Part VI

Nonhuman Primates HIV/SIV Vaccine Trials Database
VI-A

Introduction and Historical Overview of the Nonhuman Primates
HIV/SIV Vaccine Trials Database

The development of an effective vaccine against HIV is urgently needed given
the continual increase in the number of people infected with HIV, estimated to
be about 40 million, in addition to 20 million people who have already died
due to HIV since the beginning of the epidemic two decades ago. A general
consensus is that the development of an effective vaccine is the best way to tackle
this epidemic. Unfortunately, the effort to develop a good and reliable vaccine
against HIV has proven to be difficult. HIV is the most studied infectious agent
in medical history. The vaccine research is increasingly becoming an important
focus as a large number of data continue to emerge from different laboratories.
As of October 2004, a quick search using a string argument containing “HIV
or SIV and vaccine” yielded 6439 references. Using the search string “((HIV
OR SIV) AND vaccine) AND macaque”, 820 references were retrieved from
PUBMED.

Since traditional approaches for vaccine development have proven ineffec-
tive for HIV, it is important to encourage new methodologies and to increase the
numbers of studies in order to speed up the process required to develop an ef-
efective vaccine against HIV. Consequently, a large number of studies on HIV
and SIV-related vaccine are being generated. In addition, studies vary consid-
erably in the way the vaccine trials are being conducted, including the design
and formulation of vaccines, the doses, the animals used, the challenge viruses,
etc. This makes it difficult to adequately compare the studies. It is important to
continue to monitor the ever growing number of data generated by researchers
working to understand the complexity of HIV pathogenicity and to follow up the
ongoing preclinical research in animal models and phase I-III human trials.

To begin to address this problem, we have constructed a relational database
named Nonhuman Primate HIV/SIV Vaccine Trials Database to serve the scien-
tific community, particularly those engaged in vaccine development as well as
policy makers.

The published data pertaining to HIV vaccine development in nonhuman pri-
mate models have been curated and compiled in such a way that users can inter-
actively search and retrieve them online through the internet. In order to qualify
for entry in the database, the trial must meet the following criteria: 1) SIV or
HIV-based vaccine or passive immunization have been used in nonhuman pri-
mates; 2) an assessment for immunogenicity or immunotherapeutic property of
the immunogen has been performed. A challenge virus may also have been in-
jected to the immunized and control animals to assess the efficacy of the vaccine.

Historically, prior to the development of this database, Dr. Jon Warren at
the EMMES Corporation had maintained a similar database, though organized
differently, and with different data fields and somewhat different nomenclature.
The studies in that database include those published through 1999. We have
made that database accessible through the internet, and integrated it into the
search interface of the Los Alamos National Laboratory vaccine database. This
will be available to the public until we have integrated all of those studies into
the Los Alamos database.

The Los Alamos Nonhuman Primate HIV/SIV Vaccine Trials Database
home page can be accessible at http://www.hiv.lanl.gov/cgi-bin/
vaccine/public/index.cgi and is depicted in Figure VI-A-1.

The data in the database can be accessed in two ways, using the Search Form
or the Cross-Table Form which are displayed on the home page. The Search
Form allows users to retrieve technical information pertaining to vaccine studies
using multiple choice menus to construct logical arguments for searching the
database. The search argument is a combination of items chosen from the menus
which include the study Objectives, the Species or experimental animal model,
the Reference, the Vaccine and Challenge virus (Figure VI-A-2).

The search argument formulated by the user sends an electronic query to both
the Los Alamos (also known as the Current Database) and the data collected by
Jon Warren (also known as the *Previous Database*). Where the search argument cannot be applied to the *Previous Database*, a message to this effect is displayed. Of note, the *Previous Database* has fewer display choices, and the data were organized by Stage. A *Stage* is generally defined as a point in a trial where results for a group of test subjects was assessed. In some cases, stages span multiple published studies. The *Los Alamos Database* or *Current Database* does not organize data along the concept of stages, rather each published paper is treated as a distinct trial. However, in some few cases a published study may encompass multiple but directly related experiments. In such cases a suffix *experiment number* is added so that the first experiment of, say, NHP92 will be shown as NHP92.1, the second as NHP92.2, etc. In this compendium, we have selected only the information contained in the *Current Database*; a hard copy summary of Jon Warren’s final database was published in the *Journal of Clinical Primatology* under the title “Preclinical AIDS vaccine research: survey of SIV, SHIV, and HIV challenge studies in vaccinated nonhuman primates” (please see *J Med Primatol* 2002 Aug; 31(4-5):237-256).
The data entered in the database can also be retrieved using the Cross-Table Search Form. This tool was designed to allow users to retrieve data in a cross-tabulated format. For example, Table VI-A-1 shows a tabulation of the origin of vaccine immunogens (HIV-1, HIV-2, SIV or SHIV) by the subtype shows that the great majority of vaccines trials used so far are based on subtype B. The number in each bifurcation box refers to the number of studies in the database and the ratio of animals protected from infection with the challenge virus over the total number of animals immunized and challenged.

VI-A-1 Organization and contents of the compendium

This vaccine trials compendium is divided in 5 chapters.

- Vaccines
- Challenges
- Adjuvants and Stimulants
- Trial Summaries
- References

An introduction is provided at the beginning of each section.
VI-B

Vaccines

This section contains a list of vaccines used in the studies compiled in the database. We devised a simple nomenclature to group the vaccines by type of vaccine. This includes the following:

- DNA
- Live Attenuated Virus
- Recombinant Live Attenuated Virus
- Live Virus
- Cell/Tissue
- Whole (killed) Inactivated Virus
- Virus-like Particle
- Purified Viral Products
- Synthetic Protein/Peptide
- Recombinant Subunit Protein
- Recombinant Vector (virus/bacteria)
- Passive Antibody
- Other

In most cases the name and description of the vaccine, as provided by the authors of the paper, was retained. The virus (HIV, SIV or SHIV), the viral component (gene or protein) and the subtype (for HIV or HIV fragment in SHIV) were also recorded. The database trial numbers (NHP number) where the vaccine was used are listed for reference.
VI-B-1  DNA vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>bSIVgp120</td>
<td>Recombinant baculovirus expressing SIV gp120</td>
<td>NHP.33</td>
</tr>
<tr>
<td>CHO-SIVgp120</td>
<td>Recombinant Chinese hamster cells expressing SIV gp120</td>
<td>NHP.33, NHP.156</td>
</tr>
<tr>
<td>CMV SHIV dEN</td>
<td>CMV-SHIVdEN (SIVGP1 DNA) was constructed from an env and nef deletion SHIV DNA by replacing the 5’ long terminal repeat region with a cytomegalovirus promoter with an immediate-early enhancer and the 3’ long terminal repeat region with simian virus 40 poly(A).</td>
<td>NHP.326</td>
</tr>
<tr>
<td>CMVKm2-gp140TM</td>
<td>The sequence for the native subtype B HIV-1US4 envelope was modified to reflect the optimal codon usage in highly expressed human genes. Contained the oligomeric secreted membrane-bound gp140TM, which include the membrane-spanning domain of gp41 (residues1-691). The gene cassettes constructed synthetically using EcoR1 and Xba1 by the Midland Certified Reagent Company, and were cloned into plasmid vectors for DNA vaccination (pCMVKm2).</td>
<td>NHP.354</td>
</tr>
<tr>
<td>d81</td>
<td>In this vaccine the SIVmac239 env-nef expression cassette was inserted into the TK gene of the HSV-1 genome. It has a deletion in the essential ICP27 gene in addition to the deletion in TK, rendering it replication defective in Vero cells. CMV, promoter/enhancer sequences of the CMV IE gene; PA, signal sequences for poly(A) addition. The SIV sequences are from the SphI site (nucleotide 6450) rightward in SIVmac239. These include rev exon 1, the entire env ORF, rev exon 2, and the nef open reading frame.</td>
<td>NHP.54</td>
</tr>
<tr>
<td>DNA (pCMVKm2) gp140</td>
<td>Unmodified gp140. pCMVKm2 vector expressing the gp140 ectodomain form of the HIV envelope immunogen, with an intact gp120-gp41 cleavage site</td>
<td>NHP.22</td>
</tr>
<tr>
<td>DNA Vaccine pNL432-ZF1*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: larking env and nef
### DNA vaccines

**Description**
DNA vaccine derived from pNL432, an infectious molecular clone of HIV-1 in which the first two cysteine residues of the N-terminal zinc finger motif (Cys-X2-Cys-X4-His-X4-Cys) were replaced by serine residues.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>NL432</td>
<td>B</td>
<td>All (Full genome (modified))</td>
</tr>
</tbody>
</table>

**Notes**
first two amino cysteine residues of the N-terminal zinc finger motif (Cys-X2-Cys-X4-His-X4-Cys) were replaced by serine residues

**Trial(s)**
NHP.31, NHP.149.2

### DNA-gag.env

**Description**
DNA vaccines encoding SIVmac239 Gag and HIV-1-89.6P Env

**Notes**
2 constructs

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>HIV-1.89.6</td>
<td>env</td>
</tr>
<tr>
<td>HIV</td>
<td>SIVmac239</td>
<td>gag</td>
</tr>
</tbody>
</table>

**Trial(s)**
NHP.23

### DNA-pCI-rev

**Description**
Eukaryotic expression vector pCI (Promega, Charbonnieres, France) with HIV-1 primary isolate ACH320 2.1 rev cDNA. Expression checked in 293T cells.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>ACH320 2.1</td>
<td>rev</td>
</tr>
<tr>
<td>HXB2</td>
<td>5970-6045 (exon 1) and 8379-8653 (exon 2)</td>
<td></td>
</tr>
</tbody>
</table>

**Trial(s)**
NHP.276

### DNA-pCI-tat

**Description**
Eukaryotic expression vector pCI (Promega, Charbonnieres, France) with tat cDNA cloned from primary isolate ACH320 2.1. Expression checked in 293T cells.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>ACH320 2.1</td>
<td>tat</td>
</tr>
<tr>
<td>HXB2</td>
<td>5831-6045 (exon 1) and 8379-8479 (exon 2)</td>
<td></td>
</tr>
</tbody>
</table>

**Trial(s)**
NHP.276

### DNA-SIV

**Description**
This vaccine consists of five plasmids expressing different combinations of SIV mac proteins. The 5 plasmids enconded for non-infectious SIVmac239 virus particle, envelope of SIVmac239 and SIVmac251, and a monocyte/macrophage tropic isolate of SIVmac316

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>SIVmac239</td>
<td>All</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac251</td>
<td>env</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac239</td>
<td>env</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac316</td>
<td>env</td>
</tr>
</tbody>
</table>

**Trial(s)**
NHP.275

### DNA.pND14-G1.SIVmac251.env

**Description**
DNA vaccine; DNA vector using hCMV IE promoter and expressing SIVmac251 structural env gene

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>SIVmac251</td>
<td>env</td>
</tr>
</tbody>
</table>

**Trial(s)**
NHP.58

### DNA.PTH.SIVmac.J5.gptnr

**Description**
DNA vaccine; DNA vector using hCMV IE promoter expressing SIVmac251J5 structural (gag,pol) and regulatory (tat, nef and rev) genes

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**HIV Immunology and HIV/SIV Vaccine Databases 2003** 1135
### Vaccines

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>SIVmac251.J5</td>
<td>gag, pol</td>
</tr>
</tbody>
</table>

**DNA vaccines**

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA.SF162ΔV2 gp140</td>
<td>This is a DNA vector expressing the SF162ΔV2 gp140 envelope with an intact gp120-gp41 cleavage site. The DNA construct was codon optimized for high expression in mammalian cells</td>
</tr>
<tr>
<td>FMSIV</td>
<td>This is a chimeric simian-human immunodeficiency virus (SHIV) with ecotropic Friend murine leukemia virus (FMLV) env in place of SHIV env in combination with FMLV receptor, mCAT1, which is not normally expressed in primate cells. FMSIV DNA has SIV-derived LTR, gag, pol, vif, vpx and partial vpr sequences, HIV-1-derived partial vpr, tat, rev and partial env (containing the second exon of tat, the second exon of rev, and RRE) sequences and FMLV-derived env sequences.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>HIV-1.SF162</td>
<td>B</td>
<td>env</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac239</td>
<td>B</td>
<td>LTR, gag, pol, Accessory (vif,vpx)</td>
</tr>
<tr>
<td>HIV-1</td>
<td>HIV-1.MN</td>
<td>B</td>
<td>env, Accessory (vpr,tat,partial env (containing the second exon of tat, the second exon of rev, and RRE))</td>
</tr>
</tbody>
</table>

**Trial(s)**

- NHP.58
- NHP.62
- NHP.67, NHP.70, NHP.350
- NHP.16.1, NHP.16.2, NHP.363
- NHP.400
- NHP.60.1, NHP.60.3, NHP.98
- NHP.126
**DNA vaccines**

**Vaccine Name:** K81  
**Description:** This is a replication-competent HSV recombinant K81. The SIVmac239 env-nef expression cassette was inserted into the TK gene of the HSV-1 genome. CMV, promoter/enhancer sequences of the CMV IE gene; PA, signal sequences for poly(A) addition. The SIV sequences are from the SphI site (nucleotide 6450) rightward in SIVmac239. These include rev exon 1, the entire env ORF, rev exon 2, and the nef open reading frame  
**Notes:** Herpes simplex vector

**Vaccines**

**Vaccine Name:** MVA.HIVA  
**Description:** Same vaccine used in human trial in Oxford, UK and Nairobi, Kenya  
**Trial(s):** NHP.118

**Vaccine Name:** p55gagSF2  
**Description:** Virus: HIV-1  
**Strain:** HIV-1.SF2  
**Subtype:** B  
**Gene/Protein:** gag

**Vaccine Name:** pC-SIV17E-Fred (gapolenv)  
**Description:** This is a plasmid DNA vaccine encoding the SIVmac17E-Fr (which is closely related to SIVmac239) gag-pol-env, including vif, vpx, vpr, tat, and rev, except that the 5’ LTR is deleted and the 3’ LTR is truncated by 360 bp. SIV nef was truncated at the sequence for amino acid 93 by insertion of a stop codon  
**Virus:** SIV  
**Strain:** SIVmac17E-Fr  
**Gene/Protein:** env, gag

**Vaccine Name:** pC-SIVrev  
**Description:** DNA vaccine; Contains pC-SIVnef-TPA and pC-SIVnef (both constructed based on pC-SIVmac17E-Fred)  
**Trial(s):** NHP.52

**Vaccine Name:** pc-synGag (SIVmac239)  
**Description:** Contains a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct  
**Virus:** SIV  
**Strain:** SIVmac239  
**Gene/Protein:** gag

**Vaccine Name:** pc-syngp120 (SHIV-189.6p)

**Description:** A mixture of 3 plamids constructs based on the gene sequences of the gp140 envelope, p55 Gag, Nef, and Tat proteins from the HIV-2UC2 isolate. The plasmid DNA was then resuspended to 2 mg/ml in 2x phosphate buffer saline for intramuscular and intradermal immunizations or in water for intranasal immunizations and stored at &#8722;20°C.
**DNA vaccines**

*Description*
Contains a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHIV</td>
<td>HIV-1.89.6P</td>
<td>B</td>
<td>env (gp120)</td>
</tr>
</tbody>
</table>

**Vaccine Name** pc-synTat (HIV-1IIIB)

*Description*
Contain a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>HIV-1IIIB</td>
<td>B</td>
<td>Accessory (tat)</td>
</tr>
</tbody>
</table>

**Vaccine Name** pcDNA3–tet.CCR5

*Description*
This DNA vaccine encodes for CCR5 and tetanus genes.

**Vaccine Name** pcDNA3-CCR5

*Description*

**Vaccine Name** pCGag/Pol

*Description*
DNA constructs expressing HIV-1-IIIB gag/pol protein.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>HIV-1.IIIB</td>
<td>gag, pol</td>
</tr>
</tbody>
</table>

**Vaccine Name** pCI-Nef plasmid

*Description*
A mixture of six pCI-Nef plasmids expressing the nef epitopes from SIVmac251 primary isolate (BK28, SO4, SO5, SO8, SO9 and SO12)

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>SIVmac251 (BK28)</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac251 (SO4)</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac251 (SO5)</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac251 (SO8)</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac251 (SO9)</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac251 (SO12)</td>
</tr>
</tbody>
</table>

**Vaccine Name** pCMN160 (HIV-1 MN env)

*Description*
DNA constructs expressing HIV-1-MN env and rev proteins (pCMN160)

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>HIV-1.MN</td>
<td>B</td>
<td>env</td>
</tr>
</tbody>
</table>

**Vaccine Name** pCMN160 HIV-1.MN env-rev
**DNA vaccines**

**Description**  A DNA vaccine (plasmid) expressing HIV-1 MN env and rev

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.MN</th>
<th>Subtype: B</th>
<th>Gene/Protein: env</th>
</tr>
</thead>
</table>

**Trial(s)**  NHP.202

**Vaccine Name**  pCMV-gag-mod

**Description**  HIV-1SF2 p55 Gag modified to highly expressed human codons; regions with INS were inactivated. Produces a p55 Gag protein with three amino acid changes (Asn377Thr, Ile403Thr, and Lys405Arg). An optimal initiation of translation (GCCACCAUGG) was employed. This 1.527 bp SF2-gag-mod sequence was cloned into the Sall and EcoRI sites of pCMVKm2 (Chiron Corporation, Emeryville, Calif.).


<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SF2</th>
<th>Subtype: B</th>
<th>Gene/Protein: gag</th>
</tr>
</thead>
</table>

**Trial(s)**  NHP.321, NHP.354

**Vaccine Name**  pCMV-V3.S (HBV-HIV vaccine)

**Description**  HIV-1 LAI V3 inserted within the frame of HBV envelope in pCV-S2.S

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.LAI</th>
<th>Subtype: B</th>
</tr>
</thead>
</table>

**Trial(s)**  NHP.10

**Vaccine Name**  pCMV/nef

**Description**  pCMV/nef plasmid vaccine comprises the PstI-StuI Nef-encoding fragment of clone BK28 inserted into pCMV5

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac239</th>
</tr>
</thead>
</table>

**Trial(s)**  NHP.56

**Vaccine Name**  pCMV/SIVsmH4/rev-gp160

**Description**  Modified V2-deleted gp140. pCMV/km2 vector expressing the unmodified gp140 ectodomain form of the HIV envelope immunogen, with an intact gp120-gp41 cleavage site

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVsmH4</th>
<th>Gene/Protein: env, Accessory (rev)</th>
</tr>
</thead>
</table>

**Trial(s)**  NHP.371

**Vaccine Name**  pCMVKm2-Delta-V2 gp140

**Description**  The sequence for the native subtype B HIV-1US4 envelope was modified to reflect the optimal codon usage in highly expressed human genes. Contained the oligomeric secreted gp140mut (uncleaved, containing a single R522S cleavage site mutation; includes residues 1-668). The gene cassettes constructed synthetically using EcoR1 and Xba1 by the Midland Certified Reagent Company, and were cloned into plasmid vectors for DNA vaccination (pCMVKm2).

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1US4</th>
<th>Subtype: B</th>
<th>Gene/Protein: env</th>
</tr>
</thead>
</table>

**Trial(s)**  NHP.354
### Vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pCMVmCAT1</strong></td>
<td>constructed from pCMV (Clontech) by replacing the B-gal gene with a PCR fragment encoding mCAT1B (See Matano, 2000 for details)</td>
<td>HIV-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>pCSGag/Pol.SIV</strong></td>
<td>SIV gag/pol</td>
<td>SIV</td>
<td>ND</td>
<td>gag, pol</td>
</tr>
<tr>
<td><strong>pCV-tat</strong></td>
<td>DNA vaccine: the plasmid pCV-tat contains the cDNA of the HIV-1 tat gene (BH-10) under the transcriptional control of the adenovirus major late promoter and the vector pCV-0. Plasmids were purified on CsCl gradient and dialyzed for 48 h against 300 volumes of sterile PBS without calcium and magnesium.</td>
<td>HIV-1</td>
<td>BH10</td>
<td>Accessory (tat)</td>
</tr>
<tr>
<td><strong>pGA1-gag-pol DNA vaccine</strong></td>
<td>The Gag-Pol (SIVmac239) insert was cloned into the pGA1 expression vector (GenBank accession no. AF425297)</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>gag, pol</td>
</tr>
<tr>
<td><strong>pGagpol/EnvRev SIV239 DNA</strong></td>
<td>This is a DNA vaccine containing a plasmid backbone which takes advantages of a CMV promoter and a SV40 polyA signal to express SIV239 gagpol and EnvRev (in two recombinant plasmid constructs). The effect of the rev gene is thought to increase the expression of gagpolconstruct (in vitro assays)</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>env</td>
</tr>
<tr>
<td><strong>pJW4303/HXB-2.gp120</strong></td>
<td>A DNA immunogen expressing the pol gene of SHIV-IIIB</td>
<td>SHIV</td>
<td>SHIV-IIIB</td>
<td>pol</td>
</tr>
</tbody>
</table>

**Trial(s)** NHP.350, NHP.161, NHP.162, NHP.89, NHP.384, NHP.300, NHP.56
**DNA vaccines**

**Description**

Same as pHXB2gp120. This is a eukaryotic expression vector that uses enhancer and promoter elements, including intron A from the cytomegalovirus immediate-early promoter, and polyadenylation sequences from the bovine growth hormone pJW4303 supports Env expression in the absence of Rev. A stop codon introduced at the boundary of the surface (SU) and transmembrane (TM) subunits of Env followed by a BamHI site for cloning into the BamHI site in pJW4303.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.HXB2</th>
<th>Subtype: B</th>
<th>Gene/Protein: env</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** pJW4303/HXB-2.gp140

**Description**

A recombinant plasmid constructed by cloning env fragments in frame with a synthetic tissue plasminogen activator-(tPA)- leader sequence in pJW4303. This is an eukaryotic expression vector that uses enhancer and promoter elements, including intron A from the cytomegalovirus immediate-early promoter, and polyadenylation sequences from the bovine growth hormone pJW4303 supports Env expression in the absence of Rev. Contain a stop codon immediately prior to the transmembrane domain of TM.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.HXB2</th>
<th>Subtype: B</th>
<th>Gene/Protein: env</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** pMA SHIV89.6

**Description**

Mixture of 3 plasmids encoding SIVmac239 gag (pSIVoptgag), HIV-1.NL4.3 tat and rev. Plasmid pCMVNLtat, encoding the HIV-1NL4- tat, was constructed from plasmid vector pEGFP-N1 by replacing the EGFP coding sequence with the SalI-BamHI restricted tat fragment from the cDNA clone pCR2-tat1. The expression of tat is under the control of the human cytomegalovirus (CMV) immediate-early promoter. HIV-1NL4.3 rev expression is under the control of the rous sarcoma virus promoter.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac239</th>
<th>Subtype: B</th>
<th>Gene/Protein: Accessory, gag, LTR, pol (LTR, gag, pol, vpx, vpr, nef)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>Strain: HIV89.6</td>
<td>Subtype: B</td>
<td>Gene/Protein: Accessory, env (tat, rev, vpu, env)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.140</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** Pooled SIVgag/HIVtat.rev DNA vaccine

**Description**

Mixture of 3 plasmids encoding SIVmac239 gag (pSIVoptgag), HIV-1.NL4.3 tat and rev. Plasmid pCMVNLtat, encoding the HIV-1NL4- tat, was constructed from plasmid vector pEGFP-N1 by replacing the EGFP coding sequence with the Sall-BamHI restricted tat fragment from the cDNA clone pCR2-tat1. The expression of tat is under the control of the human cytomegalovirus (CMV) immediate-early promoter. HIV-1NL4.3 rev expression is under the control of the rous sarcoma virus promoter.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac239</th>
<th>Subtype: B</th>
<th>Gene/Protein: Accessory (tat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>Strain: HIV1-NL4.3</td>
<td>Subtype: B</td>
<td>Gene/Protein: Accessory (rev)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.339</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** pRS102 -SIVmac239 gag-pol proteins

**Description**

The plasmid pRS102 expresses SIVmac239 Gag and Pol proteins. The vaccine insert for pRS102 comprised a Kozak sequence, the SIV239 gag-pol region (nucleotides 1309-5753) and the Mason-Pfizer Monkey virus cytoplasmic transport element. This insert was cloned into the HindIII and Nhel sites of the eukaryotic expression vector pJW4303, and expression in transiently transfected COS cells was verified.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac239</th>
<th>Subtype: B</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** pSabRV1-SIV

**Description**

Polio virus vector expressing SIV gag, pol, env, nef, and tat in overlapping fragments.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac239</th>
<th>Subtype: B</th>
<th>Gene/Protein: env, gag, pol</th>
</tr>
</thead>
</table>

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1141
<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.322</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Name</td>
<td>pSIVNef-TPA</td>
</tr>
<tr>
<td>Description</td>
<td>DNA vaccine; Constructed based on SIVmac17E-fred + nef</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.57</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Name</td>
<td>pTHcHIV DNA</td>
</tr>
<tr>
<td>Description</td>
<td>A DNA vaccine contained an SIV gag-derived epitope, TPYDINQML, recognized by CTLs in rhesus macaques (Macaca mulatta) in the context of the Mamu-A*01 MHC class I molecule</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.118</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Name</td>
<td>pUCgp120SF2-gold particle</td>
</tr>
<tr>
<td>Description</td>
<td>Vaccine based on a modification of pCMV6agp120SF2 which has been previously described. pUCgp120 expresses gp120 of HIV-1 SF2 by using the cytomegalovirus promoter-intron A, tissue plasminogen activator signal sequences, and bovine growth hormone termination sequences; Plasmid DNA was isolated by using plasmid purification columns and endotoxin-free buffers (Qiagen, Chatsworth, Calif.). DNA was bound to 2.6-µm-diameter gold particles to a concentration of 2 µg of DNA/mg of gold</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Name</td>
<td>pV1P-HIV-1.89.6P env</td>
</tr>
<tr>
<td>Description</td>
<td>Plasmid DNA expressing HIV-1 89.6P env</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>pV1P-SIVmac239 gag</td>
<td>Plasmid DNA expressing SIVmac239</td>
</tr>
<tr>
<td>pV1R-SIVmac239-gag</td>
<td>A plasmid DNA constructed by annealing a series of overlapping oligonucleotides.</td>
</tr>
<tr>
<td>pVacc1 DNA</td>
<td>pVacc1 includes a full SIVmac239 genome with multiple mutations in the NC basic domain and the functional domains of RT and INT, under the control of the CMV promoter. A 3.1-kb Sphl-Ncol fragment that includes the env gene from pSHIV-KB9-3’ replaced the corresponding Sphl-SnaBI fragment of pVacc1 that includes the SIV env of SIVmac239. In addition, a stop codon replaced the initiation codon of the vpr gene.</td>
</tr>
<tr>
<td>pVacc4 DNA</td>
<td>The DNA plasmid pVacc4 used in the vaccination is a derivative of pVacc1; It includes a full SIVmac239 genome with multiple mutations in the NC basic domain and the functional domains of RT and INT, under the control of the CMV promoter. A 3.1-kb Sphl-Ncol fragment that includes the env gene from pSHIV-KB9-3’ replacedthe corresponding Sphl-SnaBI fragment of pVacc1 that includes the SIV env of SIVmac239. In addition, a stop codon replaced the initiation codon of the vpr gene.</td>
</tr>
<tr>
<td>rFPV</td>
<td>Designed to express the gag, pol, env and nef genes of SHIV-IIIb</td>
</tr>
<tr>
<td>SeV-gag</td>
<td>This is a Gag-expressing Sendai virus (SeV is a nonsegmented negative-strand RNA virus considered nonpathogenic for humans and nonhuman primates)</td>
</tr>
<tr>
<td>SIV Directed GLV</td>
<td>SIV GLV of PC-derived, directed inserts in the UB vector</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>Vaccine Name</td>
</tr>
<tr>
<td>----------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>NHP.120</td>
<td>SIV mac239 Gag DNA</td>
</tr>
<tr>
<td>NHP.400</td>
<td>SIV Random-GLV</td>
</tr>
<tr>
<td>NHP.120</td>
<td>SIV-HIV89.6 DNA vaccine</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>NHP.19, NHP.132, NHP.325, NHP.349</td>
<td>SIV-pcDNA3gag/pol</td>
</tr>
<tr>
<td>NHP.9.2</td>
<td>SIV-Run-Cyt. GLV</td>
</tr>
<tr>
<td>NHP.120</td>
<td>SIV/17E-Fr gag-pol-env</td>
</tr>
<tr>
<td>NHP.63</td>
<td>SIVmac17E-Fr Nef</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Description</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>SIVmac239 gag DNA</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>SIVmac239 gag DNA</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>SIVmac239 sbbvΔ3 DNA</strong></td>
<td>Contains the full genome of mac239 with a 105-bp (35-amino-acid) deletion in the 3’ nef/LTR, analogous to the common deletion observed in HIV-1 strains isolated from the Sydney Blood Bank Cohort (SBBC)</td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>SIVmac239 sbbvΔ3Delta5 DNA</strong></td>
<td>Contains the full genome of mac239 with a 105-bp (35-amino-acid) deletion in the 3’ nef/LTR, analogous to the common deletion observed in HIV-1 strains isolated from the Sydney Blood Bank Cohort (SBBC) and additional deletion at the 5’LTR</td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>V1R-SIV gag</strong></td>
<td>pUC-based vector that utilizes the human cytomegalovirus immediate-early promoter with intron A and bovine growth hormone transcription terminator/polyadenylation signal as expression regulatory elements and expresses full-length SIV gag. The SIV gag open reading frame is homologous to that of SIVmac239 and was synthesized using optimal codons for human gene expression.</td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>VEE-SIVsm (SIV MA/CA-VRP and gp160-VRP)</strong></td>
<td>VEE replicon plasmid pVR2 with SIV gag (Gly to Ala change in codon 2 ablate myristylation signal; entire env ORF (gp160; base 6587 to 9244); env lacking 3’ region encoding membrane-spanning domain and cytoplasmic tail (gp140; base 6587 to 8626)</td>
</tr>
<tr>
<td>Notes</td>
<td>gag encoding matrix-capsid (MA/CA; nucleotides 1049 to 2143, numbering from the 5’ end of the SIVsm H-4i genome)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.27</td>
</tr>
<tr>
<td>-----------</td>
<td>--------</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>vSIVgp160</td>
</tr>
<tr>
<td>Description</td>
<td>Recombinant vaccinia virus expressing SIV gp160</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Name</td>
<td>vVrgp140</td>
</tr>
<tr>
<td>Description</td>
<td>Vaccinia expressing SIVmac251 env gp140</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain:</td>
<td>SIVmac251</td>
</tr>
<tr>
<td>Gene/Protein:</td>
<td>env</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.73</th>
</tr>
</thead>
</table>
## VI-B-2 Live attenuated virus vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT-2 rx HIV-1.DH12</td>
<td>Aldrithiol-2 (AT-2)-inactivated HIV-1.DH12</td>
<td>NHP.303</td>
</tr>
<tr>
<td>AT-2 rx SIVmac239</td>
<td>Aldrithiol-2 (AT-2)-inactivated SIVmac239</td>
<td>NHP.303</td>
</tr>
<tr>
<td>DeltavpuDeltaNefSHIV-4</td>
<td></td>
<td>NHP.107, NHP.112</td>
</tr>
<tr>
<td>DeltavpuSHIV-ppc</td>
<td></td>
<td>NHP.107, NHP.112</td>
</tr>
<tr>
<td>S8-NCAZF2</td>
<td>This onstruct is based on the pCEP4 mammalian expression vector from Invitrogen Corp. (Carlsbad, Calif.); contains the complete coding region of SIV(Mne), including the nef gene. The 5’ portion of the U3 region in the 5’ long terminal repeat (LTR) and host genomic sequences upstream from the StyI site were removed. In addition, the R and U5 regions of the 3’ LTR were also deleted and replaced with the simian virus 40 (SV40) poly(A)</td>
<td>NHP.64, NHP.65.2, NHP.265</td>
</tr>
<tr>
<td>SHIV-4 (Deltavpu-Deltanef)-I</td>
<td>T-cell tropic</td>
<td>NHP.17</td>
</tr>
<tr>
<td>SHIV-dn</td>
<td>Live attenuated SHIV lacking the nef gene. The deletion is at the 5’-portion including the initial codon of the nef gene.</td>
<td>NHP.35, NHP.131</td>
</tr>
<tr>
<td>SHIV-drn</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Live attenuated virus vaccines

**Description** Live attenuated SHIV lacking the nef gene. The deletion is at the 5’-portion including the initial codon of the nef and vpr genes. The splicing of vpr was modified so that it does not function.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>mac239</td>
<td>gag, LTR, gag, pol, vif and/or vpx</td>
</tr>
<tr>
<td>HIV-1</td>
<td>NL432</td>
<td>pol (env, tat, rev and vpu)</td>
</tr>
</tbody>
</table>

**Trial(s)** NHP.28, NHP.35

### SHIV-dxrn

**Description** Live attenuated SHIV lacking the nef gene. The deletion is at the 5’-portion including the initial codon of the nef, vpr gene and the 3’ portion of vpx. The initial codon of vpx was modified to a non-sense codon.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>mac239</td>
<td>gag, LTR, gag, pol, vif and/or vpx</td>
</tr>
<tr>
<td>HIV-1</td>
<td>NL432</td>
<td>pol (env, tat, rev and vpu)</td>
</tr>
</tbody>
</table>

**Trial(s)** NHP.28, NHP.35

### SHIV-NM3n

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td></td>
<td>gag, LTR, gag, pol, vif and/or vpx</td>
</tr>
<tr>
<td>HIV-1</td>
<td></td>
<td>pol (env, tat, rev and vpu)</td>
</tr>
</tbody>
</table>

**Trial(s)** NHP.114

### SHIV-PPC (Deltavpu)

**Notes** This vaccine is dual tropic and was administered orally

**Trial(s)** NHP.17

### SIMmac239Δ2

**Description** Contains 182bp deletion in nef and a 172bp deletion upstream of U3 of LTR.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>mac239</td>
<td>gag, LTR, gag, pol, vif and/or vpx</td>
</tr>
</tbody>
</table>

**Trial(s)** NHP.207

### SIV(Mne)NC

**Description** A live attenuated SIVMne. It consists of a 12-nucleotide deletion in the gene coding for the NC protein [nucleotide positions 1772 to 1783 of the SIV(Mne) sequence (GenBank accession no. M32741) were deleted]. Also known as ΔCys 33-Cys 36 or pRB130.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>Mne</td>
<td>gag, LTR, gag, pol, vif and/or vpx</td>
</tr>
</tbody>
</table>

**Trial(s)** NHP.64, NHP.65.1, NHP.65.2, NHP.265

### SIV-IFN

**Description** This is a clone of SIVmac239 (SIVΔNU) for which a total of 513bp in the nef and U3 region has been replaced with the coding region of IFN

**Trial(s)** NHP.309

### SIV-IL4

**Description** This is a clone of SIVmac239 (SIVΔNU) for which a total of 513bp in the nef and U3 region has been replaced with the coding region of IL-4.
<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain:</th>
<th>Gene/Protein:</th>
<th>Notes</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV-PBJ6.6Δnef</td>
<td></td>
<td>SIV</td>
<td>SIV</td>
<td>All (nef disrupted)</td>
<td></td>
<td>NHP.309</td>
</tr>
<tr>
<td>SIV.GX2</td>
<td>SIV.GX2 is a nef-disrupted molecular clone. EcoRI-NdeI fragment of an SIVmacJ5 proviral clone was replaced with a PCR product that was amplified from proviral DNA isolated from an SIVmacJ5-infected macaque. This resulted in a 66 bp deletion in nef, removing the coding sequence for aa 62-83.</td>
<td>SIV</td>
<td>SIV.GX2</td>
<td>All (nef disrupted)</td>
<td>Nef gene disrupted</td>
<td>NHP.34</td>
</tr>
<tr>
<td>SIVDeltaNU</td>
<td>SIVDeltaNef is a nef deleted mac239</td>
<td>SIV</td>
<td>SIV</td>
<td></td>
<td></td>
<td>NHP.397</td>
</tr>
<tr>
<td>SIVhu</td>
<td>A pathogenic virus isolated from a lab. worker infected accidentally with biological materials from rhesus macaque infected with SIVsmB670; it has 97.9% genetic homology with parental SIVsmB670; 4 base deletion in nef gene causing a frame shift in nef</td>
<td>SIV</td>
<td>SIV.hu/SIVsmB670</td>
<td></td>
<td></td>
<td>NHP.327.1, NHP.327.2</td>
</tr>
<tr>
<td>SIVmac1A11</td>
<td>The SIVmac1A11 is a live attenuated virus. The virus stock was grown on stimulated CD4-enriched rhesus macaque peripheral blood mononuclear cells (PBMC) and had a titer of (10^5) 50% tissue culture infectious doses (TCID50)/ml.</td>
<td>SIV</td>
<td>SIVmac1A11</td>
<td></td>
<td></td>
<td>NHP.36, NHP.72</td>
</tr>
<tr>
<td>SIVmac239Δ3</td>
<td>Contains 182bp deletion in nef and a 172bp deletion upstream of U3 of LTR. It has an additional 101-bp deletion in vpr. This is is a derivatives of SIVmac239. It lacks the nef, vpr and U5 sequences.</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>LTR, gag, pol, env (Lacks nef, vpr and US)</td>
<td></td>
<td>NHP.240, NHP.294</td>
</tr>
<tr>
<td>SIVmac239Δ3</td>
<td>Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ3 is missing unique nef, vpr, and nef sequences that overlap U3. Described by Gibbs et al ARHR 10(5): 607-616 (1994).</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>All (All but nef, vpr and the U3 region overlapping with nef)</td>
<td></td>
<td>NHP.32, NHP.323</td>
</tr>
</tbody>
</table>

Vaccines

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**Vaccines Live attenuated virus vaccines**

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIVmac239Δ3+</td>
<td>Produced by infection of rhesus macaque with cloned SIVmac239Δ3 DNA. SIVmac239Δ3 is missing unique nef, vpr, and nef sequences that overlap U3. A pathogenic variant named SIVmac239Δ3+ was selected and cloned. Described by Gibbs et al ARHR 10(5): 607-616 (1994).</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>All (all but vpr, nef and LTR/U3 regions.)</td>
<td>NHP.323</td>
</tr>
<tr>
<td>SIVmac239Δ3x</td>
<td>Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ3X is missing nef, vpx, and US sequences.</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>All but nef, vpx and U</td>
<td>NHP.32</td>
</tr>
<tr>
<td>SIVmac239Δ4</td>
<td>Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ4 is missing nef, vpr, vpx, and US.</td>
<td>SIV</td>
<td>Mac239</td>
<td>All but nef, vpr, vpx, and US</td>
<td>NHP.32</td>
</tr>
<tr>
<td>SIVmac239ΔNef</td>
<td></td>
<td>SIV</td>
<td></td>
<td>Lacking nef</td>
<td>NHP.148</td>
</tr>
<tr>
<td>SIVmac239-Δnef</td>
<td>Constructed by deleting a 186-base pair fragment of the nef coding sequences of SIV mac239</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>All</td>
<td>NHP.33, NHP.34, NHP.109</td>
</tr>
<tr>
<td>SIVmac239Delta5G</td>
<td>Created by mutagenesis of the parental infectious DNA clone so that the asparagine residues for N-glycosylation at positions 79, 146, 171, 460, and 479 were converted to glutamine residues</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>All</td>
<td>NHP.39</td>
</tr>
<tr>
<td>SIVmac251ΔNef</td>
<td>Derived from the SIVmac251 BK28 clone by three modifications: (i) the premature stop codon at position 8785 in the env gene was mutated to restore a complete env ORF, (ii) the nef initiator codon ATG was mutated to ACG (cont’d, see notes), and (iii) nucleotides 9225 to 9401 in the nef region, which do not overlap either the 3’ end of env or the U3 part of the LTR, were deleted</td>
<td>SIV</td>
<td>SIVmac251</td>
<td>All</td>
<td>NHP.38, NHP.101</td>
</tr>
</tbody>
</table>
### Live attenuated virus vaccines

**Vaccine Name**: SIVmac251, 32H, (C8)

**Description**: grown in the human C8166 cell line. The nef coding region contains an in-frame deletion of four amino acids in pC8 and two conservative amino acid changes.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac251</th>
<th>Gene/Protein: All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Trial(s)**: NHP.108

**Trial(s)**: NHP.40, NHP.194.1, NHP.194.2
VI-B-3  Recombinant live attenuated virus vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>SIV 17E-CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>SIV/17E-CL is a recombinant molecular clone that contains gp120 and part of gp41 from SIV/17E-Br (a macrophage-tropic strain obtained by passage of SIVmac239 in rhesus macaques, Sharma et al., J. Infect. Dis. 66:3550, 1992) into the SIVmac239 molecular clone.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain:</td>
<td>SIVmac239</td>
</tr>
<tr>
<td>Gene/Protein:</td>
<td>Accessory, gag, pol</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain:</td>
<td>SIV/17E-Br</td>
</tr>
<tr>
<td>Gene/Protein:</td>
<td>env (gp120, gp41)</td>
</tr>
</tbody>
</table>

| Trial(s) | NHP.100 |
### VI-B-4 Live virus vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Notes</th>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-2 SBL6669</td>
<td>Isolated from the PBMCs of a patient from Gambia by cocultivation with the T cells of the neoplastic cell line HUT-78. under Franchini 30-JAN-1989 in sequence database.</td>
<td></td>
<td>HIV-2</td>
<td>SBL6669</td>
<td></td>
<td>All</td>
</tr>
<tr>
<td>RT-SHIV</td>
<td>The chimeric simian/human immunodeficiency virus (SHIV) containing the HIV-1 HXBc2 gene for reverse transcriptase (RT) in the genomic background of SIVmac239 (RT-SHIV)</td>
<td></td>
<td>HIV-1</td>
<td>HXBc2</td>
<td>B</td>
<td>pol</td>
</tr>
<tr>
<td>SIV</td>
<td>Strain: SIVmac239</td>
<td></td>
<td>SIV</td>
<td></td>
<td></td>
<td>All</td>
</tr>
<tr>
<td>HIV-1</td>
<td>Strain: HIV-1.IIIB</td>
<td>Subtype: B</td>
<td>HIV-1</td>
<td>HIV-1.IIIB</td>
<td>B</td>
<td>Accessory (tat,rev)</td>
</tr>
<tr>
<td>SIV</td>
<td>Strain: SIVmac239</td>
<td></td>
<td>SIV</td>
<td></td>
<td></td>
<td>All</td>
</tr>
<tr>
<td>SFV- Pr56gag VLP-type II</td>
<td>Components: Pr56-wt; gp120-TM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>All</td>
</tr>
<tr>
<td>SHIV-4</td>
<td>The chimeric SHIV-4 contains the gag, pol, vif, vpx, vpr and nef genes of SIVmac239 and the env, tat and rev genes of HIV-1IIIB</td>
<td></td>
<td>SIV</td>
<td></td>
<td></td>
<td>Accessory</td>
</tr>
<tr>
<td>HIV-1</td>
<td>Strain: SIVmac239</td>
<td>Subtype: B</td>
<td>HIV-1</td>
<td>HIV-1.IIIB</td>
<td>B</td>
<td>Accessory (tat,rev)</td>
</tr>
<tr>
<td>SHIV989.6</td>
<td>This is a chimeric virus containing HIV-1.89.6 env in the the SIV backbone</td>
<td></td>
<td>HIV-1</td>
<td>HIV-1.89.6</td>
<td>B</td>
<td>env (Env,tat,rev,vpu)</td>
</tr>
<tr>
<td>SHIV989.6P</td>
<td></td>
<td></td>
<td>HIV-1</td>
<td>HIV-1.89.6</td>
<td>B</td>
<td>env</td>
</tr>
<tr>
<td>SHIVIIIBc2</td>
<td></td>
<td></td>
<td>HIV-1</td>
<td>SHIVIIIBc2</td>
<td>B</td>
<td>LTR</td>
</tr>
</tbody>
</table>

**Trial(s)**
- NHP.4
- NHP.111
- NHP.77
- NHP.93
- NHP.24.1, NHP.29.1, NHP.140
- NHP.24.1
- NHP.29.1

**Virus**
- HIV-1
- HIV-2
- SIV

**Gene/Protein**
- gag, pol, Accessory (vif,vpx,vpr)
- env, Accessory (tat,rev)
- env (Env,tat,rev,vpu)
- env
- LTR, pol (gag,pol,LTR,vpx,vpr,nef)
- LTR

**Subtype**
- B
- B
- B
- B

**Vaccine Immunology and HIV/SIV Vaccine Databases 2003** 1153
<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV-Mac-32H</td>
<td>Live SIV-Mac-32H virus propagated on MT-2 cells</td>
</tr>
<tr>
<td>SIV-Mac-MPBMC</td>
<td>Not described by authors.</td>
</tr>
<tr>
<td>SIVmac251</td>
<td></td>
</tr>
<tr>
<td>SIVsmE660</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV</td>
<td>???</td>
<td>???</td>
</tr>
<tr>
<td>SIV</td>
<td>MAC-32H</td>
<td>All (All, complete genome)</td>
</tr>
<tr>
<td>SIV</td>
<td>MAC-MPBMC</td>
<td>All (all, complete genome)</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVmac251</td>
<td>All</td>
</tr>
<tr>
<td>SIV</td>
<td>SIVsmE660</td>
<td>All</td>
</tr>
</tbody>
</table>

| Trial(s) | |
|----------||
| NHP.24.1 | |
| NHP.320  | |
| NHP.320  | |
| NHP.41, NHP.194.2, NHP.345 | |
| NHP.18, NHP.41, NHP.198 | |
## VI-B-5  Cell/tissue vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT-2 inactivated SIV-loaded DC</td>
<td>AT-2 SIV (mac251) loaded dendritic cells suspended in RPMI 1640 medium</td>
<td>SIV</td>
<td>SIVmac251</td>
<td>NHP.299</td>
</tr>
<tr>
<td>SIVmac239Δ3 (cell-infected)</td>
<td>SIVmac239Δ3-infected peripheral blood mononuclear cells</td>
<td>SIV</td>
<td>NHP.305</td>
<td></td>
</tr>
</tbody>
</table>
### VI-B-6  Whole (killed) inactivated virus vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT-2-Infactivated SHIV89.6</td>
<td>Aldritiol-2 (AT-2) inactivated SHIV89.6</td>
<td>SIV</td>
<td>SHIV89.6</td>
<td>All</td>
<td>NHP.319</td>
</tr>
<tr>
<td>Fixed inactivated SIVmac251 infected cells</td>
<td>The vaccine was prepared from SIVmac251 recovered from infected a rhesus monkey, and was mixed with withC8166 cells and fixed in 0.2% of β-propiolactone</td>
<td>SIV</td>
<td>SIVmac251</td>
<td>All</td>
<td>NHP.157.1, NHP.157.2, NHP.157.3</td>
</tr>
<tr>
<td>HIV-1 GB8</td>
<td>Whole/killed inactivated HIV-1. A subtype B virus, GB8 was the first (October 1986) of a series of five sequential viral isolates isolated from a single British AIDS patient during his last 18 months of life.</td>
<td>SIV</td>
<td>GB8</td>
<td>All</td>
<td>NHP.203</td>
</tr>
<tr>
<td>SIV/DeltaB670</td>
<td>Whole killed inactivated virus harvested from H9 cells. HPLC analysis revealed that complete virus particle was represented with 2-3% of the total protein consisting of the external glycoprotein gp110 and both full length and truncated glycoprotein gp41 and gp 35, respectively, along with the predicted stoichiometric amounts of the remaining viral core proteins (p61/61, p26, p17,p14 and p9). The harvested virion was formalin inactivated.</td>
<td>SIV</td>
<td>SIVB670</td>
<td>All</td>
<td>NHP.248</td>
</tr>
<tr>
<td>SIVmac HUT-78 ((Psoralem-UV))</td>
<td>SIVmac grown in HUT-78 T-cell culture, inactivated with Psoralem and UV light</td>
<td>SIV</td>
<td>SIVmac</td>
<td>All</td>
<td>NHP.239</td>
</tr>
<tr>
<td>SIVmac251 (encapsulated)</td>
<td>Gradient-purified SIVmac251 treated with formalin, encapsulated with emulsion-based process to produce 1-10ul microphere</td>
<td>SIV</td>
<td>SIVmac251</td>
<td>All</td>
<td>NHP.200</td>
</tr>
<tr>
<td>SIVmac251, 32H, (C8)</td>
<td>Inactivated, partially purified SIVmac251 32H grown in C8166 cell line.</td>
<td>SIV</td>
<td>SIVmac251</td>
<td>All</td>
<td>NHP.203</td>
</tr>
</tbody>
</table>

---

Vaccines  Whole (killed) inactivated virus vaccines
Whole (killed) inactivated virus vaccines

<table>
<thead>
<tr>
<th>Description</th>
<th>Gradient-purified SIVmac251 grown in HuT-78 cells was treated with formalin before encapsulation by an emulsion-based process to produce 1- to 10-mm microspheres</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>SIV</td>
</tr>
<tr>
<td>Strain</td>
<td>SIVmac251</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.73</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>SIVmac251/32H (Tween/Ether)</td>
</tr>
<tr>
<td>Description</td>
<td>The virus was obtained from in-vitro passage of SIVmac251 and the product was designated SIVmac251/32H. SIVmac251/32H was then grown in C81-66 cells, then purified by column chromatography. After TE extraction, about 6 mg of the virus were dissolved in 4 ml PBS and 0.25% Tween. 4 ml of diethyl ether was added... (for details see Stahl-Hennig et al, 1992; Virology 186: 588-596)</td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
</tr>
<tr>
<td>Strain</td>
<td>SIVmac251/32H</td>
</tr>
<tr>
<td>Gene/Protein</td>
<td>All</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.97, NHP.99.2, NHP.151</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Whole inactivated HIV-1 IIIB</td>
</tr>
<tr>
<td>Description</td>
<td>A sucrose-gradient purified HIV-1 IIIB, inactivated by various methods including formaldehyde.</td>
</tr>
<tr>
<td>Virus</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Strain</td>
<td>HIV-1 IIIB</td>
</tr>
<tr>
<td>Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.204</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Whole inactivated SIVmac239 (encapsulated)</td>
</tr>
<tr>
<td>Description</td>
<td>This is a HuT-78 grown in sucrose gradient purified, formalin-inactivated and encapsulated in poly(DL-lactide-co-glycolide) microspheres. The median size of the resulting particle was 3 um</td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
</tr>
<tr>
<td>Strain</td>
<td>SIVmac239</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.74</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Whole inactivated SIVmac251</td>
</tr>
<tr>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
</tr>
<tr>
<td>Strain</td>
<td>SIVmac251</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.201.1, NHP.201.2, NHP.245.1, NHP.245.2, NHP.245.3</td>
</tr>
</tbody>
</table>
## VI-B-7  Virus-like particle vaccines

### HIV-IIIB-p55gag-VLP
- **Description**: HIV-1 isolate LAI/IIIB p55 gag protein in virus-like particle
- **Virus**: HIV-1
- **Strain**: HXB2
- **Subtype**: B
- **Gene/Protein**: gag
- **Trial(s)**: NHP.321

### HPV/SHIV-VLP
- **Description**: This is a recombinant human papilloma virus-like particle encoding HIV-1 tat and rev and SIV p27.
- **Virus**: HIV-1
  - **Strain**: HIV-1.AD8
  - **Subtype**: B
  - **Gene/Protein**: Accessory (tat)
- **Virus**: HIV-1
  - **Strain**: HIV-1.NL4.3
  - **Subtype**: B
  - **Gene/Protein**: Accessory (rev)
- **Virus**: SIV
  - **Strain**: SIVmac239
  - **Gene/Protein**: gag (gag p27)
- **Trial(s)**: NHP.339

### SFV-SIV Pr56gag VLP-type I
- **Description**: Components: Pr56-V3, CD4BR,gp41
- **Trial(s)**: NHP.77

### SIV Pr56gag VLP-type II
- **Description**: This is a pseudovirion. The gp41 transmembrane domain of the Gp160 wild-type HIV-1 glycoprotein was replaced by a heterologous Epstein-Barr virus derived type I transmembrane region, consisting of a 22 amino acid spanning transmembrane domain and a shortcytoplasmic domain, which was covalently linked to the C-terminus of gp120 by a flexible -S-G-S-G-A-G- hinge region (gp120-TM). Components: Pr56-wt; gp120-TM
- **Trial(s)**: NHP.77
### VI-B-8  Purified viral products vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>biologically active Tat protein</strong></td>
<td></td>
<td>NHP.78</td>
</tr>
<tr>
<td>gp160/BSC-40</td>
<td>This is a gp160 protein produced in BSC-40 cells infected with recombinant vaccinia virus</td>
<td>NHP.269</td>
</tr>
<tr>
<td>HIV-1 gp160</td>
<td>subunit consisting of oligomeric gp160 purified from tissue culture fluid of cells productively infected with HIV-1 IIIB</td>
<td>NHP.47</td>
</tr>
<tr>
<td>HIV-1 HXBC2 Tat</td>
<td>Contact authors</td>
<td>NHP.121</td>
</tr>
<tr>
<td>HIV-1 gp140</td>
<td>HTLV-III(451) gp140 purified by sequential affinity chromatographic steps. Amino acid sequence analysis of gp120 showed the loss of the signal peptide.</td>
<td>NHP.53, NHP.247, NHP.371</td>
</tr>
<tr>
<td>HIV-2 gp160</td>
<td>subunit consisting of oligomeric gp160 purified from tissue culture fluid of cells productively infected with HIV-2 NIHZ</td>
<td>NHP.47</td>
</tr>
<tr>
<td>HIV-2 native gp125</td>
<td>purified native HIV-2 gp125 protein</td>
<td></td>
</tr>
</tbody>
</table>
Vaccines

Vaccines Purified viral products vaccines

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHP.4</td>
<td>MVA(SIVsmH-4) gag-pol-env</td>
<td>Viral components from SIVsmH-4 env. Selected after transfection of transfer plasmid pMC03gag-pol into CEF infected with MVA-env recombinant</td>
<td>SIV</td>
<td>SIVsmH4</td>
<td>gag, pol</td>
</tr>
<tr>
<td>NHP.45</td>
<td>Native SIV gp120</td>
<td>Purified by sequential affinity chromatographic steps using a monoclonal antibody to HIV-1 gp41 and an anti-HIV-1-positive human serum; heavily glycosylated and contain complex carbohydrates</td>
<td>SIV</td>
<td>SIVsmH4</td>
<td>env (gp120)</td>
</tr>
<tr>
<td>NHP.5, NHP.205.1, NHP.205.3</td>
<td>Native SIV gp148 env</td>
<td>The glycoproteins were purified by a one-step procedure to a high level of purity by using Galanthus nivalis agglutinin (GNA).</td>
<td>SIV</td>
<td>SIVsm</td>
<td>env</td>
</tr>
<tr>
<td>NHP.125</td>
<td>p55Gag</td>
<td>p55Gag (source virus not specified, but presumed to be HIV-1 subtypeB) produced in yeast.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHP.321</td>
<td>Prt-env gp160</td>
<td>full-length, unmutated Env of HIV-1-IIIb. The IIIb Env had an apparent molecular weight of 160 kDa with gp120 and gp41 covalently attached</td>
<td>HIV-1</td>
<td>HIV-1.111B</td>
<td>B</td>
</tr>
<tr>
<td>NHP.56</td>
<td>SHIV89.6P tat</td>
<td>Contact authors</td>
<td>SHIV</td>
<td>SHIV89.6P</td>
<td>Accessory (tat)</td>
</tr>
<tr>
<td>NHP.121</td>
<td>SIVmac251 p27</td>
<td></td>
<td>SIV</td>
<td>SIVmac251</td>
<td></td>
</tr>
<tr>
<td>NHP.125</td>
<td>SIVmac251-gp120</td>
<td>The SIV gp120 was purified from the serum-free culture supernatant of SIVmac251 chronically infected Hut 78 cells by immunoaffinity column chromatography using anti-gp120 Ab</td>
<td>SIV</td>
<td>SIVmac251</td>
<td></td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Description</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>--------------</td>
<td>--------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>soluble gp160</td>
<td>HIV-1 MN strain from Pasteur Merieux Connaught, Paris</td>
<td></td>
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</tr>
</tbody>
</table>

**Trial(s)** NHP.30, NHP.328, NHP.363

**Trial(s)** NHP.78
VI-B-9  Synthetic protein/peptide vaccines

**Vaccine Name**  
C4/89.6-V3

**Description**  
Peptides were synthesized by SynPep Corporation (Dublin, Calif.) and purified by reverse-phase high-pressure liquid chromatography (HPLC). Peptides were >95% purified as determined by HPLC and mass spectrometry. SHIV-89.6 and SHIV-KB9 V3 loop peptides were synthesized C-terminal to a T-helper determinant located in the C4 region of gp120 for enhanced immunogenicity.

**Notes**  
Two additional peptides are available (89.6-V3 and 89.6P-V3) consisted of the V3 loop portions of the C4/89.6-V3 and C4/89.6P-V3 peptides lacking C4.

**Virus**  
SHIV

**Strain**  
89.6

**Subtype**  
B

**Gene/Protein**  
env (C4)

**Notes**  
Subtype is for the HIV-1 component

**Trial(s)**  
NHP.7

---

**Vaccine Name**  
C4/89.6P-V3

**Description**  
Peptides were synthesized by SynPep Corporation (Dublin, Calif.) and purified by reverse-phase high-pressure liquid chromatography (HPLC). Peptides were >95% purified as determined by HPLC and mass spectrometry. SHIV-89.6 and SHIV-KB9 V3 loop peptides were synthesized C-terminal to a T-helper determinant located in the C4 region of gp120 for enhanced immunogenicity.

**Virus**  
SHIV

**Strain**  
89.6P

**Subtype**  
B

**Gene/Protein**  
env (C4)

**Notes**  
Subtype is for the HIV-1 component

**Trial(s)**  
NHP.7

---

**Vaccine Name**  
CCR5 peptides

**Description**  
N-terminus human CCR5 N1 MDYQVSSPIYDINYYTSEPC; N-terminus human CCR5 N1/N2 MDYQVSSPIYDINYYTSEPCQKINVKQIAA; 1st extracellular loop human CCR5 X1 HYLAQRDFNMC; 2nd extracellular loop human CCR5 X2.2 YTCSSSHFYSQYQFWKKNFQT

**Trial(s)**  
NHP.68

---

**Vaccine Name**  
gp120/gp41 mimotopes

**Description**  
This is a coctail of 5 synthetic peptides (p195: KSSGKLISL, p217: CNGRLYCGP, p197: GTKLVCFAA, p287: CAGGLTCSV, p335: SGRLYDKP). p195, p217 and p197 display similarity with some discreet regions of HIV-1 in V1, C2 and gp41, respectively. Peptides p287 and p335 have no obvious sequence homology with HIV protein domains.

**Trial(s)**  
NHP.81

---

**Vaccine Name**  
o-gp140-US4

**Description**  
Oligomeric gp140US4 (o-gp140US4) was purified and characterized by immunoblot, antigen capture enzyme-linked immunosorbent assay (ELISA), CD4 binding and glycosylation profile. After the purification, o-gp140US4 was stored in citrate buffer (10 mmol/l sodium citrate, 500 mmol/l sodium chloride) at a concentration of 0.2 mg/ml for immunizations.

**Virus**  
HIV-1

**Strain**  
HIV-1

**Subtype**  
B

**Gene/Protein**  
en (gp140)

**Trial(s)**  
NHP.354
Vaccine Name: oligomeric gp130
Description: gp130 oligomers of Mac-32H
Virus: SIV
Strain: MAC-32H
Gene/Protein: env gp130
Trial(s): NHP.320

Vaccine Name: P3CSS CTL
Description: The "P3CSS CTL epitopes" were a mixture of 4 lipopeptides. The sequences are taken from the SIVmac32H consensus sequences published or provided by Neil Almond et al (AIDS Research and Human Retroviruses, 8, 77 (1992)) and used for the basis of the overlapping peptides provided by the AIDS Reagent Repository at the NIBSC, UK
Virus: SIV
Strain: SIVmac251-32H
Gene/Protein: gag

Vaccine Name: PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372
Description: Cocktail of 4 peptides each containing 1 CTL and 1 helper epitope
Notes: This vaccine is a cocktail of 4 synthetic chimeric peptides containing T helper and CTL epitopes in HIV (env) and SIV(gag or pol), respectively.
Virus: SIV
Strain: MM239
Gene/Protein: gag

Vaccine Name: Peptomer SIVmac251 (gp120: 435-452)
**Vaccines**

**Synthetic protein/peptide vaccines**

<table>
<thead>
<tr>
<th>Description</th>
<th>The SIV peptomer was constructed with an 18 amino acid peptide polymer, is representative of part of the putative CD4 binding region in SIVmac251 gp120 (amino acids 435-452: HIRQIINTWHKVGKNVYL),</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>SIV</td>
</tr>
<tr>
<td>Strain</td>
<td>SIVmac251</td>
</tr>
<tr>
<td>Gene/Protein</td>
<td>env (gp120)</td>
</tr>
<tr>
<td>MAC239</td>
<td>435-452</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.5</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Synthetic tat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>CVDPNLEPWKHPGS (tat HXB2: 3-16), CRQRRRAPDSSQNHQ(TatHXB2: 52-66) conjugated to diphtheria toxoid</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.268.1</td>
</tr>
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<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Tat 1-61</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>Virus</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Strain</td>
<td>BRU</td>
</tr>
<tr>
<td>Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Gene/Protein</td>
<td>Tat</td>
</tr>
<tr>
<td>HXB2</td>
<td>5831-6013 (amino acids 1-61 in protein)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.330</td>
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</table>

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Tat 19-53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>two amino acids different from HXB2 peptide</td>
</tr>
<tr>
<td>Virus</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Strain</td>
<td>BRU</td>
</tr>
<tr>
<td>Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Gene/Protein</td>
<td>Tat</td>
</tr>
<tr>
<td>HXB2</td>
<td>5885-5986 (19 to 53 in Protein)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.330</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Tat 19-53m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>Virus</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Strain</td>
<td>BRU</td>
</tr>
<tr>
<td>Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Gene/Protein</td>
<td>Tat</td>
</tr>
<tr>
<td>HXB2</td>
<td>5885-5986 (amino acids 19 to 53 in protein)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.330</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Tat 44-61</th>
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</thead>
<tbody>
<tr>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>Virus</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Strain</td>
<td>BRU</td>
</tr>
<tr>
<td>Gene/Protein</td>
<td>Tat</td>
</tr>
<tr>
<td>HXB2</td>
<td>5960-6013 (44 to 61 in protein)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.330</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Tat 1-20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>HXB2 Tat peptide amino acids 1-20 synthesized on ABI433A</td>
</tr>
<tr>
<td>Virus</td>
<td>HIV-1</td>
</tr>
<tr>
<td>Strain</td>
<td>HXB2</td>
</tr>
<tr>
<td>Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Gene/Protein</td>
<td>Tat</td>
</tr>
<tr>
<td>HXB2</td>
<td>5831-5890 (1-20 in Tat protein)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.330</td>
</tr>
</tbody>
</table>
### Tat8-53

**Vaccine Name:** Tat8-53  
**Description:** 2 amino acids different from same region of HXB2 peptide  
**Virus:** HIV-1  
**Strain:** BRU  
**Subtype:** B  
**Gene/Protein:** Tat  
**HXB2:** 5851-5986 (8-53 in Tat protein)  
**Trial(s):** NHP.330

### V2-MAP

**Vaccine Name:** V2-MAP  
**Description:** The V2 fragment is a gp130 at positions 168-190: KFNMTGLKRDKTKEYNET; MAP: multiple antigen peptides (branched peptide)  
**Virus:** SIV  
**Strain:** SIVmac  
**MAC239:** 168-190  
**Trial(s):** NHP.119

### V2-P3CSS

**Vaccine Name:** V2-P3CSS  
**Description:** The V2 fragment is a gp130 at positions 168-190: KFNMTGLKRDKTKEYNET  
**Virus:** SIV  
**Strain:** SIVmac  
**MAC239:** 168-190  
**Trial(s):** NHP.119

### V2.V3.HIV-1.SF2 Synth.peptides

**Vaccine Name:** V2.V3.HIV-1.SF2 Synth.peptides  
**Description:**  
**Virus:** HIV-1  
**Strain:** HIV-1.SF2  
**Subtype:** B  
**Gene/Protein:** env (V2)  
**Virus:** HIV-1  
**Strain:** HIV-1.SF2  
**Subtype:** B  
**Gene/Protein:** env (V3)  
**Trial(s):** NHP.164

### V4.32-MAP

**Vaccine Name:** V4.32-MAP  
**Description:** The V4 fragment is a gp130; MAP: multiple antigen peptides (branched peptide); gp130410-430 (V4.32), VEDRDVTNQRPKERHRRNYVP; gp130410-430 (V4.32H), VEDRNTTNQKPKEQHKRNYVP (Torres et al., 1993)  
**Virus:** SIV  
**Strain:** SIVmac  
**MAC239:** 410-430  
**Trial(s):** NHP.119
### VI-B-10  Recombinant subunit protein vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO cell-expressed HIV-1SF2 gp120</td>
<td></td>
<td>HIV-1</td>
<td>HIV-1.SF2</td>
<td>B</td>
<td>env (gp120)</td>
<td>NHP.141, NHP.193</td>
</tr>
<tr>
<td>Delta-V2 gp140 oligomeric</td>
<td>Purified oligomeric lacking the V2 region of gp140</td>
<td>HIV-1</td>
<td>HIV-1.SF162</td>
<td>B</td>
<td></td>
<td>NHP.22</td>
</tr>
<tr>
<td>Gag-Pol particles</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NHP.65.1</td>
</tr>
<tr>
<td>gp140 oligomeric</td>
<td>Purified gp140 oligomeric</td>
<td>HIV-1</td>
<td>HIVSF162</td>
<td></td>
<td></td>
<td>NHP.22</td>
</tr>
<tr>
<td>HIV BH10-tat protein</td>
<td></td>
<td>HIV-1</td>
<td>BH10</td>
<td>B</td>
<td>Accessory (tat)</td>
<td>NHP.2</td>
</tr>
<tr>
<td>HIV-1 W6.1D gp120</td>
<td>recombinant gp120 of HIV-1W6.1D from an infectious molecular clone</td>
<td>HIV-1</td>
<td>HIV-1 W6.1D</td>
<td>B</td>
<td></td>
<td>NHP.21</td>
</tr>
<tr>
<td>HIV-1.MN.rgp120</td>
<td></td>
<td>HIV-1</td>
<td>HIV-1.MN</td>
<td>B</td>
<td>env (gp120)</td>
<td>NHP.198</td>
</tr>
<tr>
<td>HIV-1.SF2 gp120/p24 Recombinant</td>
<td>Monomeric recombinant gp120 and p24 of HIV-1.SF2</td>
<td>HIV-1</td>
<td>HIV-1.F2</td>
<td>B</td>
<td>gag, env (gp120, p24)</td>
<td>NHP.198</td>
</tr>
</tbody>
</table>
### Recombinant subunit protein vaccines

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>Vaccine Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHP.164</td>
<td>HIV-189.6 Env gp140-ISCOM</td>
<td>200 µl of ISCOM matrix mixed overnight at 4°C with 25 µg of HIV-189.6 Env gp140 (produced in human 293T cells, containing gp120 and the gp41 ectodomain, and purified by lectin chromatography [University of Pennsylvania, Philadelphia]) in 250 µl of PBS.</td>
</tr>
<tr>
<td>NHP.374</td>
<td>HIV-1SF2 rgp120</td>
<td>Recombinant protein produced in Chinese hamster ovary cells</td>
</tr>
<tr>
<td>NHP.75</td>
<td>HIV-2 gp160</td>
<td>Virus HIV-2, Strain: ND, Gene/Protein: env</td>
</tr>
<tr>
<td>NHP.174</td>
<td>HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27</td>
<td>Recombinant SIVmac251 gp120 was expressed in Baculovirus-infected cells and recombinant SIV p27 was generated in pGEX-3X as a glutathione S-transferase fusion protein. With both preparations 100µg was covalently linked to HSP70 by 0.0025% glutaraldehyde (Sigma Fine Chemicals Ltd.) and 200 µg was mixed with equal concentration of HSP70; thus, a total of 400µg of HSP70 and 200µg (3)</td>
</tr>
<tr>
<td>NHP.395</td>
<td>Mono-gp120H (89.6)</td>
<td>Recombinant protein purified from plasmid expressing gp120 of HIV 89.6 strain; the proteins were tagged with histidine to facilitate their purification</td>
</tr>
<tr>
<td>NHP.11, NHP.363</td>
<td>Mono-gp120H (DH12)</td>
<td>Recombinant protein purified from plasmid expressing gp120 of HIV DH12 strain; the proteins were tagged with histidine to facilitate their purification</td>
</tr>
<tr>
<td>NHP.11</td>
<td>Monomeric rgp120</td>
<td>Monomeric rgp120 of the LAI isolate of HIV-1 was commercially produced by Intracel (Rockville, MD) by expressing HIV-1LAI gp120 DNA in CHO cells. The expression product was characterized by Western blot assay using sheep antibody to HIV-1 gp20 and sequencing. Purity of the recombinant product was &gt;98%</td>
</tr>
</tbody>
</table>
### Vaccines

**Recombinant subunit protein vaccines**

- **Vaccine Name:** Nef-Tat  
  **Description:** Nef-Tat is a full-length fusion protein of the two viral proteins. Antigens were expressed in the yeast *Pichia pastoris* as His-tagged proteins. The HIV-1 nef gene derived from the clone Bru/Lai, SIV nef was derived from the clone SIVmac239 without a premature stop codon, and the HIV-1 tat gene derived from the clone BH10  
  **Trial(s):** NHP.296

- **Vaccine Name:** Oligomeric HIV-1.89.6 gp140  
  **Description:** The 89.6 gp140 was produced from BS-C-1 cells infected with recombinant vaccinia virus vBD1 and purified by lentil lectin and Superdex 200 chromatography  
  **Virus** HIV-1  
  **Strain:** HIV-1.89.6  
  **Gene/Protein:** env  
  **Trial(s):** NHP90.1, NHP90.2

- **Vaccine Name:** Poly-gp120H  
  **Description:** Recombinant protein purified from plasmid expressing gp120 of HIV AD8, Bal, Lai, RF, 89.6 and DH12 strains; the proteins were tagged with histidine to facilitate their purification  
  **Virus** HIV-1  
  **Strain:** HIV-1 DH12  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 AD8  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 BAL  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 LAI  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 RF  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 89.6  
  **Subtype:** B  
  **Trial(s):** NHP.11

- **Vaccine Name:** Poly-gp120H (-DH12)  
  **Description:** Recombinant protein purified from plasmid expressing gp120 of HIV AD8, Bal, Lai, RF and 89.6 strains; the proteins were tagged with histidine to facilitate their purification  
  **Virus** HIV-1  
  **Strain:** HIV-1 AD8  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 BAL  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 LAI  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 RF  
  **Subtype:** B  
  **Virus** HIV-1  
  **Strain:** HIV-1 89.6  
  **Subtype:** B  
  **Trial(s):** NHP.11

- **Vaccine Name:** Recombinant gagpol particles  
  **Description:**  
  **Virus** SIV  
  **Strain:** SIVmne  
  **Gene/Protein:** gag, pol  
  **Trial(s):** NHP.134

- **Vaccine Name:** Recombinant gappolenv particles  
  **Description:**  
  **Virus** SIV  
  **Strain:** SIVmne

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**HIV Immunology and HIV/SIV Vaccine Databases 2003**
<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
<th>Trial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recombinant gp120</td>
<td>Antigen derived from the Dutch clinical HIV isolate ACH320, expressed in CHO cells</td>
<td>HIV-1</td>
<td>HIV-1.ACH320</td>
<td></td>
<td></td>
<td>NHP.134</td>
</tr>
<tr>
<td>Recombinant gp130</td>
<td>Recombinant subunit protein produced by African green monkey kidney (BSC-40) cells infected with recombinant vaccinia virus expressing the gp130 glycoprotein under the control of the late vaccinia virus 11K promoter</td>
<td>SIV</td>
<td>SIVmne</td>
<td></td>
<td></td>
<td>NHP.134</td>
</tr>
<tr>
<td>Recombinant HIV-1 env gp160 antigen</td>
<td>This is a recombinant protein (HIV-1 gp160 antigen) expressed in pMB1790</td>
<td>HIV-1</td>
<td>HIV-1.IIIB</td>
<td>B</td>
<td>env</td>
<td>NHP.204</td>
</tr>
<tr>
<td>Recombinant HIV-1 gag core (p24,p15) antigen</td>
<td>This is a recombinant protein (HIV-1 gp24 and p15 antigen) expressed in pCO1</td>
<td>HIV-1</td>
<td>HIV-1.IIIB</td>
<td></td>
<td>gag</td>
<td>NHP.204, NHP.328</td>
</tr>
<tr>
<td>Recombinant p27</td>
<td>rSIVp27 was expressed in pGEX3X as a glutathione-S-transferase fusion protein</td>
<td>SIV</td>
<td>SIVmac251</td>
<td></td>
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<td>NHP.106, NHP.185.1, NHP.185.2, NHP.201.1, NHP.201.2</td>
</tr>
<tr>
<td>rgp120</td>
<td>This protein was purified from cell culture medium containing 1%-vol fetal calf serum) conditioned by the growth of the gD-env-trunc cell line</td>
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<td>NHP.242, NHP.267</td>
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<tr>
<td>rgp120W6.1D</td>
<td>recombinant gp120W6.1D antigen derived from HIV-1 clone 320.3 isolated from a Dutch AIDS patient</td>
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<td>NHP.80</td>
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<tr>
<td>rgp140-env (HIV-1.89.6)</td>
<td></td>
<td>HIV-1</td>
<td>89.6</td>
<td>B</td>
<td>env (gp140)</td>
<td>NHP.348.1, NHP.348.2</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Description</td>
<td>Virus</td>
<td>Strain</td>
<td>Subtype</td>
<td>Gene/Protein</td>
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</tr>
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<td>--------------</td>
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<tr>
<td>rgp160</td>
<td>Recombinant subunit protein produced by African green monkey kidney (BSC-40) cells infected with recombinant vaccinia virus expressing the gp160 glycoprotein under the control of the late vaccinia virus 11K promoter</td>
<td>SIV</td>
<td>SIVmne</td>
<td></td>
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</tr>
<tr>
<td>rsgp160</td>
<td>Glycosylated This protein was produced in CHO under the transcriptional control of the SV40 early promoter. It differ from the wild type gp160 at the N terminus. The signal signal sequence and 12 amino acids of the wild type gp160 have been replaced with the signal sequence and 9 amino acids from the mature N-terminus of herpes simplex virus type 1 glycoprotein D</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>SF162ΔV2 gp140 protein</td>
<td>gp140 lacking the V2 region</td>
<td>HIV-1</td>
<td>HIV-1 IIIB</td>
<td>B</td>
<td>env (gp160)</td>
<td></td>
</tr>
<tr>
<td>SIV Nef</td>
<td></td>
<td>SIV</td>
<td>SIVmac239</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>SIV(Mne) gp160Env protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIVenv-Bgal peptides</td>
<td>This is a cocktail of 4 SIVenv epitopes (2 from gp120 and 2 from gp32). These epitopes appear to be homologous in sequence and location to the highly conserved HIV-env epitopes as well as being hydrophilic in nature. The oligonucleotides coding for these peptides were prepared and inserted at the 5’ end of the gene under the trp expression element of E. coli. The four recombinant SIVenv-B-galactosidase polipetides were expresed in bacteria and purified by HPLC.</td>
<td></td>
<td></td>
<td></td>
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</table>
### Recombinant subunit protein vaccines

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac</th>
<th>Gene/Protein: env (gp32, gp120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.94, NHP.154</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac239</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.374</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>SIVmac239 Gag-Pol-ISCOM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>25 µl SCOM matrix (Isconova, Uppsala, Sweden) mixed overnight at 4°C with either 25 µg SIVmac239 Gag-Pol in 250 µl of PBS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac239</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.374</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.89.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.349</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Soluble 89.6 gp120 protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Produced by infection of BS-C-1 cells with recombinant vaccinia virus, vBD2.13 at a multiplicity of infection of 5 plaque-forming units (pfu) per cell. Protein was purified from the media by lectin and Superdex-200 chromatography</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.89.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.349</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>tat protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>HIV-1 Tat (IIIB) expressed in Eschericia coli, purified to homogeneity by heparin-affinity chromatography and high-performance liquid chromatography and stored lyophilized at -80 °C. Purified Tat had full biological activity in several assays. Tat was resuspended in degassed buffer before use in vitro or in saline containing 20% of autologous serum for monkey injection.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.IIIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.374</td>
</tr>
</tbody>
</table>
## VI-B-11 Recombinant vector (virus/bacteria) vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>AD4-gp160(MN)</strong></td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td><strong>AD5-gp160(MN)</strong></td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>HIV-1</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>HIV-1.MN</td>
</tr>
<tr>
<td><strong>Subtype</strong></td>
<td>B</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>env</td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td>NHP.141</td>
</tr>
<tr>
<td></td>
<td><strong>Ad5-SIVgag</strong></td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>This vaccine was constructed using the adenovirus as the vector. The adenovirus vector was based on the serotype 5 that has been rendered incompetent to replicate by the deletion of E1 and E3 viral genes. The adenoviral vector, pHCMVIBGHpA1 contains Ad5 nucleotides 1-341 and 3,534-5,798 and an expression cassette containing the human cytomegalovirus promoter with intron and the bovine growth hormone poly adenylation signal (see paper for more information)</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>SIV</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>SIVmac239</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>gag</td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td>NHP.306.1, NHP.306.2</td>
</tr>
<tr>
<td></td>
<td><strong>Ad5hr-SIVmac239gag</strong></td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>Adenovirus Ad5hr with a codon-optimized Gag cDNA derived from Mac239, with silent mutations to optimize expression and eliminate the inhibitory sequences.</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>SIV</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>Mac239</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>gag (Gag)</td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td>NHP.324.1, NHP.328, NHP.363</td>
</tr>
<tr>
<td></td>
<td><strong>Ad5hr-SIVnef51-13</strong></td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>SIV</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>Mac239</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>Nef</td>
</tr>
<tr>
<td><strong>Trial(s)</strong></td>
<td>NHP.328, NHP.363</td>
</tr>
<tr>
<td></td>
<td><strong>Ad5hr-SIVsmH4 env/rev</strong></td>
</tr>
</tbody>
</table>

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### Recombinant vector (virus/bacteria) vaccines

#### Description
Ad5hr-SIVsmH4 env/rev, a replication-competent Ad5hr-SIV recombinant carrying the SIVsmH4env and rev genes in the deleted E3 region and expressing the entire SIV envelope and Rev proteins.

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain:</th>
<th>Gene/Protein: env, Accessory (rev)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.363, NHP.371</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vaccine Name
**AD7-gp160(MN)**

<table>
<thead>
<tr>
<th>Virus</th>
<th>HIV-1</th>
<th>Strain: HIV-1.MN</th>
<th>Subtype: B</th>
<th>Gene/Protein: env</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.141</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vaccine Name
**ALVAC-HIV-2 (gag,pol,gp125)**

<table>
<thead>
<tr>
<th>Virus</th>
<th>HIV-2</th>
<th>Strain: HIV-2 SBL6669</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>HIV-2</td>
<td>Strain: HIV-2 SBL6669</td>
<td>Gene/Protein: env (gp125)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vaccine Name
**ALVAC-SIV-gp**

Recombinant SIV vaccine composed of a live, weakened canarypox virus (ALVAC™) into which parts of SIV genes (gag and pol) were inserted. When ALVAC infects a human cell, the inserted SIV genes direct the cell to make SIV proteins. These proteins are packaged into SIV-like particles that bud from the cell membrane. The particles are not infectious, fool the immune system and mount immune response to SIV. As a safety precaution, ALVAC can infect but not grow in human or macaques cells.

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: ?</th>
<th>Gene/Protein: pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.345</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vaccine Name
**ALVAC-SIV-gpe (vcp180)**

The ALVAC-SIV-gpe (vcp180) was engineered to express the gag, pol, and env genes of SIVmac251(K6W).

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac251</th>
<th>Gene/Protein: env, gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.30, NHP.123, NHP.274</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vaccine Name
**ALVAC/vCP153 HIV-2 gag,pol,env**

<table>
<thead>
<tr>
<th>Virus</th>
<th>HIV-2</th>
<th>Strain: ND</th>
<th>Gene/Protein: env, gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.174</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vaccine Name
**FP-SIV-gp (FP74)**

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac239</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.9.2, NHP.345</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vaccine Name
**FPV.HIV-1.gag/pol**
**Vaccines**

**Recombinant vector (virus/bacteria) vaccines**

*Description* recombinant fowlpoxvirus (rFPV) vaccines expressing HIV-1 antigens gag and pol. The HIV-1gag/pol genes of ARV-2/SF2 strain were inserted into the FPV genome (FPV M3 strain) along with the E. coli Beta-gal and/or gpt selection and marker genes.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.ARV-2/SF2</th>
<th>Subtype: B</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.48</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** FPV.HIV-1.gag/pol-IFNgamma

*Description* recombinant fowlpoxvirus (rFPV) vaccines expressing both HIV-1 antigens and interferon-gamma. The HIV-1gag/pol genes of ARV-2/SF2 strain with the human IFNgamma gene were inserted into the FPV genome (FPV M3 strain) along with the E. coli Beta-gal and/or gpt selection and marker genes.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: ARV-2/SF2</th>
<th>Subtype: B</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.48</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** MVA SIVsmH4 gag-pol

*Description* MVA constructs expressing env, gag-pol, nef, rev and tat genes of SIVmacJ5

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVsmH4</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.3, NHP.45, NHP.46</td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** MVA-mac(J5)

*Description* MVA vectors expressing env, gag-pol, nef, rev and tat genes of SIVmacJ5

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmacJ5</th>
<th>Gene/Protein: gag, pol, env</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.51</td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** MVA-rev

*Description* Modified Vaccinia Anlkara expressing HIV-1 subtype B isolate IIIB rev cDNA.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: IIIB</th>
<th>Subtype: B</th>
<th>Gene/Protein: rev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>HXB2 5970-6045 (exon 1) and 8379-8653 (exon 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.276</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** MVA-SIV gag-pol and HIV-1 89.6 env

*Description* MVA vectors (pLW-9 and pLW-17) expressing SIV gag-pol and HIV-1 89.6 env

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: SIVmac239</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>HIV-1 Strain: HIV-1.89.6</td>
<td>Gene/Protein: env</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.24.2</td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** MVA-SIV239tat

*Description* This vector encodes the full-length SIVmac239 Tat

| Trial(s) | NHP.88 | |

**Vaccine Name** MVA-SIV251 32H tat

*Description* This vector encodes the full-length SIVmac251 32H Tat (clone J5)

| Virus | Strain: SIVmac251.32H | |
|-------|-----------------------| |
### Vaccine Name: MVA-SIVgag

**Description:**
This MVA-SIV gag vaccine was constructed by cloning the SIV gag gene into the pSC59 shuttle vector. This plasmid was designed to insert the transgene fragment into a viral thymidine kinase region and to drive the transgene from a synthetic early/late promoter. The recombinant plasmid was inserted into the MVA for immunization of monkeys.

**Virus**
SIV

**Strain:** SIVmac239

**Gene/Protein:** gag

**Trial(s):** NHP.306.1, NHP.306.2

### Vaccine Name: MVA-SIVmac239gag

**Description:**
Recombinant MVA virus VT338 contains the gag gene from SIVmac239 inserted into the deletion III region of the MVA genome under the control of the vaccinia virus 40K (H5R) promoter. The virus also contains the Escherichia coli lacZ gene under the control of the fowlpox C1 promoter for use as a colorimetric screen for recombinant viruses.

**Virus**
SIV

**Strain:** SIVmac239

**Gene/Protein:** gag

**Trial(s):** NHP.308

### Vaccine Name: MVA-SIVmacJ5 (gag-pol)

**Description:**
MVA constructs expressing gag-pol genes of SIVmac251 32H (pJ5) under the transcriptional control of the natural vaccinia virus early/late promoter P7.5 poorly immunogenic

**Virus**
SIV

**Strain:** SIVmac251 32H (pJ5)

**Gene/Protein:** gag, pol

**Trial(s):** NHP.3

### Vaccine Name: MVA-SIVSL8-tat28-35

**Description:**
This vector encodes a single Mamu-A*01-restricted CTL epitope Tat-SL8(positions 28-35)(STPESANL) inserted within the immunodominant region of hepatitis B core antigen

**Virus**
MAC239

**Strain:** SIVSL8 28-35

**Trial(s):** NHP.88

### Vaccine Name: MVA-SIVsmH-4 -env

**Description:**
MVA recombinants expressing the SIVsmH-4 env (MVA-env)

**Virus**
SIV

**Strain:** SIVsmH-4

**Gene/Protein:** env

**Trial(s):** NHP.45

### Vaccine Name: MVA-tat

**Description:**
Modified Vaccinia Ankara expressing HIV-1 IIIB strain tat cDNA

**Virus**
HIV-1

**Strain:** IIIB

**Subtype:** B

**Gene/Protein:** tat

**Trial(s):** NHP.276

### Vaccine Name: MVA.HW

---

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### Vaccines

**Description**
This is a recombinant MVA.HW expressing an MVA and SIV gag-derived epitope, TPYDINQML, recognized by CTLs in rhesus macaques (Macaca mulatta) in the context of the Mamu-A*01 MHC class I molecule.

**Virus**
- SIV

**Gene/Protein**
- gag

**Trial(s)**
- NHP.57

### Vaccine Name: MVA.pUCILSIVmac.J5

**Description**
MVA vaccine expressing SIV structural (gag,pol) and regulatory genes (tat,nef and rev).

**Virus**
- SIV

**Strain:**
- SIVmac.J5

**Gene/Protein**
- gag, pol

**Trial(s)**
- NHP.58

### Vaccine Name: MV A/HIV 48

**Description**
MVA/HIV 48 is an rMVA expressing HIV-1 clade B Gag, protease, RT, and Env constructed by homologous recombination in chick embryo fibroblasts. Contains HXB2 gag and BH10 pol. The pol sequences contained three safety mutations in RT and a truncated integrase. The env from CCR5-tropic HIV-1.ADA contained silent mutations to eliminate two copies of a TTTTTNT sequence that acts as a poxvirus transcription termination signal (See LINDA S. WYATT, et al. 2004)

**Virus**
- HIV-1

**Strain:**
- HIV-1.BH10

**Subtype:**
- B

**Gene/Protein**
- pol

**Virus**
- HIV-1

**Strain:**
- HIV-1.HXB2

**Subtype:**
- B

**Gene/Protein**
- gag

**Virus**
- HIV-1

**Strain:**
- HIV-1.ADA

**Subtype:**
- B

**Gene/Protein**
- env

**Trial(s)**
- NHP.384

### Vaccine Name: MVAgagpol

**Description**
The SIVsmH4 gag pol ORF (1049-5397) cloned into pMC03, then the product transfected into chicken embryo fibroblasts that had been infected with MVA. Plaques that stained blue upon addition of X-Gluc (CLONTECH) were purified

**Virus**
- SIV

**Strain:**
- SIVsmH4

**Gene/Protein**
- gag, pol

**Trial(s)**
- NHP.44

### Vaccine Name: MVAmacJ5-nef

**Description**
A highly immunogenic vector construct with high anti-CTL response; associated with protection

**Virus**
- SIV

**Strain:**
- SIVmac251 32H (pJ5)

**Gene/Protein**
- Accessory (nef)

**Trial(s)**
- NHP.3

### Vaccine Name: MVApIII-sp.SIVmac.J5.env

**Description**
Recombinant MVA vaccine expressing SIVmac.J5 env gene

**Virus**
- SIV

**Strain:**
- SIVmac.J5

**Gene/Protein**
- env

**Trial(s)**
- NHP.58

### Vaccine Name: NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe)

**Description**
A highly attenuated poxvirus NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe); Induce both CD4+ and CD8+ t cell responses in rhesus macaques and demonstrate effectiveness as a preventive vaccine candidate.

**Notes**
- vaccinia
Recombinant vector (virus/bacteria) vaccines

Vaccines

Virus | SIV | Strain: Mac251

Gene/Protein: env expression cassette under control of vaccinia H6 promoter and gag-pol with I3L promoter.


Trial(s) NHP9.1, NHP274

Vaccine Name: Polio (Sabin 1) - HIV-1.gag/env (2)

Virus | HIV-1 | Strain: IIB?LAI (HXB2)
Gene/Protein: gag, env (gp120,gp140 (lacking signal sequence) gp120+gp140 ectodomain, p55 fused with VP4)

Virus | HIV-1 | Strain: 92TH021
Subtype: D
Gene/Protein: env (gp120)

Virus | HIV-1 | Strain: 92TH022
Subtype: CRF02_AE
Gene/Protein: env (gp120)

Virus | HIV-1 | Strain: 92RW020
Subtype: A
Gene/Protein: env (gp120)

Virus | HIV-1 | Strain: 92BR025
Subtype: C
Gene/Protein: env (gp120)

Trial(s) NHP348.1

Vaccine Name: Polio (Sabin 1) - HIV-1.gag/env (1)

Virus | HIV-1 | Strain: 92RW020
Subtype: A
Gene/Protein: env (GP120)

Virus | HIV-1 | Strain: 92TH022
Subtype: CRF02_AE
Gene/Protein: env (gp120)

Virus | HIV-1 | Strain: 92UG021
Subtype: D
Gene/Protein: env (gp120)

Virus | HIV-1 | Strain: IIB/LAI (HXB2)
Subtype: B
Gene/Protein: gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)

Trial(s) NHP348.1

Vaccine Name: Polio (Sabin 2) - HIV-1.gag/env (3)

Virus | HIV-1 | Strain: IIB/LAI (HXB2)
Subtype: B
Gene/Protein: gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)

Virus | HIV-1 | Strain: 92UG021
Subtype: D
Gene/Protein: env (gp120)

Virus | HIV-1 | Strain: 92RW09
Subtype: A
Gene/Protein: env (gp120)

Virus | HIV-1 | Strain: 92TH026
Subtype: CRF02_AE
Gene/Protein: env (gp120)

Trial(s) NHP348.1

Vaccine Name: Polio (Sabin 2) - HIV-1.gag/env (4)

Virus | HIV-1 | Strain: IIB/LAI (HXB2)
Subtype: B
Gene/Protein: gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)

Trial(s) NHP348.1

Vaccine Name: Polio- SIVmac239gag

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<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polio-LAI/IIIB-Env</td>
<td>A mixture of 3 transformed strains of <em>Mycobacterium bovis</em> BCG expressing the SIV-MAC-251 gag, nef and env genes.</td>
<td>SIV</td>
<td>MAC251</td>
<td>-</td>
<td>Accessory, env, gag (nef, gag, env)</td>
</tr>
<tr>
<td>rBCG-SIV³</td>
<td>Recombinant fowlpox virus expressing SIVmac239 gag. The SIV gene was inserted in the BamJHI region of POXVAC-TC (Schering-Plough) strain of FPV</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>-</td>
<td>gag</td>
</tr>
<tr>
<td>Recombinant fowlpox (rFPV) SIVmac239 gag</td>
<td>Recombinant fowlpox virus expressing SIVmac239 gag. The SIV gene was inserted in the BamJHI region of POXVAC-TC (Schering-Plough) strain of FPV</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>-</td>
<td>gag</td>
</tr>
<tr>
<td>Recombinant fowlpox (rFPV) SHIV89.6P env</td>
<td>Recombinant fowlpox virus expressing SHIV89.6P env. The SHIV gene was inserted in the BamJHI region of POXVAC-TC (Schering-Plough) strain of FPV.</td>
<td>SHIV</td>
<td>SHIV89.6P</td>
<td>B</td>
<td>env</td>
</tr>
<tr>
<td>Recombinant MVA-SHIV89.6P env</td>
<td>Recombinant MVA expressing SHIV89.6P gp140 (env). The SHIV gene was inserting in the deletion III region of a plaque-purified isolate of the replication-defective strain of vaccinia virus designated MVA. The env gene was under the control of the vaccinia virus 40K(H5R) promoter.</td>
<td>SHIV</td>
<td>SHIV89.6P</td>
<td>B</td>
<td>env</td>
</tr>
<tr>
<td>Recombinant MVA-SIVmac239 gag</td>
<td>Recombinant MVA expressing SIVmac239 gag. The SIVmac239 gene was inserting in the deletion III region of a plaque-purified isolate of the replication-defective strain of vaccinia virus designated MVA. The gag gene was under the control of the vaccinia virus 40K(H5R) promoter.</td>
<td>SIV</td>
<td>SIVmac239</td>
<td>-</td>
<td>gag</td>
</tr>
<tr>
<td>Recombinant vaccinia gagpol (v-SG11)</td>
<td></td>
<td>SIV</td>
<td>SIVmne</td>
<td>-</td>
<td>gag, pol</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Description</td>
<td>Virus</td>
<td>Strain</td>
<td>Gene/Protein</td>
<td>Trial(s)</td>
</tr>
<tr>
<td>-------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------</td>
<td>------------</td>
<td>------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Recombinant vaccinia gagpolenv (v-SGE14)</td>
<td></td>
<td>SIV</td>
<td>SIVmne</td>
<td>env, gag, pol</td>
<td>NHP.134</td>
</tr>
<tr>
<td>Recombinant vaccinia gp130 (v-SE6)</td>
<td></td>
<td>SIV</td>
<td>SIVmne</td>
<td></td>
<td>NHP.134</td>
</tr>
<tr>
<td>Recombinant vaccinia virus vac-gp160 (v-SE5)</td>
<td>Recombinant vaccinia virus vac-gp160 (v-SE5) contains the coding sequence of the full-length gp160 of SIVmne molecular clone 8 (GenBank accession number M32741) in a New York City Board of Health strain (v-NY) of vaccinia virus (16, 17). v-SE5 was plaquepurified and propagated on African green monkey kidney cells (BSC-40)</td>
<td>SIV</td>
<td>SIVmne</td>
<td>env</td>
<td>NHP.134, NHP.269</td>
</tr>
<tr>
<td>Recombinant vaccinia virus-HIVgp160 (cocktail)</td>
<td>Recombinant vaccinia virus expressing gp160 of HIV-1 isolates Bal, LAI, RF (vCB43, vCB41, and vCB36, respectively), 89.6 (vBD3), DH12, and AD8 (vvDHenv and vvADenv, respectively).</td>
<td>HIV-1</td>
<td>HIV-1 BAL</td>
<td>env</td>
<td>NHP.11</td>
</tr>
<tr>
<td>HIV-1</td>
<td>Strain: HIV-1 LAI</td>
<td>Subtype: B</td>
<td>Genotype: env</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-1</td>
<td>Strain: HIV-1 RF</td>
<td>Subtype: B</td>
<td>Genotype: env</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-1</td>
<td>Strain: HIV-1 RF</td>
<td>Subtype: B</td>
<td>Genotype: env</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recombinant vaccinia virus (rVac).SHIV89.6P Env</td>
<td>Recombinant vaccinia virus expressing SHIV89.6P env, constructed by inserting the SHIV env gene in the HindIII M region of TBC-Wy Therion strain of vaccinia (see Mazzara, G. P., Destree, A.&amp;Mahr, A. (1993) Methods Enzymol. 217, 557-581).</td>
<td>SHIV</td>
<td>SHIV89.6P</td>
<td>env</td>
<td>NHP.400</td>
</tr>
</tbody>
</table>

HIV Immunology and HIV/SIV Vaccine Databases 2003
Vaccines

Recombinant vector (virus/bacteria) vaccines

**Description** The rMVA-SIVsm co-expresses the gag-pol and env of SIVsmmH4. gag-pol was under the transcriptional control of the vaccinia early-late promoter P7.5. Env was expressed using a strong synthetic vaccinia virus early-late promoter. MVA-SIVsmwas amplified on primary chicken embryo fibroblasts and purified by ultracentrifugation. Purified viruses were reconstituted in PBS and titrated by end-point dilution in CEF to obtain the TCID50, aliquotted and stored at -70 °C.

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVsmmH4</th>
<th>Gene/Protein: gag, pol, env</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.125</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** rMVA 89.6

**Description** The MVA double recombinant virus expressed both the HIV 89.6 Env and the SIV 239 Gag-Pol, which were inserted into deletion II and deletion III of MVA, respectively. The 89.6 Env protein was truncated for the COOH-terminal 115 amino acids of gp41.

**Notes** The modified H5 promoter controlled the expression of both foreign genes.

<table>
<thead>
<tr>
<th>Virus</th>
<th>HIV-1</th>
<th>Strain: HIV-1.89.6</th>
<th>Subtype: B</th>
<th>Gene/Protein: env</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>SIV</td>
<td>Strain: SIVmac329</td>
<td>Gene/Protein: gag, pol</td>
<td></td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.19, NHP.132, NHP.325, NHP.349</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** rMVA SIV239 gag-pol

**Description** this recombinant MVA expresses SIV239 Gag-Pol.

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac239</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.89</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** rMVA SIVmac239 gagpolenv

**Description** For construction of MVA-SIVgpe, chicken embryo fibroblast cells were incubated simultaneously with five infectious units each of MVA/SIV239gagpol and MVA/SIVH4wt. The latter virus expresses the SIVmac239 env gene, truncated after amino acid 733, under the control of the moderate-strength vaccinia virus promoter p7.5. A virus isolate expressing all three genes was clonally purified and amplified.

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac239</th>
<th>Gene/Protein: env, gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.294</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** rMVA-SIVmac251 32H

**Description** Recombinant MVA expressing SIVmac251 genes (gag,pol,tat,rev or nef, separately) under the transcriptional control of vaccinia virus early and late promoters P7.5 and sP.

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac251</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.52</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name** rMVA.SIVmac239gagpolHIVenv

**Description** Recombinant MVA expressing SIVmac32H tat and rev genes.

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac239</th>
<th>Gene/Protein: gag, pol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus</td>
<td>HIV-1</td>
<td>Strain: Unknown</td>
<td>Gene/Protein: env</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.366</td>
<td></td>
<td></td>
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</table>

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<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac32H</th>
<th>Gene/Protein: Accessory (tat, rev)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>rSFV-SIVmac32H.rev.tat</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Recombinant Semliki Forest Virus encoding SIVmac32H rev and tat genes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
<td>Strain:</td>
<td>Gene/Protein: Accessory (rev, tat)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.49</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac239</th>
<th>Gene/Protein: env</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>rSalmonella typhi-SIVgag</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Salmonella typhi expressing SIV gag</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
<td>Strain: SIVmac239</td>
<td>Gene/Protein: gag</td>
</tr>
<tr>
<td>Virus</td>
<td>MAC239</td>
<td>146-213</td>
<td>Gene/Protein: gag</td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
<td>Strain: SIVmac239</td>
<td>Gene/Protein: gag</td>
</tr>
<tr>
<td>Virus</td>
<td>MAC239</td>
<td>4-284</td>
<td>Gene/Protein: gag</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.308</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac239</th>
<th>Gene/Protein: gag</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>rSalmonella typhimurium-SIVgag</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Salmonella typhimurium expressing SIV gag</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
<td>Strain: SIVmac239</td>
<td>Gene/Protein: gag</td>
</tr>
<tr>
<td>Virus</td>
<td>MAC239</td>
<td>146-213</td>
<td>Gene/Protein: gag</td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
<td>Strain: SIVmac239</td>
<td>Gene/Protein: gag</td>
</tr>
<tr>
<td>Virus</td>
<td>MAC239</td>
<td>4-507</td>
<td>Gene/Protein: gag</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.308</td>
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</table>

<table>
<thead>
<tr>
<th>Virus</th>
<th>SIV</th>
<th>Strain: SIVmac</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>rVaccinia-SIVmac-env.gagpol</td>
<td></td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Recombinant vaccinia virus containing both SIVmac env and SIVmac gag-pol (vAbT386.6.1)</td>
<td></td>
</tr>
<tr>
<td>Virus</td>
<td>SIV</td>
<td>Strain: SIVmac</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.78</td>
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### Vaccines

#### Recombinant vector (virus/bacteria) vaccines

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
<th>Gene/Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHP.76</td>
<td>rVV-HIV-1.DH12env</td>
<td>Recombinant vaccinia virus expressing HIV-1 DH12 gp160 (env) protein.</td>
<td>HIV-1</td>
<td>HIV-1.DH12</td>
<td>B</td>
<td>env</td>
</tr>
<tr>
<td>NHP.303</td>
<td>rVV-SIVmacgag/pol</td>
<td>This is a recombinant vaccinia virus expressing SIV gag and pol (for additional information on this vaccine please contact Dr M. Cho directly)</td>
<td>SIV</td>
<td>SIVmac239</td>
<td></td>
<td>gag, pol</td>
</tr>
<tr>
<td>NHP.276</td>
<td>SFV-rev</td>
<td>Semliki Forest Virus from pSFV (Invitrogen, Cergy-Pontoise, France) with rev cDNA from HIV-1 primary isolate ACH320 2.1 first subcloned in pCI (Promega, Charbonnieres, France) expression vector and then re-cloned into pSFV. Recombinant SFV-rev stocks prepared on BHK-21 cells.</td>
<td>HIV-1</td>
<td>ACH320 2.1</td>
<td>B</td>
<td>rev</td>
</tr>
<tr>
<td>NHP.276</td>
<td>SFV-tat</td>
<td>Semliki Forest Virus from pSFV (Invitrogen, Cergy-Pontoise, France) containing tat cDNA from HIV-1 subtype B primary isolate ACH320 2.1 first subcloned into pCI expression vector before re-cloning into pSFV.</td>
<td>HIV-1</td>
<td>ACH320 2.1</td>
<td>B</td>
<td>tat</td>
</tr>
<tr>
<td>NHP.58</td>
<td>vAbT394</td>
<td>Recombinant vaccinia (NYCBH) expressing SIVMAC251 Gag-Pol.</td>
<td>SIV</td>
<td>MAC251</td>
<td></td>
<td>Gag-Pol</td>
</tr>
<tr>
<td>NHP.319</td>
<td>Vaccinia-rDIsSIVgag</td>
<td>A recombinant vaccinia virus DI8 expressing SIV Gag. Contains a full-length gag gene of SIVmac239 in the vector construct. rDIs expressing SIVmac239 Gag (rDIsSIVGag)</td>
<td>SIV</td>
<td>SIVmac239</td>
<td></td>
<td>gag</td>
</tr>
</tbody>
</table>
Vaccines

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.365</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>vP1047, NYVAC HIV-2.SBL-ISH gp160.gag-pol</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>To generate the NYVAC-recombinant viruses, plasmids encoding sequences for HIV-2.SBL-ISH gp160 plus gag-pol were used by invitro recombination, using the NYVAC vector vP866 as rescue virus</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>HIV-2</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>HIV-2.SBL-ISH</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>gag, pol</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.47</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>vP991, NYVAC HIV-1IIB gp120.gag-pol</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>To generate the NYVAC-recombinant viruses, plasmids encoding sequences for HIV-1 IIB gp120 (aa residues 1-511) plus gag-pol were used by invitro recombination, using the NYVAC vector vP866 as rescue virus</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>HIV-1</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>HIV-1IIB</td>
</tr>
<tr>
<td><strong>Subtype</strong></td>
<td>B</td>
</tr>
<tr>
<td><strong>HXB2</strong></td>
<td>1-511</td>
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</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.47</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>vSIVgp120</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Recombinant vaccinia virus expressing SIV gp120</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.33</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>VSV(GCh)-Env+Gag</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Recombinant vesicular stomatitis virus (VSV) encoding HIV-1.89.6 env gene and SIV gag. The VSV G protein (Indiana serotype, GI) was subtituted with the VSV Chandipura glycoprotein (GCh)</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>HIV-1</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>HIV-1.89.6</td>
</tr>
<tr>
<td><strong>Subtype</strong></td>
<td>B</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>env</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>SIV</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>SIVmac239</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>gag</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.55</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>VSV(GNJ)-Env+Gag</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Recombinant vesicular stomatitis virus (VSV) expressing HIV-1.89.6 env and SIVmac239 gag. The VSV G protein (Indiana serotype, GI) was replaced with the G protein of the VSV New Jersey serotype (GNJ)</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>SIV</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>SIVmac239</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>gag</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>HIV-1</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>HIV-1.89.6</td>
</tr>
<tr>
<td><strong>Subtype</strong></td>
<td>B</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>env</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.55</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>VSV-(GI)-Env</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Recombinant vesicular stomatitis virus (VSV) vector encoding HIV-1 env gene</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>HIV-1</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>HIV-1.89.6</td>
</tr>
<tr>
<td><strong>Subtype</strong></td>
<td>B</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>env</td>
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</table>

<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>NHP.55</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>vT107</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Recombinant vaccinia (NYCBH)expressing HIV-1 89.6 Env</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>HIV-1</td>
</tr>
<tr>
<td><strong>Strain</strong></td>
<td>89.6</td>
</tr>
<tr>
<td><strong>Subtype</strong></td>
<td>B</td>
</tr>
<tr>
<td><strong>Gene/Protein</strong></td>
<td>env (Env)</td>
</tr>
<tr>
<td>Trial(s)</td>
<td>NHP.319</td>
</tr>
<tr>
<td>----------</td>
<td>---------</td>
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</table>

Vaccines

Recombinant vector (virus/bacteria) vaccines

HIV Immunology and HIV/SIV Vaccine Databases 2003
### VI-B-12 Passive antibody vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HIV-1 ch1206</td>
<td>Passive antibody vaccines Vaccines Vaccines VI-B-12 Passive antibody vaccines Vaccine Name Anti-HIV-1 ch1206 Description Anti-HIV-1 antibodies obtaine from chimpanzees infected with HIV-1DH12. The chimpanzee was infected for 2.8 years prior to sample collection Trial(s) NHP.86.1, NHP.86.2</td>
</tr>
<tr>
<td>Anti-HIV-1 ch4750</td>
<td>Vaccine Name Anti-HIV-1 ch4750 Description Anti-HIV-1 antibodies obtaine from chimpanzees infected with HIV-1DH12, HIV-1DH20 and HIV-1DH20. The chimpanzee was infected for 3 years prior to sample collection Trial(s) NHP.86.1</td>
</tr>
<tr>
<td>Anti-HIV-1 ch911</td>
<td>Vaccine Name Anti-HIV-1 ch911 Description Anti-HIV-1 antibodies obtaine from chimpanzees infected with HIV-1 IIIB. The chimpanzee was infected for 9.9 years prior to sample collection Trial(s) NHP.86.1</td>
</tr>
<tr>
<td>Anti-HIV-2</td>
<td>Vaccine Name Anti-HIV-2 Description Antibody obtained from a Cynomolgus macaque inoculated with HIV-2 (SBL-6669) in a whole inactivated form. The monkey has subsequently shown to be protected from an autologous challenge. Virus HIV-2 Strain: HIV-2 SBL6669) Gene/Protein: All Trial(s) NHP.149.1, NHP.149.2</td>
</tr>
<tr>
<td>Anti-SHIV Plasma</td>
<td>Vaccine Name Anti-SHIV Plasma Description Pool of antiSHIV plasma from macaques infected with non-pathogenic SHIV-4. This pool consists mainly of polyclonal IgG Trial(s) NHP.87</td>
</tr>
<tr>
<td>Anti-SIVmac251</td>
<td>Vaccine Name Anti-SIVmac251 Description Antibodies generated by the immunization of pregnant macaques with whole-inactivated SIVmac251 plus montanide ISA 51 adjuvant. Virus SIV Strain: SIVmac251 Gene/Protein: All Trial(s) NHP.294</td>
</tr>
<tr>
<td>Anti-SIVmacC8</td>
<td>Vaccine Name Anti-SIVmacC8 Description Pool of antibodies collected from 4 cynomolgous macaques (L103, L106) inoculated with 10^4 TCID50 of 9/90 live attenuated virus SIVmacC8, prepared in C8166 cell. all macaques were shown to be infected and were subsequencently challenged with SIVmac5M and SHIV-4. The challenge did not induce superinfection. Serum collected from the 4 monkeys was stored at -70°C and used as reagent. Trial(s) NHP.215</td>
</tr>
<tr>
<td>C/1 anti-V3</td>
<td>Vaccine Name C/1 anti-V3 Description This is a mouse-human IgG1 chimeric monoclonal antibody. It contains the intact variable region of the murine 0.5 β monoclonal antibody which is directed to the V3 loop of HIV-1 IIIB variant gp120 and has potent in vitro IIIB-specific virus-neutralizing activity.</td>
</tr>
</tbody>
</table>
### Passive antibody vaccines

<table>
<thead>
<tr>
<th>Virus</th>
<th>Strain: HIV-1.IIIB</th>
<th>Subtype: B</th>
<th>Gene/Protein: env (V3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial(s)</td>
<td>NHP.152.1, NHP.152.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Vaccine Name**: Chimp anti-HIV IgG  
**Description**: Antibodies were obtained from chimpanzees that were infected with a variety of HIV-1 isolates and subsequently developed high-titer neutralizing antibodies.  
**Trial(s)**: NHP.249

**Vaccine Name**: Chimp-anti-HIV-IgG  
**Description**: The authors [Nishimura et al J Virol 76(5): 2123-30 (2002)] state that the IgG was harvested in 2000, from chimpanzee 4750 which had been infected in 1993 with 3 different HIV-1 strains including HIV-1 strain DH12.  
**Trial(s)**: NHP.354, NHP.394

**Vaccine Name**: F105/2G12/2F5 mab  
**Description**: Cocktail of 3 monoclonal antibodies (F105, 2G12 and 2F5)  
**Trial(s)**: NHP.85, NHP.117

**Vaccine Name**: HIVIG  
**Description**: Anti-HIV-1 immunoglobulin obtained by plasmapheresis from HIV-1 infected individuals. The neutralising antibody titer was above or equal to 1:128. Virus-sterilized coagulation factors by application of solvents and detergents were used to inactivate the virus in the plasma.  
**Notes**: derived from the pooled plasma of several HIV-1 positive donors  
**Trial(s)**: NHP.8, NHP.82.1, NHP.82.2, NHP.361

**Vaccine Name**: IgG1 b12  
**Description**: Human antibody (IgG1, ) recognizing an epitope overlapping the CD4 binding site of gp120 , contained <1 IU of endotoxin/ml  
**Trial(s)**: NHP.6, NHP.15, NHP.304

**Vaccine Name**: mAb B4  
**Description**: This is a monoclonal antibody directed against HIV receptor complex; Broad neutralizing activity against HIV; Provides postexposure prophylaxis to hu-peripheral blood leukocyte (PBL)-severe combined immunodeficient mice and chimpanzees; Recognized a complex receptor site for HIV on the T cell surface including CD4; Preferentially neutralizes primary HIV-1 isolates compared with T cell line-adapted strains, including SI and NSI-inducing phenotypes, representatives from HIV-1 subtypes A-G, HIV-2, SIV, and SHIV  
**Trial(s)**: NHP.84

**Vaccine Name**: Monoclonal antibody 2F5  
**Description**:  
**Notes**: 2F5 is an subclass IgG1. recognizes the gp41 sequence ELDKWA that is conserved among many HIV-1 strains  
**Trial(s)**: NHP.8, NHP.15, NHP.82.1, NHP.82.2, NHP.304

**Vaccine Name**: Monoclonal antibody 2G12  
**Description**: 2G12 is a subclass IgG1. Binds to a conformationally sensitive epitope in the C3-V4 region of gp120
<table>
<thead>
<tr>
<th>Trial(s)</th>
<th>Vaccine Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHP.8, NHP.15, NHP.82.1, NHP.82.2, NHP.304</td>
<td>Monoclonal antibody 4E10</td>
<td>This is a human monoclonal antibody that recognizes the conserved HIV-1 gp41 epitope</td>
</tr>
<tr>
<td>NHP.304</td>
<td>Monoclonal antibody F105</td>
<td>Obtained by fusion of antibody-producing EBV-transformed cells with the HMMA2.11TG/O cell line; This is an IgG1 kappa antibody that binds to the surfaces of cells infected with all HIV-1 strains tested: MN, RF, IIIB, and SF2, but not uninfected cells</td>
</tr>
<tr>
<td>NHP.15</td>
<td>SIVIG</td>
<td>Approximately 16 g of IgG purified from 1.5 liters of plasma obtained by plasmapheresis from a single long-term nonprogressing Macaca mulatta macaque, infected with the F236 isolate of SIVsm and remaining clinically healthy for more than 6 years</td>
</tr>
<tr>
<td>NHP.377</td>
<td>SIVIG-1</td>
<td>Antibody preparation from pooled plasma from SIVmac251-infected macaques. The preparation contains 15 mg/ml of purified IgG, a titer of 68,000 gp120; 31,00 anti-p27 and 1.15 ug/ml 50% neutralization titer</td>
</tr>
<tr>
<td>NHP.83</td>
<td>SIVIG-2</td>
<td>Antibody preparation from pooled plasma from SIVmac251-infected macaques. The preparation contains 16 mg/ml of purified IgG, a titer of 170,000 gp120; 30,00 anti-p27 and 0.6 ug/ml 50% neutralization titer</td>
</tr>
</tbody>
</table>
### VI-B-13 Other vaccines

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Description</th>
<th>Virus</th>
<th>Strain</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CD4 Immunoadhesin (CD4-IgG)</strong></td>
<td>A chimeric consisting of the N-terminal two immunoglobulin-like regions of CD4 joined to the Fc region of human IgG1. This is used as a CD4 analogue because it has a half life longer than CD4. In human, the complexe results in 25 folds increase of concentration of CD4-IgG in the blood compared with recombinant CD4.</td>
<td>HIV-1</td>
<td>HIV-1.IIIB</td>
<td>B</td>
</tr>
<tr>
<td><strong>Crosslinked gp120-CD4</strong></td>
<td>HIV-1 IIIB gp120 and CD4 chemically crosslinked with 0.5 mM bis(sulfosuccinimidyl)suberate (BS3, Sigma)</td>
<td>HIV-1</td>
<td>HIV-1.IIIB</td>
<td>B</td>
</tr>
<tr>
<td><strong>Crosslinked gp140-CD4</strong></td>
<td>HIV-1 IIIB gp140 and CD4 chemically crosslinked with 0.5 mM bis(sulfosuccinimidyl)suberate (BS3, Sigma)</td>
<td>HIV-1</td>
<td>HIV-1.IIIB</td>
<td>B</td>
</tr>
<tr>
<td><strong>HIV-1 HXBc2 Tat Toxoid</strong></td>
<td>Contact authors</td>
<td>HIV-1</td>
<td>HXBc2</td>
<td><strong>Gene/Protein:</strong> Accessory (tat)</td>
</tr>
<tr>
<td><strong>inactivated Tat toxoid</strong></td>
<td>Contact authors</td>
<td>HIV-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SHIV89.6P tat toxoid</strong></td>
<td>Contact authors</td>
<td>SHIV</td>
<td>SHIV89.6P</td>
<td>B</td>
</tr>
</tbody>
</table>
VI-C

Challenges

This chapter contains a list of challenge viruses used in the studies compiled in the database. Challenge viruses are grouped into the following categories:

- SHIV
- SIV
- HIV-1
- HIV-2

In most cases, the name and description of challenge viruses were retained as provided by the authors in the paper reporting the trial. For HIV-1, HIV-2 and simian/human synthetic recombinant viruses, the subtype of the HIV-1 or HIV-2 portion(s) of the genome has been recorded. In addition, the studies in which each challenge virus was used are also shown for each challenge virus.

Viruses used in primate models of AIDS and vaccine studies are tremendously variable in infectivity, sequence diversity, and pathogenicity. For example, the SHIV89.6P virus is much more rapidly lethal to Rhesus macaques than the SHIV-89.6 virus from which it was derived [1,2]. The SHIV89.6P acutely pathogenic virus has mutations which alter the carboxy terminus of the env gp41 protein and also alter the Nef protein. Similarly, some of the PBJ isolates are far more acutely lethal than the SMM9 stock from which they were derived [3,4].

The database contains links to genetic sequences of challenge viruses whenever such sequences are available. Caution should be used in interpreting such links because the sequence may not be 100% identical to the challenge virus. Even with an infectious molecular clone of a virus, the challenge dose is often created from culturing the clone though several amplification passages which could result in an accumulation of mutations.

References


## VI-C-1 SHIV Challenges

<table>
<thead>
<tr>
<th>Strain</th>
<th>Description</th>
<th>HIV Subtype</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHIV-BX08</td>
<td>The SHIV-BX08 construct is a chimeric virus derived from SIV-MAC239 (gag, pol, vif, vpx and nef genes), HIV-1 isolate BX08 (env gp120), and HIV-1 isolate LAI (env gp41, tat and rev). Although SHIV-BX08m has been used in numerous studies, no DNA sequences are available for the BX08 virus.</td>
<td>B</td>
<td>NHP.276</td>
</tr>
<tr>
<td>SHIV-C2/1</td>
<td>SHIV-C2/1 is an SHIV-89.6 variant isolated by passaging the peak of initial plasma viremia from an infected cynomologus macaque as described in J Gen Virol 80(5):1231-40 (1999) by Shinohara et al. The original pSHIV, containing the SHIV-89.6P (and not the 89.6 as implied by Shinohara in J Gen Virol) was kindly provided by Y. Lu at the Harvard AIDS Institute (Boston, Mass. <a href="mailto:yichenlu@hsph.harvard.edu">yichenlu@hsph.harvard.edu</a>).</td>
<td>B</td>
<td>NHP.365</td>
</tr>
<tr>
<td>SHIV-DH12clone7</td>
<td>Infectious molecular clone derived from SHIV-DH12R-PS1 which in turn was derived from HIV-MD14YE [Igarashi et al PNASU 96(24): 14049-14054 (1999)].</td>
<td>B</td>
<td>NHP.386</td>
</tr>
<tr>
<td>SHIV-DH12clone8</td>
<td>Infectious molecular clone derived from SHIV-DH12R-PS1 which in turn was derived from HIV-MD14YE [Igarashi et al PNASU 96(24): 14049-14054 (1999)].</td>
<td>B</td>
<td>NHP.386</td>
</tr>
<tr>
<td>SHIV-IIIB/HXB2</td>
<td>Also known as SHIV-4, Described in J AIDS 5: 639-646 (1992) by Li et al. SIV-Mac239 virus with HIV-1 HXB2 env inserted. Described in J Virol 70(5):3198-3206 (1996) only as the aren plasmid from which SHIV-89.6 was created by replacing part of HXB2 gp160 with the same region for another HIV-1 subtype B virus with different tropism.</td>
<td>B</td>
<td>NHP.14, NHP.16.1, NHP.16.2, NHP.47, NHP.56</td>
</tr>
<tr>
<td>SHIV-Ku2</td>
<td>SHIV-Ku2 is a chimeric virus containing the HIV-1 IIIB strain (HXBc2) envelope gene and SIVmac239 gag and pol genes, and is pathogenic in rhesus macaque</td>
<td>B</td>
<td>NHP.1, NHP.79, NHP.107</td>
</tr>
</tbody>
</table>

Notes:
<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV-MD14YE (DH12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Derived from SHIV-1DH12, but with the HIV-1 nef gene replaced by SIV-Mac239 nef with two mutations R17Y and Q17E. The SIV nef R17Y mutation is known to create virus that depletes macaque T-cells self-activates T-cells such that the virus can replicate in non-stimulated PBMCs. R17Y creates SH2 binding ITAM motif YXXLXXXXXYXXL.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Notes</td>
<td>The tat, rev and env genes and the remainder of the vpr gene were derived mostly from HIV-1DH12, except for a small segment (145 bp) at the SIV/HIV-1 junction in vpr) that is of HIV-1NL4-3 origin.</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.86.1, NHP.86.2, NHP.387, NHP.389</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV-NM-3rN</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Notes</td>
<td>The subtype relates to the HIV component only</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.28, NHP.31, NHP.35, NHP.322</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV-vpu+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Described in Li et al J Virol 69(11):7061-7 (1995) PubMed ID 7474126. SHIV-4 modified by site-directed mutagenesis to correct defective vpu. HIV-1 subtype B clone HXB2 has a defective vpu gene due to an ATG to ACG mutation in the vpu start codon. ThisSHIV has a corrected start codon, plus a P5Q mutation in vpu.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.15, NHP.85, NHP.117</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV.229(mn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>The SHIV229(mn) is based on SHIVIIIB encoding HIV-1HXBc2 tat, rev and env on a SIVmac239 backbone, passaged through M. nemestrina in vivo to become pathogenic. The challenge stock was generated by expanding the SHIV229(mn) on PHA-activated M. nemestrina PBMC.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.339</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV.DH12 (MD1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>This chimeric simian-human immunodeficiency virus (SHIVs) carries envelope glycoproteins from a T cell-macrophage dual-tropic primary isolate (human immunodeficiency virus type 1 [HIV-1] strain DH12) in the SIVmac239 backbone. DH12 is also known as MD1. MD14 is derived from MD1 by replacing the DH12 nef with Mac239 nef.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.11</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV.DH12R-PS1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>This SHIV was obtained from the nonpathogenic SHIVDH12 (SHIVMD1) (Shibata, JID 176:362-73 1997). This highly pathogenic SHIVDH12R was isolated at week 68 from rhesus monkey 565Z (Igarashi et al PNASU 96(24):14049-14054 1999). Virus isolated at week 52 from animal 565Z also induced an irreversible and extremely rapid depletion of CD4+ T lymphocytes following its inoculation into rhesus monkey PS1 and was designated SHIVDH12R-PS1.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.157.3, NHP.303, NHP.391</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV.KU1</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Strain</td>
<td>SHIV.VMD1</td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------------------</td>
</tr>
<tr>
<td>Description</td>
<td>It carries a portion of the U3 LTR, the R-U5 LTR, gag, pol, vif, and vpx, and approximately 20% of vpr from SIVmac239. The remainder of vpr, tat, rev, env, and nef and a portion of the U3 LTR are derived from HIV-1; most of the HIV-1 sequences came from a T-cell/macrophage dual-tropic primary isolate HIV-1DH12 except for small segments at SIV-HIV-1 junctions (145 bp in vpr; 27 bp in nef) that were derived from HIV-1NL43. NRE, negative regulatory element. Shibata et al. J Inf Dis 176:362 (1997)</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.87, NHP.112</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV.SF13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Described in AIDS 10(12): 1331-7 (1996) PubMed ID 8902061. This SHIV is a SIV-Mac239 LTR-Gag-Pol and Nef with HIV-1 subtype B clone SF13 Tat-Rev-Vpu-Env. The SF13 clone is from the same patient as the HIV-1 SF2 clone.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.207, NHP.389, NHP.394</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV.W6.1D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>SIV.W6.1d was constructed by replacing an NheI-to-AvrII fragment encompassing Env gp160, of SHIV-4 with the W6.1D cloned Env from HIV-1 subtype B isolate 320.3 which is a dual-tropic virus from a Dutch AIDS patient.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.80</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV162P4</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.6, NHP.62</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>This SHIV contains the tat, rev, vpu, and env genes of HIV-1 subtype B isolate SF33. The SHIV-SF33 construct was then passaged in Rhesus macaque to generate SHIV-SF33A. See also the entry with accession number AF401229, from this same SHIV construct.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.268.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV33A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>This SHIV contains the tat, rev, vpu, and env genes of HIV-1 subtype B isolate SF33. The SHIV-SF33 construct was then passaged in Rhesus macaque to generate SHIV-SF33A. See also the entry with accession number AF401229, from this same SHIV construct.</td>
</tr>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.268.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>SHIV89.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Subtype</td>
<td>B</td>
</tr>
<tr>
<td>Trials</td>
<td>NHP.7, NHP.15, NHP.90.1, NHP.114, NHP.126, NHP.319</td>
</tr>
</tbody>
</table>

| Strain         | SHIV89.6P                          |

**Notes** This is an extremely virulent chimeric virus. Has an open vpu in addition to numerous mutations in the env and nef. Replicates efficiently in macrophage cultures and at extremely high titers in monkeys, with loss of CD4+ T cells and AIDS.
### Description
Parental SHIV was SHIV-4 (also known as SHIV-IIIB/HXB2) from which env of HXB2 was replaced by env of 89.6 (also HIV-1 subtype B but different tropism). Described in J Virol 70(5): 3198-3206 (1996) by Reimann et al. Passaged to gain pathogenicity as described in J Virol 71(6): 4218-25 (1997) by Karlsson et al.

**HIV Subtype**
B

**Notes**

**Trials**
NHP.2, NHP.7, NHP.16.2, NHP.17, NHP.19, NHP.23, NHP.24.2, NHP.28, NHP.36, NHP.37, NHP.55, NHP.56, NHP.60.1, NHP.60.3, NHP.79, NHP.80, NHP.89, NHP.90.2, NHP.107, NHP.117, NHP.121, NHP.126, NHP.131, NHP.132, NHP.304, NHP.306.1, NHP.306.2, NHP.325, NHP.348.2, NHP.349, NHP.366, NHP.374, NHP.400

---

### SHIV89.6PD

**HIV Subtype**
B

**Trials**
NHP.8, NHP.34, NHP.70, NHP.72, NHP.78, NHP.81, NHP.82.1, NHP.82.2, NHP.326, NHP.398

---

### SHIV89.6v

**Description**
This is a stock virus from the SHIV89.6 after passage in rhesus macaques through intra vaginal inoculation and brief culture in rhesus PBMC. The stock concentration was determined as $10^3$ TCID50/ml by culture on CEMx174 cells and p27 production

**HIV Subtype**
B

**Trials**
NHP.20

---

### SHIVSF162-PC

**Description**
SHIVSF162-PC is derived from SHIVSF162 by replacing V1-V5 with V1-V5 from a passaged SHIVSF162 that was more infectious and pathogenic (SHIVSF162-P3).

**HIV Subtype**
B

**Trials**
NHP.312

---

### SHIVHan2

**Description**
Described in AIDS 10(12): 1331-7 (1996) PubMed ID 8902061. This SHIV is a SIV-Mac239 LTR-Gag-Pol and Nef with HIV-1 subtype B clone pNL43 Tat-Rev-Vpu-Env, from which the SacII-HindIII region (most of env) was replaced by HIV-1 subtype B isolate Han2.

**HIV Subtype**
B

**Trials**
NHP.80

---

### SHIVsbg0.1

**Trials**
NHP.10
### VI-C-2 SIV Challenges

<table>
<thead>
<tr>
<th>Strain</th>
<th>Description</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SIV mac251 (European) stock 5</strong></td>
<td>prepared by passaging the European SIVmac251-32H 11/88 challenge virus once through rhesus PBMC</td>
<td>NHP.119</td>
</tr>
<tr>
<td><strong>SIV(Mne) Cell-free</strong></td>
<td></td>
<td>NHP.269</td>
</tr>
<tr>
<td><strong>SIV(Mne) clone E11S</strong></td>
<td></td>
<td>NHP.64, NHP.65.1, NHP.65.2, NHP.94, NHP.134, NHP.154, NHP.265, NHP.269</td>
</tr>
<tr>
<td><strong>SIVDeltaB670</strong></td>
<td>The virus was described by Mickey Corb in a paper published by Gormus et. al. in the Journal of Infectious Diseases, Vol 160, No 3, Sept 1989. The virus came from mangabey A022 (naturally infected with SIV), was passed to rhesus macaque 8664, then passed to B670. Sooty mangabey A022 came from Yerkes to Tulane and appears to have been born at Yerkes.</td>
<td>NHP.63, NHP.248</td>
</tr>
<tr>
<td><strong>SIVmac (not determined)</strong></td>
<td></td>
<td>NHP.239, NHP.240</td>
</tr>
<tr>
<td><strong>SIVmac220</strong></td>
<td>Viral challenge (SIVmac 220) which is a cell-free virus stock prepared from the spleen of a rhesus monkey infected with the J5 molecular clone of SIVmac 251 (32H)</td>
<td>NHP.106, NHP.397</td>
</tr>
<tr>
<td><strong>SIVmac239</strong></td>
<td></td>
<td>NHP.16.2, NHP.18, NHP.39, NHP.54, NHP.61, NHP.67, NHP.69, NHP.88, NHP.148, NHP.308</td>
</tr>
<tr>
<td><strong>SIVmac239/nef-open</strong></td>
<td></td>
<td>NHP.52, NHP.309</td>
</tr>
<tr>
<td><strong>SIVmac251</strong></td>
<td></td>
<td>NHP.9.1, NHP.13, NHP.32, NHP.33, NHP.38, NHP.51, NHP.57, NHP.66, NHP.73, NHP.74, NHP.108, NHP.109, NHP.120, NHP.123, NHP.148, NHP.157.1, NHP.157.2, NHP.200, NHP.201.2, NHP.205.1, NHP.205.2, NHP.205.3, NHP.245.1, NHP.245.2, NHP.245.3, NHP.294, NHP.300, NHP.324.1, NHP.327.1, NHP.327.2, NHP.353, NHP.363</td>
</tr>
<tr>
<td><strong>SIVmac251 (561)</strong></td>
<td>This challenge stock was prepared by culturing PHA-activated peripheral blood mononuclear cells (PBMC) from a Mamu-A*01-positive infected macaque (561L) exposed to SIVmac251 by the vaginal route. The SIVmac251 (561) was titered in vivo in rhesus macaques by inoculating 6 animals with different dilutions of virus stock via the rectal route. 6/6 animals inoculated with the virus (0.5 ml diluted to 1.5 ml with RPMI medium) became infected, evidenced by high plasma viremia and a drop in CD4 counts.</td>
<td>NHP.30, NHP.274</td>
</tr>
<tr>
<td><strong>SIVmac251 (J5)</strong></td>
<td></td>
<td>NHP.126, NHP.185.2</td>
</tr>
<tr>
<td><strong>SIVmac251 (32H)</strong></td>
<td></td>
<td>NHP.5, NHP.41, NHP.49, NHP.97, NHP.99.2, NHP.116, NHP.151, NHP.152.1, NHP.152.2, NHP.185.1, NHP.194.1, NHP.203, NHP.205.2</td>
</tr>
<tr>
<td>Strain</td>
<td>Notes</td>
<td>Trials</td>
</tr>
<tr>
<td>----------------</td>
<td>-----------------------------------------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>SIVmac251,32H.spl</td>
<td>virus stock was prepared from a spleen homogenate of a rhesus monkey inoculated with SIVmac251, 32H and titrated in vitro in human T cells and in vivo in rhesus monkeys</td>
<td>NHP.40</td>
</tr>
<tr>
<td>SIVmac251BK28</td>
<td>molecular clone grown in monkey PBMC</td>
<td>NHP.40</td>
</tr>
<tr>
<td>SIVmac32H.IXc</td>
<td>Pathogenic cell-associated SIV from primary, uncultured rhesus monkey PBMC</td>
<td>NHP.58</td>
</tr>
<tr>
<td>SIVmac8980</td>
<td>SIVmac 8980 grown in rhesus monkey PBMC and analyzed for CCR5 coreceptor binding using the &quot;Ghost system&quot; (see Trkola A et al., J Virol 1998;72:1876-85).</td>
<td>NHP.395</td>
</tr>
<tr>
<td>SIVmacJ5M</td>
<td></td>
<td>NHP.215</td>
</tr>
<tr>
<td>SIVmacR71</td>
<td></td>
<td>NHP.107</td>
</tr>
<tr>
<td>SIVmne clone A2-clone 5</td>
<td></td>
<td>NHP.41</td>
</tr>
<tr>
<td>SIVsm</td>
<td>SIV-sm described by Fultz et al Proc Nat Acad Sci 83(14):5286-90 (1986) PubMed ID 3014542 from an infected macaque at Yerkes. This SIV-sm is from the same animal from which the SIV-SMM9 virus was obtained. J. Virol. 66(1): 414-9 (1992) PubMed ID 1727495 cites Fultz (1986) as the source of SMM9.</td>
<td>NHP.4, NHP.68, NHP.93, NHP.125, NHP.194.2</td>
</tr>
<tr>
<td>SIVsmB670</td>
<td></td>
<td>NHP.36, NHP.203</td>
</tr>
<tr>
<td>SIVsmE660</td>
<td></td>
<td>NHP.18, NHP.27, NHP.37, NHP.44, NHP.45, NHP.59, NHP.377</td>
</tr>
</tbody>
</table>
### VI-C-3 HIV-1 Challenges

<table>
<thead>
<tr>
<th>Strain</th>
<th>Description</th>
<th>HIV Subtype</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 Han2</td>
<td>Isolate HAN was isolated from a 39 year old homosexual German patient with AIDS related complex, in 1986. This patient died from complications of AIDS in 1987. HAN was highly cytopathic in MT-2 T cell line, it was able to productively infect MT-4, H9 or Jurkat cell lines. Genomic DNA from infected MT-2 cells was used to prepare a lambda phage genomic library. Two full-length clones, HAN/2 and HAN/3 were purified. HAN/3 was used for DNA sequencing, and has a defective env gene.</td>
<td>B</td>
<td>NHP.21</td>
</tr>
<tr>
<td>HIV-1 IIIB</td>
<td></td>
<td>B</td>
<td>NHP.71, NHP.202, NHP.242, NHP.247, NHP.267, NHP.361</td>
</tr>
<tr>
<td>HIV-1 S016</td>
<td></td>
<td>B</td>
<td>NHP.141</td>
</tr>
<tr>
<td>HIV-1 DH12</td>
<td></td>
<td>B</td>
<td>NHP.84, NHP.392</td>
</tr>
<tr>
<td>HIV-1 LA1</td>
<td></td>
<td>B</td>
<td>NHP.48, NHP.204</td>
</tr>
<tr>
<td>HIV-1 SF2</td>
<td></td>
<td>B</td>
<td>NHP.141, NHP.193</td>
</tr>
<tr>
<td>LA V-1 or NY5</td>
<td></td>
<td>B</td>
<td>NHP.249</td>
</tr>
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</table>
VI-C-4  HIV-2 Challenges

<table>
<thead>
<tr>
<th>Strain</th>
<th>Description</th>
<th>HIV Subtype</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-2 (UC2-10568)</td>
<td>HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d’Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboons 9429, 12281 and 10568.</td>
<td>A</td>
<td>NHP.310</td>
</tr>
<tr>
<td>HIV-2 (UC2-11966)</td>
<td>HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d’Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons 9429, 12281, 10568, 11999 and 11966.</td>
<td>A</td>
<td>NHP.310</td>
</tr>
<tr>
<td>HIV-2 (UC2-11999)</td>
<td>HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d’Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons 9429, 12281, 10568 and 11999.</td>
<td>A</td>
<td>NHP.310</td>
</tr>
<tr>
<td>HIV-2 (UC2-12281)</td>
<td>HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d’Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboons 9429 and 12281.</td>
<td>A</td>
<td>NHP.310</td>
</tr>
<tr>
<td>HIV-2 (UC2-12741)</td>
<td>HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d’Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons 9429, 12281, 10568, 11999, 11966 and 12741.</td>
<td>A</td>
<td>NHP.310</td>
</tr>
<tr>
<td>HIV-2 (UC2-9429)</td>
<td>HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d’Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboon 9429.</td>
<td>A</td>
<td>NHP.310, NHP.378</td>
</tr>
<tr>
<td>HIV-2.SBL6669</td>
<td></td>
<td>A</td>
<td>NHP.47, NHP.149.1, NHP.174</td>
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</tbody>
</table>

HIV Immunology and HIV/SIV Vaccine Databases 2003
## Adjuvants and Stimulants

As part of the vaccines database, we developed a separate and general database table and search interface for adjuvants and stimulants. The majority of the data on adjuvants was obtained from the National Institute of Allergy and Infectious Diseases. We are indebted to Dr. Carl Alving for making the adjuvant data available. In this vaccine compendium, we have listed only the adjuvants which were used in the Nonhuman Primate HIV/SIV Vaccine Trials Database. For information about other adjuvants and stimulants, the reader is advised to use the Adjuvant/Stimulant search form at [http://www.hiv.lanl.gov/cgi-bin/vaccine/public/adjuvant_search.cgi?process=start](http://www.hiv.lanl.gov/cgi-bin/vaccine/public/adjuvant_search.cgi?process=start).

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adju-Phos</td>
<td>Aluminum phosphate gel</td>
<td>NHP.330</td>
</tr>
<tr>
<td>Adjumer™</td>
<td>Synthetic Solid: beige to off white powder. Aqueous solution: clear, colorless liquid</td>
<td>NHP.72, NHP.78</td>
</tr>
<tr>
<td>Alum</td>
<td>Crystalline aluminum hydroxide gel. Known mineralogically as boehmite. Obtained by precipitation of aluminum hydroxide under alkaline conditions. White gelatinous precipitate in aqueous suspension.</td>
<td>NHP.97, NHP.99.2, NHP.151, NHP.162, NHP.185.1, NHP.185.2, NHP.198, NHP.205.3, NHP.248, NHP.349, NHP.362</td>
</tr>
<tr>
<td>AS-2 adjuvant</td>
<td></td>
<td>NHP.21</td>
</tr>
<tr>
<td>B7-2</td>
<td>The gene product encoded by B7-2 is a co-stimulatory molecule for GM-CSF. The genes had been cloned by PCR from baboon peripheral blood mononuclear cells (PBMC) and were sequenced, then sub-cloned into the mammalian expression vector, pND-14.</td>
<td>NHP.378</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td></td>
<td>NHP.2, NHP.16.1, NHP.202, NHP.322</td>
</tr>
<tr>
<td>Bupivacaine-HCl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Name</td>
<td>Description</td>
<td>Trials</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------------------------------------------------------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>BWZL</td>
<td>Mixtures of incomplete Freund’s adjuvant; IFA; FIA: mixtures of mineral oil (Marcol 52) and emulsifier (Arlacel A [mannide monooleate]) as an 80% mineral oil, and 15% emulsifier emulsion. Manufactured by Statens Seruminstitut, Copenhagen, Denmark. Thick viscous liquid without color.</td>
<td>NHP.300, NHP.204</td>
</tr>
<tr>
<td>CCR5 peptides</td>
<td>N-terminal (aa 1-20): Met-Asp-Tyr-Gln-Ser-Pro-ILe-Tyr-Asp-ILe-Tyr-Tyr-Thr-Ser-Glu-Pro-Cys</td>
<td></td>
</tr>
<tr>
<td></td>
<td>First loop (aa 89-102): His-Tyr-Ala-Ala-Ala-Gln-Trp-Asp-Phe-Gly-Asn-Thr-Met-Cys-Gln</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Second loop (aa 178-197): Cys-Ser-Ser-His-Phe-Pro-Tyr-Ser-Gln-Tyr-Gln-Ile-Ile-Asp-Tyr-Thr-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lys-Asn-Phe-Gln-Thr-Leu-Lys Neosystem Laboratories (Strasbourg, France)</td>
<td></td>
</tr>
<tr>
<td>CpG 2006</td>
<td>Euorgenec, Seraing, Belgium</td>
<td>NHP.395</td>
</tr>
<tr>
<td>CRL1005</td>
<td>ABA block polymer with mean values of x = 8 and y = 205. SOURCE: Linear chain polymers are synthesized by condensation of propylene oxide and ethylene glycol initiator in the presence of a cesium salt catalyst to form polyoxypropylene chain, followed by condensation of ethylene oxide on either end of the chain. Individual polymeric species of triblock nonionic block copolymers result from controlled synthesis of chains with pre-determined length. Clear, colorless to slightly yellow, viscous liquid.</td>
<td>NHP.306.1, NHP.306.2</td>
</tr>
<tr>
<td>Diphtheria toxoid</td>
<td></td>
<td>NHP.268.1</td>
</tr>
<tr>
<td>DL-PGL</td>
<td>Polyester poly (DL-lactide-co-glycolide)</td>
<td>NHP.218</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>Granulocyte-macrophage colony stimulating factor; Sargramostim (yeast-derived rh-GM-CSF)</td>
<td></td>
</tr>
</tbody>
</table>
**Description**  

**Trials**  
NHP.68, NHP.106

**Name** IFN-gamma in pCDNA3  
**Trials** NHP.16.1

**Name** IL-12 DNA  
**Description** The rhesus macaque IL-12 expression plasmid was derived from the plasmid pSFG.hIL12.p40.Lp35, which expresses human IL-12, by substituting the sequences encoding the human p40 and p35 subunits with the corresponding rhesus macaque sequences, positioned in the same configuration to produce plasmid pRM.IL-12.p40-p35. In this plasmid, the IL-12 p40 and -30 subunits are produced as a fusion protein in which the p35 subunit, deleted of its leader sequence, is fused to the p40 subunit by a Gly6Ser linker. IL-12 production by rmIL-12.p40.Lp35 was tested in 293T transfection supernatant by ELISA.

**Trials** NHP.366

**Name** IL-12/GMCSF plasmid (Sykes)  
**Description** Plasmids expressing the human cytokine IL-12 and GMCSF. Constructed by amplifying the cDNA coding sequences from pED and pXM vectors. EcoRI and SalI sites were incorporated into the end of the cDNAs encoding GMCSF and IL-12 subunit p35 by PCR (for more information contact authors) Sykes et al.

**Trials** NHP.120

**Name** IL-2 in pCDNA3  
**Trials** NHP.16.1

**Name** IL-2/lg plasmid  
**Trials** NHP.23, NHP.60.1, NHP.60.3, NHP.98, NHP.126, NHP.366, NHP.400

**Name** IL-2/lg protein  
**Trials** NHP.24.1, NHP.60.1, NHP.98, NHP.126

**Name** IL-4  
**Trials** NHP.106, NHP.309

**Name** IL-4 in pCDNA3  
**Trials** NHP.16.1

**Name** Interferon-γ  
**Other Names** Actimmune® (rhIFN-gamma, Genentech, Inc.); immune interferon; IFN-γ gamma-interferon  
**Description** Noncovalent dimer. Low resolution crystal structure available. Monomer consists of 140 amino acids, no glycosylation or cysteines in human form. Murine form is a covalent dimer (one cysteine per monomer). Ealick, S. E. et al., 1991, Three-dimensional structure of recombinant human interferon-g , Science, 252: 698- 702. Sequence of human interferon-gamma: QDPYVKEAENLKNRTFYQAGHSDVADGTLFLGILKNWKEESDRKIMQSQIVSFYFKLFRKDDQSI QRSVEIKGEDNNKFNFSLNLRKRDDEFKLTNYSVTDLNVRKAIHELIQMAELSPAAKTGKRKRS QMLFRGRASQ Both human (rhIFN-gamma) and murine (rmuIFN-gamma) forms are expressed in Escherichia coli and distributed in a completely pure state. Clear aqueous solution.

**Trials** NHP.309

**Name** Interleukin-2  
**Other Names** IL-2; T-cell growth factor; aldesleukin (des-alanyl-1, serine-125 human interleukin 2); Proleukin®; Teceleukin®

**HIV Immunology and HIV/SIV Vaccine Databases 2003**  
1201
**Vaccines**

**Adjuvants and Stimulants**

**Description**

**Trials**
NHP.106, NHP.126, NHP.245.3

---

**Name** ISCOM(s)™
**Other Names** Immune stimulating complexes

**Description**
ISCOMs are a complex composed of typically 0.5% Quillaja saponins, 0.1% cholesterol, 0.1% phospholipid, and antigen in phosphate-buffered saline (PBS). Occasionally, surfactants are used t are ISCOMs (such as Mega 10) but are removed from the final formulation before use. The adjuvant-active components of ISCOMs are derived by aqueous extraction of the bark of Quillaja saponaria and are further purified by chromatography. Quil A is a purified form of this. Further chromatographic purification provides components with high adjuvant activity and ISCOM-forming properties (see Iscoprep 7.0.3 TM ). ISCOMs form a clear product in solution.

**Trials**
NHP.75, NHP.125, NHP.164, NHP.374

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**Name** Kehole Limpet Hemocyanin
**Description**

**Trials**
NHP.320

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**Name** Lipid-based Adjuvant
**Other Names** LBA

**Description**
Data not available Mannhalter et al, 1991

**Trials**
NHP.362

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**Name** Liposomes
**Other Names** Liposomes (L) containing protein or Th-cell and/ or B-cell peptides, or microbes with or without co-entrapped interieukin-2, BisHOP or DOTMA (see below). A, [L (Antigen)]; B, [L (IL-2 or DOTMA or BisHOP + Antigen)]; C, [L (Antigen)-mannose]; D, [L (Th-cell)

**Description**
A: Multilamellar liposomes prepared by the dehydration-rehydration method (average diameter 600-800 nm) composed of egg phosphatidy1choline (PC) or distearoyl phosphatidylcholine (DSPQ and equimolar cholesterol and containing antigens such as tetanus toxoid and synthetic Th-cell peptides. 13: As in A with IL-2 (10^3 - 10^4 Cetus units) co-entrapped with the antigen in the aqueous phase or with 1,2-bis (hexadecylcycloxy)-3-trimethylaminopropane-HCL (BisHOP) or N(2,3-dioleyloxy)-NNN-triethylammonium (DOTMA) incorporated into the lipid phase of liposomes (0.8: 1.0: 0.2 molar ratio for PC or DSPC, cholesterol and DOTMA or BisHOP). C, as in A with marmosylated albumin covalently coupled to the surface of antigen-containing liposomes. D: As in A with Th-cell and B-cell peptides co-entrapped in the aqueous phase. E: Giant liposomes (average diameter 5-9 μm) prepared as in A or by a solvent-spherele evaporation method, composed of PC or DSPC, cholesterol, triolein (TO), and phosphatidylglycerol (PG) (4: 4: 1: 2 molar ratio) and containing killed or live Bacillus subtilis or killed Bacille Calmette-Guérin (BCG) with or without co-entrapped tetanus toxoid. PC, DSPC, and PG in pure form from Lipid Products, Nuthill, Surrey, U. K.; TO in pure form from Sigma Chemical Co., Poole, Dorset, U. K.; recombinant interleukin-2 (des-Ala1-Ser125 mutein; 3 x 10 6 Cetus units/ mg) obtained from Cetus Corporation, Emeryville, CA; BisHOP and DOTMA obtained from Syntex Research, Palo Alto, CA. White, opalescent colloidal suspensions (A-E).

**Trials**
NHP.61, NHP.94

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**Name** LT(R192G)
**Other Names** mutant heat-labile E. coli enterotoxin

**Description**

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<table>
<thead>
<tr>
<th>Name</th>
<th>Other Names</th>
<th>Description</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTK63</td>
<td>mutared E. coli heat-labile enterotoxin</td>
<td></td>
<td>NHP.1</td>
</tr>
<tr>
<td>MF59</td>
<td>None</td>
<td>Squalene/ water emulsion. Composition: 43 mg/mL squalene, 2.5 mg/mL polyoxymethylene sorbitan monooleate (Polysorbate 80), 2.4 mg/mL sorbitan trioleate (Span 85). Chiron Corporation, Emeryville, CA. White liquid.</td>
<td>NHP.22, NHP.23, NHP.62, NHP.75, NHP.141, NHP.193, NHP.354</td>
</tr>
<tr>
<td>MONTANIDE ISA 51</td>
<td>Purified IFA; Incomplete Freund’s adjuvant</td>
<td>Mannide oleate (mostly mannide monooleate, esters of mannitol and oleic acids -an example shown below) (MONTANIDE 80) in mineral oil solution (DRAKEOL 6VR). Manufactured by SEPPIC. Limpid clear yellow liquid.</td>
<td>NHP.1, NHP.119</td>
</tr>
<tr>
<td>MONTANIDE ISA 720</td>
<td>metabolizable oil adjuvant</td>
<td>A highly refined emulsifier from the mannide monooleate family (an example of mannide monooleate shown below) in a natural metabolizable oil solution. The exact nature of the emulsifier and the metabolizable in MONTANIDE ISA 720 is proprietary, but can be disclosed under specific agreement with SEPPIC. manufactured by SEPPIC. Yellow, odorless liquid</td>
<td>NHP.330</td>
</tr>
<tr>
<td>MPL™</td>
<td>3-Q-desacyl-4</td>
<td>MPL™is composed of a series of 4'-monophosphoryl lipid A species that vary in the extent and position of fatty acid substitution. The hexaacyl structure shown below is the most highly acylated and most abundant component in MPLO. Species with five and four fatty acids are also present. All structures contribute to the adjuvant activity of MPLO. Derived from the lipopolysaccharide (LPS) of Salmonella minnesota R595. Obtained by treatment of LPS with mild acid and base hydrolytic conditions, and chromatographic purification of the resulting 3D-MLA. Colorless, odorless white powder.</td>
<td>NHP.306.1</td>
</tr>
<tr>
<td>MTP-PE</td>
<td>N-acetyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1,2-dipalmitoyl-sn-glycero-3-(hydroxy-phosphoryloxy)) ethylamide, mono sodium salt.</td>
<td>Chemical synthesis by Ciba-Geigy Ltd., Basel, Switzerland. White powder.</td>
<td>NHP.141</td>
</tr>
<tr>
<td>p-Hydroxybenzoique acid methyl ester</td>
<td></td>
<td></td>
<td></td>
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</table>
## Adjuvants and Stimulants

<table>
<thead>
<tr>
<th>Name</th>
<th>Trials</th>
</tr>
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<tbody>
<tr>
<td><strong>pCIL-10</strong></td>
<td>NHP.71</td>
</tr>
<tr>
<td><strong>pCIL12</strong></td>
<td>NHP.71, NHP.276</td>
</tr>
<tr>
<td><strong>pCMVmCAT1</strong></td>
<td>NHP.67, NHP.70</td>
</tr>
<tr>
<td><strong>pCMVN</strong></td>
<td>NHP.70</td>
</tr>
<tr>
<td><strong>Peptomer-NP</strong></td>
<td>NHP.5</td>
</tr>
<tr>
<td><strong>PLG</strong></td>
<td>NHP.321</td>
</tr>
<tr>
<td><strong>QS-21</strong></td>
<td>NHP.11, NHP.14, NHP.53, NHP.81, NHP.303, NHP.371</td>
</tr>
<tr>
<td><strong>Quil-A</strong></td>
<td>NHP.157.1, NHP.157.2</td>
</tr>
<tr>
<td><strong>Rehydragel HPA</strong></td>
<td>NHP.47, NHP.174, NHP.201.1, NHP.201.2, NHP.203, NHP.204, NHP.242, NHP.306.1</td>
</tr>
<tr>
<td><strong>RIBI</strong></td>
<td>NHP.94, NHP.119, NHP.162, NHP.320</td>
</tr>
<tr>
<td><strong>Ribilike adjuvant system (MPL, TMD,CWS)</strong></td>
<td>NHP.68</td>
</tr>
<tr>
<td><strong>SAF-1</strong></td>
<td>NHP.68</td>
</tr>
</tbody>
</table>

**Other Names**
- polyactide coglycolide
- Stimulon™QS-21 Adjuvant.
- High Protein Adsorbency Aluminum Hydroxide Gel; alum
- Crystalline aluminum oxyhydroxide AlOOH, known mineralogically as boehmite. the structure consists of corrugated sheets of aluminum octahedra. Synthetic oxyhydroxide of aluminum (aluminum hydroxide) prepared by acid-base precipitation. Translucent, thixotropic, colloidal aqueous gel supplied sterile.
- SAF-m; Syntex Adjuvant Formulation
- Composed of threonyl-MDP (0.05-1%) in an emulsion vehicle [5% squalane, 2.5% Pluronic® L121, 0.2% Polysorbate 80 and phosphate buffered saline (pH 7.4)]. See individual components. White, fluid, oil-in-water emulsion.

**Description**
- A complex but purified mixture of Quillaja saponins which are glycosides of Quillaic acid and carbohydrates. The Higuchi formula of Quil A is shown below. Purified extract from the bark of the South American tree Quillaja saponaria Molina. Lyophilized powder. Color is light brownish, almost white.
- Composed of threonyl-MDP (0.05-1%) in an emulsion vehicle [5% squalane, 2.5% Pluronic® L121, 0.2% Polysorbate 80 and phosphate buffered saline (pH 7.4)]. See individual components. White, fluid, oil-in-water emulsion.
<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Squalene 2</strong></td>
<td>Found in shark liver oil and some vegetable oils. Intermediate in the biosynthesis of cholesterol. Clear oil, colorless. Faint, agreeable odor.</td>
<td>NHP.245.1</td>
</tr>
</tbody>
</table>
VI-E

Trial Summaries

This chapter contains a listing of studies compiled in the database. There are currently 388 trials in the relational database created at LANL and 218 trials carried over from Jon Warren’s database. This listing is a printed version of the results of searching our database with the default settings (find any or all) and the Trial Summary display format. Each summary contains data from the following fields unless they are empty in the database:

- Trial number
- Title
- Authors
- Citation and PubMed ID number
- Objectives
- Species/subspecies
- Vaccine name, type, formulation and route of inoculation
- A short description of the vaccine
- Challenge virus name and route
- A summary of the main findings

The database itself contains much more detailed information for each trial, including information about each group of animals.

<table>
<thead>
<tr>
<th>NHP.1</th>
<th>(11726972)</th>
<th>Mucosal AIDS vaccine reduces disease and viral load in gut reservoir and blood after mucosal infection of macaques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal</td>
<td>Nat Med 2001 Dec;7(12):1320-6</td>
<td></td>
</tr>
<tr>
<td>Objectives</td>
<td>Challenge, Immunogenicity To compare whether a mucosal vaccine could induce mucosal CTLs and protect rhesus macaques against mucosal infection with SHIV more effectively than the same vaccine given subcutaneously.</td>
<td></td>
</tr>
<tr>
<td>Species/Subspecies</td>
<td>Macaca mulatta (Rhesus macaque)</td>
<td></td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372</td>
<td></td>
</tr>
<tr>
<td>Type</td>
<td>Synthetic Protein/Peptide</td>
<td></td>
</tr>
<tr>
<td>Routes</td>
<td>Intrarectal, Subcutaneous</td>
<td></td>
</tr>
<tr>
<td>SHIV-KU2 Route</td>
<td>Intrarectal</td>
<td></td>
</tr>
<tr>
<td>Main Findings</td>
<td>• Mucosal SIV specific CTL can be induced by intrarectal immunization of macaques with synthetic-peptide vaccine coupled with LT(R192G) adjuvant.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• CTL response correlates with helper response.</td>
<td></td>
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<tr>
<td></td>
<td>• CD4+ T cells preserved better in animal mucosally immunized than in animals immunized by subcutaneous route and control.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• In contrast with subcutaneous immunization, intrarectal immunization reduced viral load to undetectable level.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NHP.2</th>
<th>(11282197)</th>
<th>Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P)</th>
</tr>
</thead>
</table>

HIV Immunology and HIV/SIV Vaccine Databases 2003
Trial Summaries


**Journal** Vaccine 2001 Apr 6;19(20-22):2862-77

**Objectives** Challenge, Immunogenicity To test the immunogenicity and protective value of a tat-expressing vector containing defined unmethylated CpG sequences (pCV-tat) in cynomolgus monkeys challenged with SHIV.

**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)

**Vaccine Name** HIV BH10-tat protein **Type:** Recombinant Subunit Protein **Routes:** Intradermal, Intramuscular

**Vaccine Name** pCV-tat **Type:** DNA **Routes:** Intradermal, Intramuscular

**Challenge** SHIV89.6P **Route:** Intravenous

**Main Findings**

- Intramuscular inoculation of the pCV-tat contained primary infection with HIV89.6P virus.
- Control of CD4 T cell decline in all the vaccinated monkeys.
- Correlation between undetectable virus replication and negative virus isolation in all cases with anti-tat CTLs.
- CD8-mediated non-cytolytic antiviral activity not present in all protected animals.
- CpG-rich tat DNA vaccine, potential for cross-clade application in human as a therapeutic and preventive vaccine.

NHP.3 (11514732) **Induction of simian immunodeficiency virus (SIV)-specific CTL in rhesus macaques by vaccination with modified vaccinia virus Ankara expressing SIV transgenes: influence of pre-existing anti-vector immunity**

**Authors** Sharpe S, Polyanskaya N, Dennis M, Sutter G, Hanke T, Erfle V, Hirsch V, Cranage M

**Journal** J Gen Virol 2001 Sep;82(Pt 9):2215-23

**Objectives** Immunogenicity To assess the immunogenicity of an MVA vaccine expressing structural and regulatory genes of SIV, and the influence of pre-existing immunity to vector in immunized Mamu A*01 MHC class 1 rhesus monkeys.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** MVA-SIVmacJ5 (gag-pol) **Type:** Recombinant Vector (virus/bacteria) **Route:** Intramuscular

**Vaccine Name** MVAmacJ5-nef **Type:** Recombinant Vector (virus/bacteria) **Route:** Intraocular

**Vaccine Name** MVA SIVsmH4 gag-pol **Type:** Recombinant Vector (virus/bacteria) **Route:** Intraocular

**Main Findings**

- MVA SIVmacJ5 gag-pol construct was poorly immunogenic.
- Nab weak and transient.
- SIV-specific CTL detected in all animals immunized with MVA-SIV vaccines, 4-8 weeks post immunization (not in control animals). One immunization is enough and boosting does not increase the magnitude of immune response.
- MVA-SIV nef produced the strongest response compared to MVA-SIVat and MVA-SIVrev.

NHP.4 (11413371) **Cross-protection against mucosal simian immunodeficiency virus (SIVsm) challenge in human immunodeficiency virus type 2-vaccinated cynomolgus monkeys**


**Journal** J Gen Virol 2001 Jul;82(Pt 7):1601-12

**Objectives** Challenge, Immunogenicity To compare the efficacy of a live attenuated HIV-2 vaccine alone versus boosting with live non-pathogenic HIV-2 following priming with ALVAC HIV-2 (recombinant canarypox virus expressing HIV-2 env, gag and pol).

**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)

**Vaccine Name** HIV-2 SBL6669 **Type:** Live Virus **Route:** Intravenous

**Vaccine Name** ALVAC-HIV-2 (gag,pol,gp125) **Type:** Recombinant Vector (virus/bacteria) **Route:** ND

**Vaccine Name** HIV-2 native gp125 **Type:** Purified Viral Products **Route:** ND

**Challenge** SIVsm **Route:** Intrarectal
**Main Findings**

- Vaccination with an ALVAC HIV-2 vaccine followed by exposure to live HIV-2 could induce cross-protection against mucosal infection with SIVsm and seemed to be more efficient than immunization with a live HIV-2 vaccine only.

---

**NHP5** (11429125) **A conformational C4 peptide polymer vaccine coupled with live recombinant vector priming is immunogenic but does not protect against rectal SIV challenge**

**Authors** Patterson LJ, Robey F, Muck A, Van Remoortere K, Aldrich K, Richardson E, Alvord WG, Markham PD, Cranage M, Robert-Guroff M

**Journal** AIDS Res Hum Retroviruses 2001 Jun 10;17(9):837-49

**Objectives** Challenge, Immunogenicity To compare SIV peptomer and native gp120 subunit boosts following two adenovirus type 5 host range (Ad5hr)-SIVenv recombinant priming immunizations.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** Peptomer SIVmac251 (gp120: 435-452) **Type:** Synthetic Protein/Peptide **Routes:** Subcutaneous, Intramuscular

**Vaccine Name** Ad5hr-SIVenv **Type:** Recombinant Vector (virus/bacteria) **Routes:** Intratracheal, Oral, Intranasal

**Vaccine Name** Native SIV gp120 **Type:** Purified Viral Products **Route:** Intramuscular

**Challenge** SIVmac251(32H) **Route:** Intrarectal

**Main Findings**

- Peptomer immunization elicited peptomer and SIV gp120-specific binding antibodies.
- Only native gp120 boosting elicited SIV neutralizing antibodies.
- Upon intrarectal challenge with SIVmac32H, all nine macaques became infected.
- The solely envelope-based vaccine conferred no protection.

---

**NHP6** (11483779) **Antibody protects macaques against vaginal challenge with a pathogenic R5 simian/human immunodeficiency virus at serum levels giving complete neutralization in vitro**


**Journal** J Virol 2001 Sep;75(17):8340-7

**Objectives** Challenge, Immunogenicity To evaluate the role of passive intravenous transfer of the human neutralizing monoclonal antibody b12 to provide dose-dependent protection to macaques vaginally challenged with the R5 virus SHIV162P4.

**Species/Subspecies** Macaca (sp)

**Vaccine Name** IgG1 b12 **Type:** Passive Antibody **Route:** Intravenous

**Challenge** SHIV162P4 **Route:** Vaginal or perivaginal

**Main Findings**

- Passive immunization with b12 antibody protects monkeys from challenge with SHIV.
- The immunization with b12 antibodies induced sterile protection in vaccinees.

---

**NHP7** (11287566) **Vaccine-elicited V3 loop-specific antibodies in rhesus monkeys and control of a simian-human immunodeficiency virus expressing a primary patient human immunodeficiency virus type 1 isolate envelope (a)**

**Authors** Letvin NL, Robinson S, Rohne D, Axthelm MK, Fenton JW, Bilksa M, Palker TJ, Liao HX, Haynes BF, Montefiori DC

**Journal** J Virol 2001 May;75(9):4165-75

**Objectives** Challenge, Immunogenicity To evaluate the role of vaccine elicited antibodies in the protection against SHIV containing the envelope of a primary isolate of HIV.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** C4/89.6-V3 **Type:** Synthetic Protein/Peptide **Route:** Intramuscular

**Vaccine Name** C4/89.6P-V3 **Type:** Synthetic Protein/Peptide **Route:** Intramuscular

**Challenge** SHIV89.6, SHIV89.6P **Route:** Intravenous

**Main Findings**
• SHIV-89.6 not suitable to assess viral set point between vaccinees and controls.
• Both peptides (vaccine and mock) were immunogenic - the mock C4/scrbl-V3 was immunogenic due to the presence of C4 fragment in the peptide.
• Immunization with the C4/89.6-V3 peptide generated 10-fold-higher titre of V3-specific antibodies than infection with SHIV-89.6.
• Neutralization of immunogens (C4/89.6-V3, C4/89.6P) induced Ab were virus specific (SHIV-89.6 and SHIV-89.6P, respectively).

<table>
<thead>
<tr>
<th>NHP8</th>
<th>Protection of macaques against vaginal transmission of a pathogenic HIV-1/SIV chimeric virus by passive infusion of neutralizing antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Authors</td>
<td>Mascola JR, Stiegler G, VanCott TC, Katinger H, Carpenter CB, Hanson CE, Beary H, Hayes D, Frankel SS, Birx DL, Lewis MG</td>
</tr>
<tr>
<td>Journal</td>
<td>Nat Med 2000 Feb;6(2):207-10</td>
</tr>
<tr>
<td>Objectives</td>
<td>Challenge, Passive Immunization To evaluate the protective effect of HIV-1 specific antibodies using the SHIV-macaque vaginal challenge model.</td>
</tr>
<tr>
<td>Species/Subspecies</td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Monoclonal antibody 2G12  Type: Passive Antibody  Route: Intravenous</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Monoclonal antibody 2F5  Type: Passive Antibody  Route: Intravenous</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>HIVIG  Type: Passive Antibody  Route: Intravenous</td>
</tr>
<tr>
<td>Challenge</td>
<td>SHIV89.6PD  Route: Vaginal or perivaginal</td>
</tr>
</tbody>
</table>
| Main Findings | • 14 antibody-treated macaques were either completely protected against infection or against pathogenic manifestations of HIV-infection  
• Some types of antibody response could play a role in protection against mucosal transmission of HIV-1  
• 5/5 control animals were viremic upon SHIV challenge and had decline CD4+ T cells |

<table>
<thead>
<tr>
<th>NHP.9.1</th>
<th>Viremia control following antiretroviral treatment and therapeutic immunization during primary SIV251 infection of macaques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Authors</td>
<td>Hel Z, Venzon D, Poudyal M, Tsai WP, Giuliani L, Woodward R, Chougnet C, Shearer G, Altman JD, Watkins D, Bischofberger N, Abimiku A, Markham P, Tartaglia J, Franchini G</td>
</tr>
<tr>
<td>Objectives</td>
<td>Challenge, Immunogenicity, Immunotherapy To explore the effect of therapeutic immunization in the context of ART during primary infection using the simian immunodeficiency virus (SIV251) macaque model.</td>
</tr>
<tr>
<td>Species/Subspecies</td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>NYV AC-SIV-gag-pol-env (NYVAC-SIV-gpe)  Type: Recombinant Vector (virus/bacteria)  Route: Intramuscular</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>SIVmac251  Route: Intravenous</td>
</tr>
</tbody>
</table>
| Main Findings | • Vaccination of Rhesus macaques with the highly attenuated poxvirus-based NYVAC-SIV vaccine expressing structural genes elicited vigorous virus-specific CD4+ and CD8+ T cell responses in macaques that responded effectively to ART.  
• Following discontinuation of a six-month ART regimen, viral rebound occurred in most animals, but was transient in six of eight vaccinated animals.  
• Viral rebound was also transient in four of seven mock-vaccinated control animals. |

<table>
<thead>
<tr>
<th>NHP.9.2</th>
<th>Prior DNA immunization enhances immune response to dominant and subdominant viral epitopes induced by a fowlpox-based SIVmac vaccine in long-term slow-progressor macaques infected with SIVmac251</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal</td>
<td>Virology 2003 Jul 20;312(1):181-95</td>
</tr>
<tr>
<td>Objectives</td>
<td>Immunogenicity, Immunotherapy, Chemotherapy To investigate whether a combination of DNA and recombinant poxvirus vaccine can induce high level of virus-specific CD4+ T-cell response and broadens the cytolytic activity in SIVmac251-infected macaques.</td>
</tr>
<tr>
<td>Species/Subspecies</td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>FP-SIV-gp (FP74)  Type: Recombinant Vector (virus/bacteria)  Route: Intramuscular</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>SIV-pcDNA3gag/pol  Type: DNA  Routes: Intradermal, Intramuscular</td>
</tr>
</tbody>
</table>
• The combination of a DNA expressing the gag and pol genes (DNA-SIV-gp) of SIVmac239 followed by a recombinant fowlpox expressing the same SIVmac genes (FP-SIV-gp) was significantly more immunogenic than two immunizations of FP-SIV-gp in SIVmac251-infected macaques treated with ART.
• The DNA/FP combination significantly expanded and broadened Gag-specific T-cell responses.
• The combination of these vaccine modalities also induced a sizeable expansion in most macaques of Gag-specific CD8-(CD4+) T-cells able to produce TNF-alpha.

**NHP.10** (11257382)

**Expansion of HBV-specific memory CTL primed by dual HIV/HBV genetic immunization during SHIV primary infection in rhesus macaques**

**Authors** Borgne SL, Michel ML, Camugli S, Corre B, Le Grand R, Riviere Y

**Journal** Vaccine 2001 Mar 21;19(17-19):2485-95

**Objectives** Challenge, Immunogenicity To evaluate the humoral and cellular immune response to immunization with HIV/HBV vaccine and the protection against SHIV challenge.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** pCMV-V3.S (HBV-HIV vaccine)  
**Type:** DNA  
**Route:** Intradermal

**Challenge** SHIVsbg0.1  
**Route:** Intravenous

**Main Findings**
- DNA-immunized primates and control challenged with SHIV were all infected.
- Peak viremia correlates with HBV envelop specific CTL precursor detected in primary infection.
- HBV or SHIV specific cytotoxicity corresponded in part to CD8 T cells presenting a memory phenotype.

**NHP.11** (11160726)

**Polyvalent envelope glycoprotein vaccine elicits a broader neutralizing antibody response but is unable to provide sterilizing protection against heterologous Simian/human immunodeficiency virus infection in pigtailed macaques**


**Objectives** Challenge, Immunogenicity To compare the breadth of NAb and protective immune response following vaccination of pigtailed macaques with envelope protein(s) derived from either single or multiple viral isolates against the challenge with SHIVDH12.

**Species/Subspecies** Macaca nemestrina (pigtailed macaque)

**Vaccine Name** Recombinant vaccinia virus-HIVgp160 (cocktail)  
**Type:** Recombinant Vector (virus/bacteria)  
**Route:** Intradermal

**Vaccine Name** Poly-gp120H  
**Type:** Recombinant Subunit Protein  
**Route:** Intramuscular

**Vaccine Name** Poly-gp120H (-DH12)  
**Type:** Recombinant Subunit Protein  
**Route:** Intramuscular

**Vaccine Name** Mono-gp120H (89.6)  
**Type:** Recombinant Subunit Protein  
**Route:** Intramuscular

**Vaccine Name** Mono-gp120H (DH12)  
**Type:** Recombinant Subunit Protein  
**Route:** Intramuscular

**Challenge** SHIVDH12 (MD1)  
**Route:** Intravenous

**Main Findings**
- Mixtures of HIV-1 envelope glycoproteins elicit broader immune responses than individual Env immunogens.
- 5/8 animals immunized with polyvalent vaccines made NAb against three or more viral strains.
- NAb activity almost entirely homologous to strains used in the vaccine.
- No sterilizing protection against heterologous SHIV challenge.
- Protection of animals against SIV or HIV-1 infection correlates with the presence of NAbs, not gp120 binding activity.

**NHP.12** (11145897)

**DNA vaccination of macaques with several different Nef sequences induces multispecific T cell responses**

**Authors** Couillin I, Letourneur F, Lefebvre P, Guillet JG, Martinon F


**Objectives** Immunogenicity To study the ability of DNA vaccine to induce a wide spectrum of TCL responses to recognize several epitopes and multiple isolates.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)
Trial Summaries

**Vaccine Name** pCI-Nef plasmid  
**Type:** DNA  
**Route:** Intradermal

- DNA immunization with several sequences elicits multispecific T cell responses that recognize several epitopes expressed in the different Nef immunogens.
- DNA immunization with Nef sequences induced interferon-gamma (IFN-gamma) secreting cell responses directed against several regions of Nef.
- CD8+ T cells were predominantly involved in anti-Nef IFN-gamma secreting cell responses.

**NHP.13** (11462016)  
**Protection against simian immunodeficiency virus vaginal challenge by using Sabin poliovirus vectors**

**Authors**  

**Journal**  

**Objectives**  
Challenge, Immunogenicity  
To assess the immunogenicity and protection of a vector-based vaccine (polio Sabin 1 and 2) coupled with SIV genes against vaginal challenge with highly pathogenic SIVmac251.

**Species/Subspecies**  
Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**  
pSabRV1-SIV  
**Type:** DNA  
**Route:** Intranasal

**Vaccine Name**  
pSabRV2-SIV  
**Type:** DNA  
**Route:** Intranasal

**Challenge**  
SIVmac251  
**Route:** Vaginal or perivaginal

**Main Findings**
- 4/7 vaccinated animals exhibited substantial protection against the vaginal SIV challenge.
- All 12 control monkeys became SIV positive (infection).
- No virological evidence of infection following challenge in 2/7 SabRV-SIV-vaccinated monkeys, indicating complete protection.
- Two additional SabRV-SIV-vaccinated monkeys exhibited a pronounced reduction in postacute viremia to <10^3 copies/ml, suggesting that the vaccine elicited an effective cellular immune response.
- 3/6 control animals developed clinical AIDS by 48 weeks postchallenge. In contrast, all seven vaccinated monkeys remained healthy as judged by all clinical parameters.

**NHP.14** (11134278)  
**Immunogenicity and protective efficacy of oligomeric human immunodeficiency virus type 1 gp140**

**Authors**  
Earl PL, Sugiura W, Montefiori DC, Broder CC, Lee SA, Wild C, Lifson J, Moss B

**Journal**  

**Objectives**  
Challenge, Immunogenicity  
To test the immunogenicity and protective efficacy of oligomeric gp140 in the rhesus macaque model, against homologous challenge with SHIV-HXB2.

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Vaccine Name**  
HIV-1 IIIB gp140  
**Type:** Purified Viral Products  
**Route:** Intramuscular

**Challenge**  
SHIV-IIIB/HXB2  
**Route:** Intravenous

**Main Findings**
- Strong neutralizing antibodies against a homologous virus and modest neutralization of heterologous laboratory-adapted isolates were elicited.
- No neutralization of primary isolates.
- 3/4 vaccinated macaques exhibited no evidence of virus replication.
- Infected animals demonstrated high, sustained neutralizing antibody titers to the challenge strain, while those that were protected exhibited waning titers.

**NHP.15** (11462019)  
**Postnatal passive immunization of neonatal macaques with a triple combination of human monoclonal antibodies against oral simian-human immunodeficiency virus challenge**

**Authors**  

**Journal**  

**Objectives**  
Challenge, Passive Immunization  
To develop prophylaxis against mother-to-child of SIV by postnatal passive immunization of neonatal macaques with a triple combination of human monoclonal antibodies.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Monoclonal antibody 2G12 Type: Passive Antibody Route: Intravenous
Vaccine Name Monoclonal antibody 2F5 Type: Passive Antibody Route: Intravenous
Vaccine Name IgG1 b12 Type: Passive Antibody Route: Intravenous
Vaccine Name Monoclonal antibody F105 Type: Passive Antibody Route: Intravenous
Challenge SHIV89.6, SHIV-vpu+ Route: Oral
Main Findings
• Two neonates macaques passively immunized with monoclonal antibodies (F105, 2G12, and 2F5), were protected from oral SHIV-vpu+ challenge, while four untreated control animals became persistently infected.
• Among SHIV89.6P-challenged animals, the MAb combination was partially successful in preventing infection.
• Half of the treated infants were protected from the acute, severe T-cell depletion.

NHP.16.1 (11257383) Modulation of antigen-specific cellular immune responses to DNA vaccination in rhesus macaques through the use of IL-2, IFN-gamma, or IL-4 gene adjuvants
Authors Kim JJ, Yang JS, Manson KH, Weiner DB
Objectives Challenge, Immunogenicity To examine the effects of cytokine gene adjuvants to enhance the level of cell-mediated immune responses generated by a multicomponent DNA vaccine in the rhesus macaque primate model.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name HIV env MN/rev(pCEnv) Type: DNA Route: Intramuscular
Vaccine Name pCSGag/Pol.SIV Type: DNA Route: Intramuscular
Challenge SHIV-IIIB/HXB2 Route: Intravenous
Main Findings
• Coadministration of IL-2 and IFN-gamma cDNA enhances antigen-specific T cell-mediated immune response.
• Antibody-specific responses can be driven to a higher level through the use of cytokine genetic adjuvants in rhesus macaques.
• Overall, low CTL response.
• The stimulated T cells from vaccinated rhesus macaques produced higher levels of IFN-gamma than the control animals.
• 3/8 immunized and challenged animals were protected from SHIV challenge.
• Protection to SHIV challenge was associated with CTL.

NHP.16.2 (11437655) Protection from immunodeficiency virus challenges in rhesus macaques by multicomponent DNA immunization
Authors Kim JJ, Yang JS, Nottingham LK, Lee DJ, Lee M, Manson KH, Wyand MS, Boyer JD, Ugen KE, Weiner DB
Journal Virology 2001 Jul 5;285(2):204-17
Objectives Challenge, Immunogenicity To test the ability of rhesus macaques immunized with DNA vaccines encoding HIV env/rev and SIV gag/pol to control infection with SIVmac239.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name HIV env MN Type: –
Vaccine Name HIV envreV(pCEnv) Type: DNA Route: Intramuscular
Vaccine Name pCSGag/Pol.SIV Type: DNA Route: Intramuscular
Challenge SIVmac239, SHIV89.6P, SHIV-IIIB/HXB2 Route: Intravenous
Main Findings
• Following the pathogenic challenges, all three vaccinated animals were negative for viral coculture and antigenemia and were negative by PCR.
• The control animals exhibited antigenemia by 2 weeks postchallenge and exhibited greater than 10 logs of virus/10^6 cells in limiting dilution coculture.
NHP.17  (11145906)  **Sequential immunization of macaques with two differentially attenuated vaccines induced long-term virus-specific immune responses and conferred protection against AIDS caused by heterologous simian human immunodeficiency Virus (SHIV(89.6)P)**

**Authors**  Kumar A, Lifson JD, Li Z, Jia F, Mukherjee S, Adany I, Liu Z, Piatak M, Sheffer D, McClure HM, Narayan O

**Journal**  Virology 2001 Jan 5;279(1):241-56

**Objectives**  Challenge, Immunogenicity To investigate the immunological response and protection in rhesus macaques sequentially immunized with live vaccines $\Delta$vpu$\Delta$nefSHIV-4 (vaccine-I) and $\Delta$vpu SHIVPPC (vaccine-II).

**Species/Subspecies**  Macaca mulatta (Rhesus macaque)

**Vaccine Name**  SHIV-4 (Deltavpu-Deltanef)-I  Type: Live Attenuated Virus  Route: Subcutaneous

**Vaccine Name**  SHIV-PPC (Deltavpu)  Type: Live Attenuated Virus  Route: Oral

**Challenge**  SHIV89.6P  Route: Intravenous

**Main Findings**

- The vaccine viruses did not replicate productively in the PBMCs of the vaccinated animals.
- 4/4 vaccinees developed binding antibodies against both vaccine envelope glycoproteins but neutralizing antibodies were elicited by only one vaccine; and virus-specific CTLs that recognized homologous as well as heterologous pathogenic SHIVs.
- 3 naive control animals were infected with the challenged strain and 2/3 controls were immunocompromised and succumbed to AIDS 6mpc.
- 4/4 vaccinees became infected with challenge virus but virus in these animals replicated approximately 200- to 60,000-fold less efficiently than in control animals and eventually, plasma viral RNA became undetectable in three of the four vaccinates.

NHP.18  (11581387)  **Role of CD8(+) lymphocytes in control of simian immunodeficiency virus infection and resistance to rechallenge after transient early antiretroviral treatment**


**Objectives**  Challenge, Immunogenicity, Immunotherapy To study the role of CD8+ in the control of SIV infection and rechallenge after transient early antiretroviral therapy.

**Species/Subspecies**  Macaca mulatta (Rhesus macaque)

**Vaccine Name**  SIVsmE660  Type: Live Virus  Route: Intravenous

**Challenge**  SIVsmE660, SIVmac239  Route: Intravenous

**Main Findings**

- Animals that controlled plasma viremia following transient postinoculation treatment showed substantial resistance to subsequent intravenous rechallenge with homologous (SIVsmE660) and highly heterologous (SIVmac239) SIV isolates, up to more than 1 year later, despite the absence of measurable neutralizing antibody.

NHP.19  (11393868)  **Control of a mucosal challenge and prevention of AIDS by a multiprotein DNA/MVA vaccine**

**Authors**  Amara RR, Villinger F, Altman JD, Lydy SL, O

**Journal**  Science 2001 Apr 6;292(5514):69-74

**Objectives**  Challenge, Immunogenicity To assess the protective value of an immunization scheme consisting of DNA priming followed by a recombinant modified vaccinia Ankara (rMVA) booster.

**Species/Subspecies**  Macaca mulatta (Rhesus macaque)

**Vaccine Name**  SIV-HIV89.6 DNA vaccine  Type: DNA  Routes: Intradermal, Intramuscular

**Vaccine Name**  rMVA 89.6  Type: Recombinant Vector (virus/bacteria)  Routes: Intradermal, Intramuscular

**Challenge**  SHIV89.6P  Route: Intrarectal

**Main Findings**
Two DNA inoculations at 0 and 8 weeks and a single rMVA booster at 24 weeks effectively controlled an intrarectal challenge administered 7 months after the booster.

**NHP.20** (11507204) Evidence for early local viral replication and local production of antiviral immunity upon mucosal simian-human immunodeficiency virus SHIV(89.6) infection in Macaca nemestrina

**Authors** Ambrose Z, Larsen K, Thompson J, Stevens Y, Finn E, Hu SL, Bosch ML


**Objectives** Immunogenicity, Immunotherapy To study the differences in viremia, CD4 T-cell percentages, and mucosal and systemic anti-SHIV humoral and cellular immune responses during primary infection of animals infected either intravenously or intravaginally.

**Species/Subspecies** Macaca nemestrina (pigtailed macaque)

**Challenge** SHIV89.6v  Route: Intravenous, Vaginal or perivaginal

**Main Findings**
- SHIV Positive viral cocultures, peripheral blood mononuclear cell viral load peaks, and CD4 cell declines were delayed by 1 week in the intravaginally inoculated animals compared to the animals infected intravenously, demonstrating delayed viral spreading to the periphery.
- Mucosal anti-SHIV antibody levels were greater in magnitude and arose more rapidly and mucosal CD8(+) T-cell responses were enhanced in the intravaginally inoculated animals.

**NHP.21** (11424009) Protection from secondary human immunodeficiency virus type 1 infection in chimpanzees suggests the importance of antigenic boosting and a possible role for cytotoxic T cells

**Authors** Balla-Jhaghoorsingh SS, Mooij P, ten Haaft PJ, Bogers WM, Teeuwen VJ, Koopman G, Heeney JL


**Objectives** Challenge, Immunogenicity To investigate correlates of protection against secondary and subsequent HIV infection.

**Species/Subspecies** Pan troglodytes verus (chimpanzee), Macaca (sp)

**Vaccine Name** HIV-1 W6.1D gp120  Type: Recombinant Subunit Protein  Route: Intramuscular

**Challenge** HIV-1 Han2  Route: Intravenous

**Main Findings**
- After exposure to an infectious dose of heterologous primary isolate, 4/8 HIV-1 seropositive chimpanzees resisted secondary infection, whereas 2 naive controls became readily infected.
- Only animals who were immunologically boosted were protected.
- Protection from heterologous secondary exposure appeared to be related to the repertoire of the cytolytic CD8+ T cell responses to HIV-1.

**NHP.22** (11356960) The ability of an oligomeric human immunodeficiency virus type 1 (HIV-1) envelope antigen to elicit neutralizing antibodies against primary HIV-1 isolates is improved following partial deletion of the second hypervariable region


**Objectives** Immunogenicity To investigate whether the modified, SF162V2-derived envelope may elicit higher titers of cross-reactive neutralizing antibodies than the unmodified SF162-derived envelope.

**Species/Subspecies** Macaca mulatta (Rhesus macaque), Macaca (sp)

**Vaccine Name** Delta-V2 gp140 oligomeric  Type: Recombinant Subunit Protein  Route: Intramuscular

**Vaccine Name** DNA (pCMVKm2) gp140  Type: DNA  Routes: Intradermal, Intramuscular

**Vaccine Name** pCMVKm2-Delta-V2 gp140  Type: DNA  Routes: Intradermal, Intramuscular

**Vaccine Name** gp140 oligomeric  Type: Recombinant Subunit Protein  Route: Intramuscular

**Main Findings**
Trial Summaries

- Modified immunogen was more effective in eliciting potent binding and neutralizing antibodies, against homologous and several heterologous primary HIV-1 isolates.

<table>
<thead>
<tr>
<th>NHP.23 (11595290)</th>
<th>Vaccine-elicited immune responses prevent clinical AIDS in SHIV(89.6P)-infected rhesus monkeys</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Barouch DH, Fu TM, Montefiori DC, Lewis MG, Shiver JW, Letvin NL</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To study the role of adjuvant IL-2/Ig, a fusion protein consisting of IL-2 and the Fc portion of IgG, in DNA vaccines encoding SIVmac239 Gag and HIV-189.6P Env.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>DNA-gag.env Type: DNA Route: Intramuscular</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SHIV89.6P Route: Intravenous</td>
</tr>
</tbody>
</table>

- Animals immunized with DNA vaccines plus IL-2/Ig plasmid or protein developed significantly higher levels of p11C- and p41A-specific CTLs.
- No prevention of infection in vaccinees upon intravenous challenge with SHIV89.6.
- Control of viremia to nearly undetectable levels in vaccinees.
- Control monkeys developed high levels of viremia and exhibited a rapid loss of CD4+ T cells, significant clinical disease progression, and death in half of the animals by day 140 following challenge.

<table>
<thead>
<tr>
<th>NHP.24.1 (11160750)</th>
<th>Elicitation of high-frequency cytotoxic T-lymphocyte responses against both dominant and subdominant simian-human immunodeficiency virus epitopes by DNA vaccination of rhesus monkeys</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>Immunogenicity To compare the CTL response to vaccination with plasmid DNA, live recombinant vector and infection with simian-human immunodeficiency virus (SHIV).</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>rMVASIV239gagpol.HIV89.6env Type: Recombinant Vector (virus/bacteria) Route: Intramuscular</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SHIV89.6 Type: Live Virus Route: Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SHIV89.6P Type: Live Virus Route: Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SHIVIII.B2 Type: Live Virus Route: Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>pV1P-SIVmac239 gag Type: DNA Route: Intramuscular</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>pV1P-HIV-1.89.6P env Type: DNA Route: Intramuscular</td>
</tr>
</tbody>
</table>

- The p11C-specific CTL response was high frequency and dominant and the p41A-specific CTL response was low frequency and subdominant in both SHIV-infected monkeys and in monkeys vaccinated with recombinant modified vaccinia virus Ankara vectors expressing these viral antigens.
- Vaccination with plasmid DNA, but not vaccination with a live recombinant vector or infection with SHIV, elicits potent CTL responses against both dominant and subdominant epitopes in rhesus monkeys.
- Plasmid DNA vaccination leads to high-frequency CTL responses specific for both of env p41A and Gag p11C epitopes.

<table>
<thead>
<tr>
<th>NHP.24.2 (11333896)</th>
<th>Reduction of simian-human immunodeficiency virus 89.6P viremia in rhesus monkeys by recombinant modified vaccinia virus Ankara vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To study the immune responses elicited in rhesus monkeys by a recombinant poxvirus vaccine and the degree of protection afforded against a pathogenic simian-human immunodeficiency virus SHIV-89.6P challenge.</td>
</tr>
</tbody>
</table>
**Species/Subspecies**
- Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- MVA-SIV gag-pol and HIV-1 89.6 env

**Type**: Recombinant Vector (virus/bacteria)

**Route**: Intramuscular

**Challenge**
- SHIV89.6P

**Route**: Intravenous

**Main Findings**
- Immunization with MVA vectors expressing SIVmac239 gag-pol and HIV-1 89.6 env elicited potent Gag-specific CTL responses but no detectable SHIV-specific NAb responses.
- MVA-vaccinated monkeys had high-frequency secondary CTL responses, high-titer secondary SHIV-89.6-specific NAb responses, rapid SHIV-89.6P-specific NAb responses, partial preservation of CD4+ T lymphocytes, reduced setpoint viral RNA levels, and no clinical disease or mortality by day 168 postchallenge (in contrast to control animals).

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**NHP.27**  (10590126)

**Vaccination of macaques against pathogenic simian immunodeficiency virus with Venezuelan equine encephalitis virus replicon particles**

**Authors**

**Journal**

**Objectives**
- Challenge, Immunogenicity

To evaluate the immunogeneicity and protective value of an SIV vaccine in VEE vector against SIV challenge.

**Species/Subspecies**
- Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- VEE-SIVsm (SIV MA/CA-VRP and gp160-VRP)

**Type**: DNA

**Routes**: Intravenous, Subcutaneous

**Challenge**
- SIVsmE660

**Route**: Intravenous

**Main Findings**
- 4/4 vaccinees were protected against disease for at least 16 mpc (intravenous) with a pathogenic SIV swarm, while two of four controls required euthanasia at 10 and 11 weeks.
- Vaccination reduced the mean peak viral load 100-fold.

---

**NHP.28**  (10600597)

**Protection of macaques against a SHIV with a homologous HIV-1 Env and a pathogenic SHIV-89.6P with a heterologous Env by vaccination with multiple gene-deleted SHIVs**

**Authors**

**Journal**
- Virology 1999 Dec 20;265(2):252-63

**Objectives**
- Challenge, Immunogenicity

To evaluate the potential of SHIVs as anti-HIV-1 live attenuated virus vaccines.

**Species/Subspecies**
- Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- SHIV-drn

**Type**: Live Attenuated Virus

**Route**: Intravenous

**Challenge**
- SHIV-NM-3rN, SHIV89.6P

**Main Findings**
- In 4 macaques that had been vaccinated with SHIV-drn and challenged with SHIV-NM-3rN, no challenge virus was detected by DNA PCR in, or recovered from, two of the macaques. In the other two, challenge virus was detected once and twice, respectively.
- Plasma viral loads were much lower than those in unvaccinated controls.
- Another four macaques vaccinated with SHIV-dxrn, control of infection was evident but less than that of SHIV-drn-vaccinated macaques.
- When the two SHIV-drn-vaccinated macaques were challenged with pathogenic SHIV-89.6P, which has an HIV-1 Env that is antigenically different from that of SHIV-drn, replication of the challenge virus was restricted.
- Protection involved not only neutralizing antibodies and killer cell activity, but also other unknown specific and nonspecific immunity elicited by the infection.

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**NHP.29.1**  (12584336)

**Simian-Human Immunodeficiency Virus SHIV89.6-Induced Protection against Intravaginal Challenge with Pathogenic SIVmac239 Is Independent of the Route of Immunization and Is Associated with a Combination of Cytotoxic T-Lymphocyte and Alpha Interferon Responses**

**Authors**
- Abel K, Compton L, Rourke T, Montefiori D, Lu D, Rothaeusler K, Fritts L, Bost K, Miller CJ

**Journal**

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**HIV Immunology and HIV/SIV Vaccine Databases 2003**

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### Trial Summaries

**Objectives** Challenge, Immunogenicity To compare the mucosal (intranasal, intravaginal) vs. intravenous immunization with live nonpathogenic SHIV89.6 in rhesus macaques subsequently challenged intravaginally with SIVmac239.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** SHIV89.6 Type: Live Virus Routes: Intravenous, Vaginal or perivaginal, Intranasal

**Main Findings**
- The route of immunization did not affect mucosal challenge outcome after a prolonged period of systemic infection with the nonpathogenic vaccine virus.
- Protection from the SIV challenge was associated with the induction of multiple host immune effector mechanisms: vaccinated-protected animals had higher frequencies of SIV Gag-specific cytotoxic T lymphocytes and gamma interferon-secreting cells during the acute phase postchallenge than the vaccinated unprotected ones.
- Vaccinated-protected animals had a more pronounced increase in peripheral blood mononuclear cell IFN-gamma mRNA levels than did the vaccinated-unprotected animals in the first few weeks after challenge.

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**NHP.29.2** (14694116) **Gamma interferon-mediated inflammation is associated with lack of protection from intravaginal simian immunodeficiency virus SIVmac239 challenge in simian-human immunodeficiency virus 89.6-immunized rhesus macaques**

**Authors** Abel K, La Franco-Scheuch L, Rourke T, Ma ZM, De Silva V, Fallert B, Beckett L, Reinhart TA, Miller CJ


**Objectives** Challenge, Immunogenicity To determine the relationship between IFN-Γ-related host immune responses and challenge virus replication in lymphoid tissues of SHIV89.6-vaccinated and unvaccinated rhesus macaques after challenge with SIVmac239.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Main Findings**
- Vaccinated-protected monkeys had low tissue viral RNA (vRNA) levels.
- Vaccinated-unprotected animals had moderate tissue vRNA levels.
- Unvaccinated animals had high tissue vRNA levels.
- Vaccinated-protected monkeys had slightly increased tissue IFN-Γ mRNA levels and a high frequency of IFN-Γ secreting T cells responding to in vitro SIVgag peptide stimulation.

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**NHP.30** (11739694) **ALVAC-SIV-gag-pol-env-based vaccination and macaque major histocompatibility complex class I (A*01) delay simian immunodeficiency virus SIVmac-induced immunodeficiency**


**Objectives** Challenge, Immunoxygenity To assess whether immunization with an ALVAC-based vaccine expressing the SIVmac251 Gag, Pol, and Env and subsequent boosting with subunit gp120 could confer immunity and prevent or contain SIVmac251 replication following a mucosal exposure to SIVmac251.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** ALVAC-SIV-gpe (vcp180) Type: Recombinant Vector (virus/bacteria) Routes: Intrarectal, Intramuscular, Intranasal

**Vaccine Name** SIVmac251-gp120 Type: Purified Viral Products Routes: Intrarectal, Intramuscular, Intranasal

**Challenge** SIVmac251 (561) Route: Intrarectal

**Main Findings**
- MHC-I Mamu-A*01 genotype and vaccination of rhesus macaques with ALVAC-SIV-gag-pol-env (ALVAC-SIV-gpe) restrict SIVmac251 replication, preserve CD4+ T cells, and delay disease progression following intrarectal challenge exposure of the animals to SIVmac251.
- ALVAC-SIV-gpe immunization induced CTL responses cumulatively in 67% of the immunized animals.
- Significant delay in CD4+ T-cell loss was observed in Mamu-A*01-positive macaques.
- Neither boosting the ALVAC-SIV-gpe with gp120 immunizations nor administering the vaccine by the combination of mucosal and systemic immunization routes increased significantly the protective effect of the ALVAC-SIV-gpe vaccine.
**NHP.31** (11017793) **DNA vaccination of macaques by a full genome HIV-1 plasmid which produces noninfectious virus particles**

**Authors** Akahata W, Ido E, Shimada T, Katsuyama K, Yamamoto H, Uesaka H, Ui M, Kuwata T, Takahashi H, Hayami M


**Objectives** Challenge, Immunogenicity To evaluate the humoral and cell-mediated immune response to a DNA vaccine containing full genome of HIV-1.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** DNA Vaccine pNL432-ZF1*

**Type:** DNA  **Route:** Intramuscular

**Challenge** SHIV-NM-3rN  **Route:** Intravenous

**Main Findings**
- Immunological responses against HIV-1 were elicited in all of the vaccinated monkeys: stable anti-HIV-1 Env antibodies were raised in two monkeys and CTL activities were induced in the other monkeys. After homologous challenge of the macaques intravenously 54 weeks with 100 TCID50 of SHIV-NM-3rN, in all of the vaccinated macaques, the peak plasma viral loads were two to three orders of magnitude lower than those of the naive controls.

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**NHP.32** (10233957) **Highly attenuated vaccine strains of simian immunodeficiency virus protect against vaginal challenge: inverse relationship of degree of protection with level of attenuation**

**Authors** Johnson RP, Lifson JD, Czajak SC, Cole KS, Manson KH, Glickman R, Yang J, Montefiori DC, Montelaro R, Wyand MS, Desrosiers RC


**Objectives** Challenge, Immunogenicity To compare 3 levels of attenuation of SIV-based vaccine and their ability to protect against mucosal challenge with pathogenic SIV.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- SIVmac239  **Type:** Live Attenuated Virus  **Route:** Intravenous
- SIVmac239Δ3  **Type:** Live Attenuated Virus  **Route:** Intravenous
- SIVmac239Δ4  **Type:** Live Attenuated Virus  **Route:** Intravenous

**Challenge** SIVmac251  **Route:** Intravenous, Vaginal or perivaginal

**Main Findings**
- All three vaccines elicited strong protective effect up to 1 year from immunization to challenge.
- Degree of protection correlated inversely with the level of attenuation.
- Protection against vaginal challenge was easier to achieve than protection against intravenous challenge.
- Protection associated with high antibody avidity indices.
- Protection in absence of detectable serum Nab was associated with CTL response in immunized animals. No vaccine virus recovered in 11 of 12 vaccinees.

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**NHP.33** (11085585) **Enhanced safety and efficacy of live attenuated SIV vaccines by prevaccination with recombinant vaccines**

**Authors** Jones L, Ahmad S, Chan K, Verardi P, Morton WR, Grant R, Yilma T


**Objectives** Challenge, Immunogenicity To evaluate the safety of a live attenuated vaccine (delta nef) in macaques pre-immunized with a recombinant DNA vaccine.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- SIVmac239-Δnef  **Type:** Live Attenuated Virus  **Route:** Intravenous
- vSIVgp120  **Type:** Recombinant Vector (virus/bacteria)  **Route:** Intradermal
- CHO-SIVgp120  **Type:** DNA  **Route:** Intramuscular
- vSIVgp160  **Type:** DNA  **Route:** Intradermal
- bSIVgp120  **Type:** DNA  **Route:** Intramuscular
- SIVmac251  **Route:** Intravenous

**Main Findings**
- In the case of intravenous or intrarectal challenge with the chimeric SIV/HIV strains SHIV(89.6P) or SHIV(KU2), respectively, MHC-I Mamu-A*01-positive macaques did not significantly restrict primary viremia.
Vaccines

Trial Summaries

- Preimmunized macaques advanced to disease SLOWER than controls after challenge with virulent SIV.
- 5 animals survived for 3 years without disease and only the vaccine virus (SIVΔnef) could be isolated at this time.
- In another experiment, preimmunized animals had lower virus loads and no disease compared to controls.

<table>
<thead>
<tr>
<th>NHP.34</th>
<th>Limited protection from a pathogenic chimeric simian-human immunodeficiency virus challenge following immunization with attenuated simian immunodeficiency virus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Lewis MG, Yalley-Ogunro J, Greenhouse JJ, Brennan TP, Jiang JB, VanCott TC, Lu Y, Eddy GA, Binx DL</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To test the ability of two live attenuated SIV constructs with single deletion to stimulate protective immunity in macaques.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque), Macaca nemestrina (pigtailed macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIVmac239-Δnef <strong>Type:</strong> Live Attenuated Virus <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIV-PBJ6.6Δnef <strong>Type:</strong> Live Attenuated Virus <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SHIV89.6PD <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td></td>
</tr>
<tr>
<td>- Each construct generated high levels of specific immunity in all of the immunized animals.</td>
<td></td>
</tr>
<tr>
<td>- SIV239Δnef grew to high levels in all immunized animals. The SIVPBj6.6Δnef was effectively controlled by all of the immunized animals.</td>
<td></td>
</tr>
<tr>
<td>- Challenge strain: SIV89.6PD.</td>
<td></td>
</tr>
<tr>
<td>- Vaccination with attenuated SIV can protect macaques from disease and in some cases from infection by a highly pathogenic SHIV. Inability to control the immunizing virus may result in rapid disease progression.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>NHP.35</th>
<th>Protective immunity of gene-deleted SHIVs having an HIV-1 Env against challenge infection with a gene-intact SHIV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Ui M, Kuwata T, Igarashi T, Miyazaki Y, Tamara K, Shimada T, Nakamura M, Uesaka H, Yamamoto H, Hayami M</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To assess the level of immunogenicity and protection of a SHIV-deleted live attenuated vaccine virus against a gene-intact SHIV challenge virus.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SHIV-dn <strong>Type:</strong> Live Attenuated Virus <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SHIV-dmn <strong>Type:</strong> Live Attenuated Virus <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SHIV-dxrn <strong>Type:</strong> Live Attenuated Virus <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SHIV-NM-3rN <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td></td>
</tr>
<tr>
<td>- Protective immunity of live attenuated SHIV vaccine is inversely dependent upon the level of attenuation of the virus.</td>
<td></td>
</tr>
<tr>
<td>- Most immunized macaques had HIV-1 env and/or SIV gag-specific CTL responses.</td>
<td></td>
</tr>
<tr>
<td>- 10/12 vaccinated macaques had NK cell activities higher than those of normal macaques (&lt;10%): NK cells may be involved in protection against challenge.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NHP.36</th>
<th>Induction of long-term protective effects against heterologous challenge in SIVhu-infected macaques</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Villinger F, Switzer WM, Parekh BS, Otten RA, Adams D, Shanmugam V, Bostik P, Mayne AE, Chikkala NF, McClure HM, Novembre F, Yao Q, Heneine W, Folks TM, Ansari AA</td>
</tr>
<tr>
<td><strong>Journal</strong></td>
<td>Virology 2000 Dec 5;278(1):194-206</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To measure the immunogenicity and protective effect of a live attenuated vaccine SIVhu (isolated from a human accidentally exposed) against challenge with SHIV89.6P.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIVhu <strong>Type:</strong> Live Attenuated Virus <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SIVsmB670, SHIV89.6P <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td></td>
</tr>
</tbody>
</table>
• SIVhu which accidentally infected human had a truncated nef which failed to repair itself and added additional stop codons post-infection.
• Infection with SIVhu was associated with minimal acute viral replication, followed by undetectable plasma viral loads and only intermittent PCR detection up to 5 ypi.
• 3/3 animals infected with SIVhu remained healthy and with stable CD4(+) lymphocyte levels and undetectable plasma viral loads at >20 months post-SIV89.6p challenge.

NHP.37  (10482586) Protection by live, attenuated simian immunodeficiency virus against heterologous challenge
Authors Wyand MS, Manson K, Montefiori DC, Lifson JD, Johnson RP, Desrosiers RC
Objectives Challenge, Immunogenicity To examine the ability of a live, attenuated deletion mutant (SIVmac2393), which is missing nef and vpr genes, to protect against challenge by heterologous strains SHIV89.6p and SIVsmE660.
Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca (sp)
Vaccine Name SIVmac239∆3  Type: Live Attenuated Virus  Route: Intravenous
Challenge SIVsmE660, SHIV89.6P  Route: Intravenous
Main Findings
• By the criteria of CD4+ cell counts and disease, strong protection against the SHIV89.6p challenge was observed in 4/4 vaccinated monkeys (group 1).

NHP.38  (11152522) Persistence of pathogenic challenge virus in macaques protected by simian immunodeficiency virus SIVmacDeltanef
Authors Khatissian E, Monceaux V, Cumont MC, Kiency MP, Aubertin AM, Hurtrel B
Objectives Challenge, Immunogenicity To investigate virological and immunological characteristics of five rhesus macaques immunized with a nef-inactivated SIVmac251 molecular clone (SIVmac251nef) and challenged 15 months later with the pathogenic SIVmac251 isolate.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac251∆Nef  Type: Live Attenuated Virus  Route: Intravenous
Challenge SIVmac251  Route: Intravenous
Main Findings
• No total protection against homologous virus challenge but control of infection with challenge virus in the absence of a secondary immune response.
• Challenge and vaccine viruses may persist in a replication-competent form for long periods after the challenge, possibly resulting in recombination between the two viruses.

NHP.39  (11287551) Quintuple deglycosylation mutant of simian immunodeficiency virus SIVmac239 in rhesus macaques: robust primary replication, tightly contained chronic infection, and elicitation of potent immunity against the parental wild-type strain
Authors Mori K, Yasutomi Y, Ohgimoto S, Nakasone T, Takamura S, Shioda T, Nagai Y
Journal J Virol 2001 May;75(9):4023-8
Objectives Challenge, Immunogenicity To assess the immunogenicity and protection effect of a deglycosylated SIVmac239 mutant vaccine.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac239Delta5G  Type: Live Attenuated Virus  Route: Intravenous
Challenge SIVmac239  Route: Intravenous
Main Findings
• Monkeys infected with the mutant tolerated a challenge infection with wild-type SIV very well.
• Analyses of host responses following challenge revealed no neutralizing antibodies against the challenge virus but strong secondary responses of cytotoxic T lymphocytes against multiple antigens, including Gag-Pol, Nef, and Env.
• Quintuple deglycosylation mutant appeared to represent a novel class of SIV live attenuated vaccine.
<table>
<thead>
<tr>
<th>NHP.40</th>
<th>(10191194) Long-lasting protection by live attenuated simian immunodeficiency virus in cynomolgus monkeys: no detection of reactivation after stimulation with a recall antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Sernicola L, Corrias F, Koanga-Mogtomo ML, Baroccelli S, Di Fabio S, Maggiorella MT, Belli R, Michelini Z, Macchia I, Cesolini A, Cioc L, Verani P, Titti F</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To determine the breadth of the protection after repeated challenges of monkeys with SIV.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca fascicularis (cynomolgus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIVmac251, 32H, (C8) <strong>Type:</strong> Live Attenuated Virus  <strong>Route:</strong> Intravenous</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SIVmac251BK28, SIVmac251,32H.spl  <strong>Route:</strong> Intravenous</td>
</tr>
</tbody>
</table>
| **Main Findings** | • Monkeys immunized with live attenuated C8 vaccine were protected from consecutive challenge with SIVmac251, SIVmac32H.  
• The C8 virus remained genotypically stable, and depletion of CD4+ cells was not observed during 3 years of follow-up. |

<table>
<thead>
<tr>
<th>NHP.41</th>
<th>(10998338) Replication of simian immunodeficiency virus (SIV) in ex vivo lymph nodes as a means to assess susceptibility of macaques in vivo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Journal</strong></td>
<td>Virology 2000 Sep;275(2):391-7</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To investigate whether infectability of ex vivo lymph nodes could predict resistance and/or susceptibility to SIV infection.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca (sp)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIVmac251  <strong>Type:</strong> Live Virus  <strong>Route:</strong> Mucosal</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SIVsmE660  <strong>Type:</strong> Live Virus  <strong>Route:</strong> Mucosal</td>
</tr>
</tbody>
</table>
| **Main Findings** | • Six macaques, apparently uninfected, following low-dose exposure to the pathogenic SIV(mac251) and SIV(SME660) by the mucosal route, were re-exposed to a less pathogenic SIV(MNE): 4/6 macaques resisted viral infection.  
• PBMC and lymph-node resistance or susceptibility to infection ex vivo correlate with in vivo infectivity. |

<table>
<thead>
<tr>
<th>NHP.42</th>
<th>(10593484) Antigen-specific cytokine responses in vaccinated Macaca nemestrina</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Mulvania T, Lynch JB, Robertson MN, Greenberg PD, Morton WR, Mullins JI</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity Macaca nemestrina vaccinated with a minimally pathogenic HIV-2 strain KR. Group 1 was then inoculated with a non-infectious stock of a pathogenic strain, HIV-2287.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca nemestrina (pigtailed macaque)</td>
</tr>
</tbody>
</table>
| **Main Findings** | • Both groups 1 and 2 were subsequently challenged with an infectious stock of HIV-2287.  
• 5/6 group 1 animals were protected against CD4 decline.  
• 3/6 animals in group 2 were protected.  
• Analysis of CTL responses demonstrated strong activity against HIV-2(KR)-Gag in group 1.  
• Strong correlation between CTL responses and antigen-specific T-helper (Th) type 1 responses. |

<table>
<thead>
<tr>
<th>NHP.43</th>
<th>(10593486) An anti-HIV strategy combining chemotherapy and therapeutic vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity, Immunotherapy .</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td></td>
</tr>
</tbody>
</table>
• Chemotherapy/therapeutic vaccination regimen induced a significant reduction in the steady-state level of viremia in one out of two chronically infected rhesus macaques.
• Chemotherapeutic treatment alone did not achieve reduction of viremia in two chronically infected animals. The nature of the immune responses assumed to have been induced by vaccination in one out of the two monkeys remains to be elucidated.

### NHP.44 (10684264)
**Immunization with a modified vaccinia virus expressing simian immunodeficiency virus (SIV) Gag-Pol primes for an anamnestic Gag-specific cytotoxic T-lymphocyte response and is associated with reduction of viremia after SIV challenge**

**Objectives** Challenge, Immunogenicity To explore the immunogenicity and protective efficacy of rMVA expressing the SIV gag-pol proteins in rhesus monkeys expressing the MHC class I allele, MamuA*01.

<table>
<thead>
<tr>
<th>Species/Subspecies</th>
<th>Macaca mulatta (Rhesus macaque)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Name</td>
<td>MVA_{gag-pol}</td>
</tr>
<tr>
<td>Type</td>
<td>Recombinant Vector (virus/bacteria)</td>
</tr>
<tr>
<td>Route</td>
<td>Intravenous</td>
</tr>
<tr>
<td>Challenge</td>
<td>SIVsmE660</td>
</tr>
<tr>
<td>Route</td>
<td>Intravenous</td>
</tr>
</tbody>
</table>

**Main Findings**
- MVA-gag-pol-immunized macaques exhibited a rapid and substantial anamnestic CTL response specific for the p11C, C-M Gag epitopes.
- The level at which CTL stabilized after resolution of primary viremia correlated inversely with plasma viral load set point (P = 0.03).
- The magnitude of reduction in viremia in the vaccinees was predicted by the magnitude of the vaccine-elicited CTL response prior to SIV challenge.

### NHP.45 (10684290)
**Comparative efficacy of recombinant modified vaccinia virus Ankara expressing simian immunodeficiency virus (SIV) Gag-Pol and/or Env in macaques challenged with pathogenic SIV**

**Objectives** Challenge, Immunogenicity To evaluate the protective effects of prior immunization with MVA-SIV recombinant vaccines as a sole immunogen without boosting with Env protein and to optimize expression of Gag-Pol.

<table>
<thead>
<tr>
<th>Species/Subspecies</th>
<th>Macaca mulatta (Rhesus macaque)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Name</td>
<td>MVA-SIVsmH-4 -env</td>
</tr>
<tr>
<td>Type</td>
<td>Recombinant Vector (virus/bacteria)</td>
</tr>
<tr>
<td>Route</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>MVA(SIVsmH-4 )_{gag-pol-env}</td>
</tr>
<tr>
<td>Type</td>
<td>Purified Viral Products</td>
</tr>
<tr>
<td>Route</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>MVA SIVsmH4 gag-pol</td>
</tr>
<tr>
<td>Type</td>
<td>Recombinant Vector (virus/bacteria)</td>
</tr>
<tr>
<td>Route</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Challenge</td>
<td>SIVsmE660</td>
</tr>
<tr>
<td>Route</td>
<td>Intravenous</td>
</tr>
</tbody>
</table>

**Main Findings**
- Although all animals became infected post challenge, plasma viremia was significantly reduced in animals that received the MVA-SIV recombinant vaccines as compared with animals that received nonrecombinant MVA (P = 0.0011 by repeated-measures analysis of variance).
- Immunization significantly modifies viral load following SIV challenge.
- Recombinant MVA has considerable potential as a vaccine vector for human AIDS.

### NHP.46 (9707609)
**Recombinant modified vaccinia virus Ankara-simian immunodeficiency virus gag pol elicits cytotoxic T lymphocytes in rhesus monkeys detected by a major histocompatibility complex class I/peptide tetramer**

**Authors** Seth A, Ourmanov I, Kuroda MJ, Schmitz JE, Carroll MW, Wyatt LS, Moss B, Forman MA, Hirsch VM, Letvin NL  
**Journal** Proc Natl Acad Sci U S A 1998 Aug 18;95(17):10112-6  
**Objectives** Immunogenicity To explore the utility of MVA as a vector for eliciting AIDS virus-specific CTL in the SIV/rhesus monkey model.

<table>
<thead>
<tr>
<th>Species/Subspecies</th>
<th>Macaca mulatta (Rhesus macaque)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Name</td>
<td>MVA SIVsmH4 gag-pol</td>
</tr>
<tr>
<td>Type</td>
<td>Recombinant Vector (virus/bacteria)</td>
</tr>
<tr>
<td>Route</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>
Intramuscular immunization with recombinant MVA-SIVSM gag pol elicited a Gag epitope-specific CTL response readily detected in peripheral blood lymphocytes by using a functional killing assay. Moreover, those immunizations also elicited a population of CD8+ T lymphocytes in the peripheral blood that bound a specific major histocompatibility complex class I/peptide tetramer.

Tetramer staining may be a useful technology for monitoring CTL generation in vaccine trials in nonhuman primates and in humans.


Authors Patterson LJ, Peng B, Abimiku AG, Aldrich K, Murty L, Markham PD, Kalyanaraman VS, Alvord WG, Tartaglia J, Franchini G, Robert-Guroff M


Objectives Challenge, Immunogenicity To evaluate the immunization with attenuated poxvirus-HIV-1 recombinants followed by protein boosting in rhesus monkeys model.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name vP991, NYVAC HIV-1IIIIB gp120,gag-pol Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

Vaccine Name vP1047, NYVAC HIV-2.SBL-I SY gp160,gag-pol Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

Vaccine Name HIV-1 gp160 Type: Purified Viral Products Route: Intramuscular

Vaccine Name HIV-2 gp160 Type: Purified Viral Products Route: Intramuscular

Challenge HIV-2.SBL6669, SHIV-IIIB/HXB2 Route: Intravenous

Main Findings

- Both immunization groups developed homologous binding antibodies.
- Homologous Nab only observed in NYVAC-HIV-2-immunized macaques.
- No cross-reactive neutralizing antibodies detected.
- Immunization groups displayed cross-reactive CTL.
- Significant CD8AA observed for only one NYVAC-HIV-2-immunized macaque.
- Both immunizations significantly reduced viral burdens and partially protected against HIV-2 challenge.
- Humoral antibody and/or CTL and CD8AA associated with protection against homologous HIV-2 challenge.
- No significant protection observed in the SHIV-challenged macaques, although NYVAC-HIV-1 immunization resulted in significantly lower viral burdens compared with controls.

NHP.48 (10717345) A recombinant avipoxvirus HIV-1 vaccine expressing interferon-gamma is safe and immunogenic in macaques

Authors Kent SJ, Zhao A, Dale CJ, Land S, Doyle BB, Ramshaw IA

Journal Vaccine 2000 Apr 28;18(21):2250-6

Objectives Immunogenicity, Immunotherapy To construct and assess FPV.gag/pol-IFNgamma as a therapeutic vaccine for safety and immunogenicity in Macaca nemestrina previously infected with HIV-1.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name FPV.HIV-1.gag/pol-IFNgamma Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

Vaccine Name FPV.HIV-1.gag/pol Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

Challenge HIV-1.LAI Route: Intravenous

Main Findings

- FPV.gag/pol-IFNgamma vaccinations were safe and enhanced T cell proliferative responses to Gag antigens (but not control tetanus antigens).
- Enhanced CTL responses to gag/pol antigens were also observed following IFNgamma expressing vaccinations.
- Since cellular immunity may be critical to controlling or preventing HIV-1 infection, these observations suggest that avipox vectors co-expressing IFNgamma should be further evaluated as therapeutic or preventive HIV-1 vaccines.
### NHP.51 (11555138) Effect of vaccination with recombinant modified vaccinia virus Ankara expressing structural and regulatory genes of SIV(macJ5) on the kinetics of SIV replication in cynomolgus monkeys

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**
rMV A-mac(J5)
**Type:** Recombinant Vector (virus/bacteria)
**Route:** Intramuscular

**Challenge**
SIV mac251
**Route:** Intravenous

**Main Findings**
- Vaccination with rMV A-J5 performed at week 0, 12, and 24 induced a moderate proliferative response to whole SIV, a detectable humoral response to all but Nef SIV antigens, and failed to induce neutralizing antibodies.
- All control monkeys were infected by week two and seroconverted by weeks four to eight.
- In contrast a sharp increase of both humoral and proliferative responses at two weeks post-challenge was observed in vaccinated monkeys compared to control monkeys.
- Although all vaccinated monkeys were infected, vaccination with rMV A-J5 appeared to partially control viral replication during the acute and late phase of infection as judged by cell- and plasma-associated viral load.

### NHP.52 (12072518) Immunization of rhesus macaques with a DNA prime/modified vaccinia virus Ankara boost regimen induces broad simian immunodeficiency virus (SIV)-specific T-cell responses and reduces initial viral replication but does not prevent disease progression following challenge with pathogenic SIVmac239

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity To test the immunogenicity and protective value of a DNA prime/modified vaccinia virus Ankara boost regimen immunization in rhesus macaques against intrarectal challenge with simian immunodeficiency virus (SIV) mac239.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- pC-SIVrev **Type:** DNA **Route:** Intradermal
- rMVA-SIVmac251 32H **Type:** Recombinant Vector (virus/bacteria) **Routes:** Intrarectal, Intradermal
- pC-SIV17E-Fred (gagpolenv) **Type:** DNA **Route:** Intradermal
- SIVmac17E-Fr Nef **Type:** DNA **Route:** Intradermal
- SIVmac239/nef-open **Route:** Intrarectal

**Main Findings**
- Immunization resulted in induction of virus-specific CD8+ and CD4+ responses in all vaccinees.
- Anamnestic nab responses against laboratory-adapted SIVmac251 developed after the challenge.
- No neutralizing antibodies against SIVmac239.
- Vaccinated animals had significantly reduced peak viremia compared with controls (P<0.01).
Most animals had gradual CD4 depletion and progressed to disease despite the induction of virus-specific CTL responses and reduced peak viral loads.

NHP.53  
**Crosslinked HIV-1 envelope-CD4 receptor complexes elicit broadly cross-reactive neutralizing antibodies in rhesus macaques**

**Authors**  

**Journal**  
Proc Natl Acad Sci U S A. 2002 Aug 21

**Objectives**  
Immunogenicity To evaluate the immunogenicity of crosslinked gp120-CD4 complexes in rhesus monkeys.

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Vaccine Name**  
Crosslinked gp120-CD4  
Type: Other  
Route: Intramuscular

**Main Findings**  
- The animals immunized with anti-env-CD4 exhibited a broad pattern of neutralization of primary viruses regardless of coreceptor usage and genetic subtype.
- anti-env-CD4 neutralization more biased toward primary isolates than laboratory adapted strains, unlike anti-env which neutralized only laboratory adapted strains.
- anti-Env-CD4 antisera failed to neutralize SHIV89.6, SHIV89.6P, and SHIVKU2 in the human PBMC-based assays and SIVmac239 in assays with either human or macaque PBMCs.

NHP.54  
**Vaccine protection against simian immunodeficiency virus by recombinant strains of herpes simplex virus**

**Authors**  

**Journal**  
J Virol 2000 Sep;74(17):7745-54

**Objectives**  
Challenge, Immunogenicity To develop and use replication-competent and replication-defective strains of recombinant herpes simplex virus (HSV) that express envelope and Nef antigens of SIV.

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Vaccine Name**  
K81  
Type: DNA  
Routes: Subcutaneous, Intramuscular

**Vaccine Name**  
d81  
Type: DNA  
Routes: Intradermal, Intramuscular

**Challenge**  
SIVmac239  
Route: Intrarectal

**Main Findings**  
- The HSV recombinants induced antienvelope antibody responses that persisted at relatively stable levels for months after the last administration.
- 2/7 rhesus vaccinated monkeys were solidly protected, and another showed a sustained reduction in viral load following rectal challenge with pathogenic SIVmac239 at 22 weeks following the last vaccine administration.

NHP.55  
**An effective AIDS vaccine based on live attenuated vesicular stomatitis virus recombinants**

**Authors**  
Rose NF, Marx PA, Luckay A, Nixon DF, Moretto WJ, Donahoe SM, Montefiori D, Roberts A, Buonocore L, Rose JK

**Journal**  
Cell 2001 Sep 7;106(5):539-49

**Objectives**  
Challenge, Immunogenicity To test live attenuated vesicular stomatitis virus vectors expressing SIV ?env and gag genes in rhesus monkeys.

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque), Macaca (sp)

**Vaccine Name**  
VSV-(GI)-Env  
Type: Recombinant Vector (virus/bacteria)  
Routes: Oral, Intramuscular

**Vaccine Name**  
VSV(GCh)-Env+Gag  
Type: Recombinant Vector (virus/bacteria)  
Routes: Oral, Intramuscular

**Vaccine Name**  
VSV(GNJ)-Env+Gag  
Type: Recombinant Vector (virus/bacteria)  
Routes: Oral, Intramuscular

**Challenge**  
SHIV89.6P  
Route: Intravenous

**Main Findings**  
- Vectors with glycoproteins from different VSV serotypes boosted response.
- 7/8 controls progressed to AIDS at about 148 dpc with severe loss of CD4+ T cells, high viral loads.
• 7/8 vaccinees infected with SHIV89.6P remained healthy up to 14 mpc (low or undetectable viral loads).

**NHP.56** (10229229) **Neutralizing antibody-independent containment of immunodeficiency virus challenges by DNA priming and recombinant pox virus booster immunizations**

**Authors** Robinson HL, Montefiori DC, Johnson RP, Manson KH, Kalish ML, Lifson JD, Rizvi TA, Lu S, Hu SL, Mazzara GP, Panicali DL, Herndon JG, Glickman R, Candido MA, Lydi SL, Wyand MS, McClure HM

**Journal** Nat Med 1999 May;5(5):526-34

**Objectives** Challenge, Immunogenicity To compare 8 different protocols for their ability to protect against immunodeficiency virus challenges in rhesus macaques.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- pRS102 - SIVmac239 gag-pol proteins
  - Type: DNA
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal
- pCMV/nef
  - Type: DNA
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal
- pJW4303/HXB-2.dpol
  - Type: DNA
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal
- pJW4303/HXB-2.gp140
  - Type: DNA
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal
- pJW4303/HXB-2.gp120
  - Type: DNA
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal
- Prt-env gp160
  - Type: Purified Viral Products
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal
- rFPV
  - Type: DNA
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular
- SHIV89.6P, SHIV-IIIB/HXB2
  - Route: Intravenous

**Main Findings**
- Intradermal DNA priming followed by recombinant fowl pox virus booster immunizations was a more efficient protocol in inducing immune response and containment of challenge infection than the gene gun inoculation method.

**NHP.57** (10438842) **Effective induction of simian immunodeficiency virus-specific cytotoxic T lymphocytes in macaques by using a multiepitope gene and DNA prime-modified vaccinia virus Ankara boost vaccination regimen**

**Authors** Hanke T, Samuel RV, Blanchard TJ, Neumann VC, Allen TM, Boyson JE, Sharpe SA, Cook N, Smith GL, Watkins DI, Cranage MP, McMichael AJ

**Journal** J Virol 1999 Sep;73(9):7524-32

**Objectives** Challenge, Immunogenicity To test multi-CTL epitope gene and a DNA prime-MVA boost vaccination regimen in rhesus macaques.

**Species/Subspecies** Macaca mulatta (Rhesus macaque), Macaca (sp)

**Vaccine Name**
- pTH.HW DNA
  - Type: DNA
  - Route: Intradermal (Gene Gun DNA-coated gold beads)
- MV A.HW
  - Type: Recombinant Vector (virus/bacteria)
  - Route: Intradermal
- SIVmac251
  - Route: Intrarectal

**Challenge** SIVmac251

**Main Findings**
- High SIV gag specific-CTL response by immunization, capable of killing SIV-infected cells in vitro.
- After intrarectal challenge with pathogenic SIVmac251, 2/3 vaccinated animals were infected.
- Correlates of protective immunity not defined.
- DNA prime-MVA boost regimen is an effective protocol for induction of CTLs in macaques.

**NHP.58** (11085589) **A vaccine strategy utilizing a combination of three different chimeric vectors which share specific vaccine antigens**


**Objectives** Immunogenicity Overcomes an anti-vector immune response with chimeric vectors that have in common only the specific antigens for immunization.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- DNA.PTH.SIVmac.J5.gptnr
  - Type: DNA
  - Route: Intradermal
- DNA.pND14-G1.SIVmac251.env
  - Type: DNA
  - Route: Intradermal
- MVA.pUCII.SIVmac.J5
  - Type: Recombinant Vector (virus/bacteria)
  - Routes: Intradermal, Intramuscular

Challenge: SIVmac32H.1Xc  Route: Intravenous

Main Findings:
- Anti-vector immune response to foreign genes of engineered vectors may preclude sufficient ‘priming’ or immunogenicity, or impair optimal ‘boosting’ upon repeated immunization.
- Describes a new strategy that avoids increased anti-vector responses, allows the use of combinations of vectors to present the same or related antigen differently to the immune system and at alternative sites.
- New strategy induces optimal type of immunity against the pathogen.

NHP.59  (10906202) Simian immunodeficiency virus (SIV) gag DNA-vaccinated rhesus monkeys develop secondary cytotoxic T-lymphocyte responses and control viral replication after pathogenic SIV infection


Journal: VIROLYS 2000 Aug;74(16):7485-95

Objectives: Challenge, Immunogenicity To use plasmid DNA construct to elicit protective immunity in SIV/macaque model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: V1R-SIV gag  Type: DNA  Route: Intramuscular

Challenge: SIVsmE660  Route: Intravenous

Main Findings:
- Soluble major histocompatibility class I/peptide tetramers and peptide-specific killing assays are used to monitor CD8(+) T-lymphocyte responses to a dominant SIV Gag epitope in rhesus monkeys.
- Codon-optimized SIV gag DNA vaccine construct elicits high-frequency SIV-specific CTL response in peripheral blood and lymph node lymphocytes.
- After IV challenge with SIVsm E660, gag plasmid DNA-vaccinated monkeys have better containment of viral replication by 50 dpc.

NHP.60.1  (11039923) Control of viremia and prevention of clinical AIDS in rhesus monkeys by cytokine-augmented DNA vaccination


Objectives: Challenge, Immunogenicity Reports the protective efficacy of vaccine-elicited immune responses against a pathogenic SHIV-89.6P challenge in rhesus monkeys.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239 gag DNA  Type: DNA  Route: Intramuscular

Vaccine Name: HIV-1.89.6P env DNA  Type: DNA  Route: Intramuscular

Challenge: SHIV89.6P  Route: Intravenous

Main Findings:
- The monkeys that received the DNA vaccines plus IL-2/Ig protein or IL-2/Ig plasmid demonstrated markedly higher vaccine-elicited CTL responses than the animals that received the DNA vaccines alone.
- All monkeys that received DNA vaccines augmented with IL-2/Ig were infected, demonstrated potent secondary CTL responses, stable CD4+ T cell counts, preserved virus-specific CD4+ T cell responses, low to undetectable setpoint viral loads, and no evidence of clinical disease or mortality by 140 dpc
- After the final immunization at week 40, the vaccinated monkeys developed significant circulating p11C- and p41A-specific CD8+ T lymphocytes, in contrast with the control monkeys that had no detectable circulating tetramer-positive CD8+ T lymphocytes.

NHP.60.2  (11797012) Eventual AIDS vaccine failure in a rhesus monkey by viral escape from cytotoxic T lymphocytes
### Trial Summaries

<table>
<thead>
<tr>
<th>NHP.60.3 (12021371)</th>
<th>Prior vaccination increases the epitopic breadth of the cytotoxic T-lymphocyte response that evolves in rhesus monkeys following a simian-human immunodeficiency virus infection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Santra S, Barouch DH, Kuroda MJ, Schmitz JE, Krivulka GR, Beaudry K, Lord CI, Lifton MA, Wyatt LS, Moss B, Hirsch VM, Letvin NL</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIVmac239 gag DNA Type: DNA</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>HIV-1.89.6P env DNA Type: DNA</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SHIV89.6P Route:</td>
</tr>
</tbody>
</table>
| **Main Findings**   | - rMVA vaccination elicited high-frequency CTL responses to dominant epitopes but with substantially lower frequency to subdominant epitopes.  
- Animals immunized with DNA plus IL-2/Ig plasmid showed higher frequency p41A-specific CTL responses than animals immunized with DNA alone and controls. |

<table>
<thead>
<tr>
<th>NHP.61 (11044096)</th>
<th>Effective induction of simian immunodeficiency virus-specific systemic and mucosal immune responses in primates by vaccination with proviral DNA producing intact but noninfectious virions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Wang SW, Kozlowski PA, Schmelz G, Manson K, Wyand MS, Glickman R, Montefiori D, Lifson JD, Johnson RP, Neutra MR, Aldovini A</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity Reports a pilot evaluation of a DNA vaccine producing genetically inactivated SIV particles in primates, focuses on eliciting mucosal immunity.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>pVacc1 DNA Type: DNA Routes: Intrarectal, Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SIVmac239 Route: Intrarectal</td>
</tr>
</tbody>
</table>
| **Main Findings**   | - IgA in rectal secretions of macaques that received the DNA vaccine intradermally and at the rectal mucosa are higher than in natural infection.  
- CTL responses were low and sporadic.  
- After rectal challenge with cloned SIVmac239, some animals with high SIV-specific IgA levels became infected.  
- High levels of IgA alone are not sufficient to prevent the establishment of chronic infection, although mucosal IgA responses may reduce the infectivity of the initial viral inoculum. |

<table>
<thead>
<tr>
<th>NHP.62 (11152527)</th>
<th>DNA vaccination with the human immunodeficiency virus type 1 SF162DeltaV2 envelope elicits immune responses that offer partial protection from simian/human immunodeficiency virus infection to CD8(+) T-cell-depleted rhesus macaques</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Cherpelis S, Shrivastava I, Gettie A, Jin X, Ho DD, Barnett SW, Stamatos L</td>
</tr>
<tr>
<td><strong>Journal</strong></td>
<td>J Virol 2001 Feb;75(3):1547-50</td>
</tr>
</tbody>
</table>
### Trial Summaries

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Challenge, Immunogenicity To conduct DNA immunization of macaques with the SF162V2 envelope, then challenge with SHIV162P4.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species/Subspecies</td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>DNA.SF162AV2 gp410  Type: DNA  Routes: Intradermal, Intramuscular</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>SF162AV2 gp410 protein  Type: Recombinant Subunit Protein  Routes: Intradermal, Intramuscular</td>
</tr>
<tr>
<td>Challenge</td>
<td>SHIV162P4  Route: Intravenous</td>
</tr>
</tbody>
</table>

**Main Findings**

- Immunization elicited lymphoproliferative responses and potent neutralizing antibodies.
- Animals were depleted of their CD8+ T lymphocytes and then challenged intravenously with SHIV162P4.
- Compared to unvaccinated animals, vaccinated macaques had lower peak viremia levels, rapidly cleared plasma virus, and delayed seroconversion.

---

**NHP.63** (11884556) **Induction of mucosal protection against primary, heterologous simian immunodeficiency virus by a DNA vaccine**

| Authors | Fuller DH, Rajakumar PA, Wilson LA, Trichel AM, Fuller JT, Shipley T, Wu MS, Weis K, Rinaldo CR, Haynes JR, Murphey-Corb M |
| Journal | J Virol 2002 Apr;76(7):3309-17 |
| Objectives | Challenge, Immunogenicity To analyze immunogenicity and protective efficacy of a DNA vaccine containing SIV strain 17E-Fr (SIV/17E-Fr) gag-pol-env in rhesus macaques. |
| Species/Subspecies | Macaca mulatta (Rhesus macaque) |
| Vaccine Name | SIV/17E-Fr gag-pol-env  Type: DNA  Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal |
| Challenge | SIVDeltaB670  Route: Intrarectal |

**Main Findings**

- First report of mucosal protection against a primary pathogenic, heterologous isolate of SIV using a commercially viable vaccine approach.
- Vaccinated and naive control monkeys were challenged intrarectally with SIV strain DeltaB670 (SIV/DeltaB670), whose env is 15% dissimilar to that of the vaccine strain.
- Postchallenge, in 4/7 vaccinees no SIV viral RNA or DNA sequences were found in the peripheral blood, and anamnestic antibody responses were absent.

---

**NHP.64** (11085583) **Mucosal challenge of Macaca nemestrina with simian immunodeficiency virus (SIV) following SIV nucleocapsid mutant DNA vaccination**

| Objectives | Challenge, Immunogenicity  |
| Species/Subspecies | Macaca nemestrina (pigtailed macaque) |
| Vaccine Name | SIV(Mne)NC  Type: Live Attenuated Virus  Route: Intramuscular |
| Vaccine Name | S8-NCZF2  Type: Live Attenuated Virus  Routes: Subcutaneous, Intramuscular |
| Challenge | SIV(Mne) clone E11S  Route: Intrarectal |

**Main Findings**

- Challenged mucosally, all 12 macaques became infected, the 4 immunized animals greatly restricted their viral replication.
- One immunized animal that controlled replication remains antibody negative, no disease evident 46 wpc.

---

**NHP.65.1** (11090194) **Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost**

| Objectives | Challenge, Immunogenicity To evaluate SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost. |
| Species/Subspecies | Macaca nemestrina (pigtailed macaque) |
| Vaccine Name | SIV(Mne)NCZF2 DNA  Type: Live Attenuated Virus  Route: Intramuscular |
Vaccine Name | SIV(Mne) gp160Env protein | Type: Recombinant Subunit Protein | Route: Intramuscular
---|---|---|---
Vaccine Name | Gag-Pol particles | Type: Recombinant Subunit Protein | Route: Intramuscular
Challenge | SIV(Mne) clone E11S | Route: Intravenous

Main Findings
- Background: 11 pigtailed macaques were inoculated with nucleocapsid mutant SIV expressing DNA, intramuscularly (i.m.) in one study and i.m. and subcutaneously in another study. Six control animals received vector DNA lacking SIV sequences.
- Post IV challenge, all control animals became infected and 3/4 developed progressive SIV disease.
- 2 ypc, most immunized animals had low postacute levels of plasma SIV RNA, no CD4+ T-cell depletion or clinical evidence of progressive disease (see experiment 2 for additional information).

NHP.65.2 (11090194) Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost

Objectives | Challenge, Immunogenicity
Species/Subspecies | Macaca nemestrina (pigtailed macaque)
Vaccine Name | SIV(Mne)NC ∆ZF2 DNA | Type: Live Attenuated Virus | Routes: Subcutaneous, Intramuscular
Vaccine Name | S8-NC ∆ZF2 | Type: Live Attenuated Virus | Routes: Subcutaneous, Intramuscular
Challenge | SIV(Mne) clone E11S | Route: Intravenous

Main Findings
- The vaccine induced only modest and inconsistent humoral responses and no cellular immune responses prior to challenge.
- Following iv challenge with 20 animal infectious doses of the pathogenic SIV(Mne) in a long-term study, all control animals became infected and 3/4 animals developed progressive SIV disease leading to death.
- All 11 NC mutant SIV DNA-immunized animals became infected following challenge but decreased initial peak plasma SIV RNA levels compared to those of control animals.

NHP.66 (11689679) Vaccination with attenuated simian immunodeficiency virus by DNA inoculation

Authors | Kent SJ, Dale CJ, Preiss S, Mills J, Campagna D, Purcell DF
Journal | J Virol 2001 Dec;75(23):11930-4
Objectives | Challenge, Immunogenicity To evaluate attenuated proviral DNA vaccine in macaques.
Species/Subspecies | Macaca nemestrina (pigtailed macaque)
Vaccine Name | SIVmac239 sbbvΔ3 DNA | Type: DNA | Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular
Vaccine Name | SIVmac239 sbbvΔ3Delta5 DNA | Type: DNA | Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular
Challenge | SIVmac251 | Route: Intrarectal

Main Findings
- Innoculated with wild-type simian immunodeficiency virus strain mac239 (SIV(mac239)) DNA or SIV(mac239) DNA containing a single deletion in the 3’ nef-long terminal repeat overlap region (nef/LTR) led to sustained SIV infections and AIDS.
- Injection of SIV(mac239) DNA containing identical deletions in both the 5’ LTR and 3’ nef/LTR resulted in attenuated SIV infections and substantial protection against subsequent mucosal SIV(mac251) challenge.

NHP.67 (10869776) Induction of protective immunity against pathogenic simian immunodeficiency virus by a foreign receptor-dependent replication of an engineered avirulent virus

Authors | Matano T, Kano M, Odawara T, Nakamura H, Takeda A, Morikawa M, Sato T, Nagai Y
Journal | Vaccine 2000 Aug 1;18(28):3310-8
## Trial Summaries

### NHP.68 (11118363)
**Induction of immune responses and break of tolerance by DNA against the HIV-1 coreceptor CCR5 but no protection from SIVsm challenge**

**Authors**

**Journal**
Virology 2000 Dec 20;278(2):400-11

**Objectives**
Challenge, Immunogenicity To explore genetic immunization to induce an immune response directed to CCR5 structures and break immunological tolerance toward endogenous CCR5.

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**
- pcDNA3-CCR5  
  Type: DNA  
  Route: Intradermal (Gene Gun DNA-coated gold beads)
- pcDNA3–tet.CCR5  
  Type: DNA  
  Route: Intradermal (Gene Gun DNA-coated gold beads)
- CCR5 peptides  
  Type: Synthetic Protein/Peptide  
  Route: Intramuscular

**Challenge**
SIVsm  
Route: Intrarectal

**Main Findings**
- Intramucosal immunization of cynomolgus macaques with CCR5 DNA followed by boosts with CCR5 peptides induced prominent IgG and IgA antibody responses.
- The CCR5-specific antibodies neutralized the infectivity of primary human R5 HIV-1 strains, and the macaque SIVsm.
- CCR5 gene and CCR5 peptide immunizations induced B- and T-cell responses.
- Tolerance was broken against endogenous macaque CCR5.
- Neither protection against nor enhancement of SIVsm infection was achieved.

### NHP.69 (10894297)
**Elicitation of protective immunity against simian immunodeficiency virus infection by a recombinant Sendai virus expressing the Gag protein**

**Authors**

**Journal**
AIDS 2000 Jun 16;14(9):1281-2

**Objectives**
Challenge, Immunogenicity To use recombinant SeV expressing the Gag antigen of SIV, SeV/SIVgag, to elicit protective immunity.

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**
SeV-gag  
Type: DNA  
Route: Intranasal

**Challenge**
SIVmac239  
Route: Intravenous

**Main Findings**
- The vaccinated animals and controls were all infected by the challenge virus SIVmac239. Only animals immunized with SeV-SIV-gag were able to control infection by reducing the viral load to below detectable level.

### NHP.70 (11689672)
**Rapid appearance of secondary immune responses and protection from acute CD4 depletion after a highly pathogenic immunodeficiency virus challenge in macaques vaccinated with a DNA prime/Sendai virus vector boost regimen**

**Authors**
Matano T, Kano M, Nakamura H, Takeda A, Nagai Y

**Journal**
J Virol 2001 Dec;75(23):11891-6
**Objectives**
Challenge, Immunogenicity To test the immunogenicity and protective effect of a SHIV-DNA prime vaccine followed by a single booster with a Gag-expressing Sendai virus (SeV-Gag).

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
SeV-gag
*Type:* DNA
*Route:* Intranasal

**Vaccine Name**
FMSIV
*Type:* DNA
*Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

**Challenge**
SHIV89.6PD
*Route:* Intravenous

**Main Findings**
- All naive control macaques showed acute CD4(+) T-cell depletion at 2 wpc (iv SHIV89.6PD).
- All vaccinated macaques with prime/boost regimen were protected from depletion and showed greatly reduced peak viral loads.
- Vaccination with DNA alone or SeV-Gag alone did not confer protection.
- Differences in secondary responses between the protected and unprotected macaques was clear at 1 wpc.
- Rapid secondary responses reduce peak viral loads and protect from acute CD4(+) T-cell depletion.

---

**NHP.71 (10983638) Therapeutic immunization of HIV-infected chimpanzees using HIV-1 plasmid antigens and interleukin-12 expressing plasmids**

**Authors**

**Journal**

**Objectives**
Immunogenicity, Immunotherapy To assess HIV-1 DNA vaccination and co-immunization with interleukin (IL)-12 and IL-10 as immunotherapy in the HIV-1 infected chimpanzee model system.

**Species/Subspecies**
Pan Troglodytes (Chimpanzee)

**Vaccine Name**
pCMN160 (HIV-1 MN env)
*Type:* DNA
*Route:* Intramuscular

**Vaccine Name**
pCGag/Pol
*Type:* DNA
*Routes:* Intramuscular

**Challenge**
HIV-1 IIIB
*Route:*

**Main Findings**
- No evidence of systemic toxicity associated with DNA immunization or the cytokine-expressing plasmids.
- IL-12/HIV-1 DNA vaccinated animals enhanced proliferative responses to multiple HIV-1 antigens at multiple time points.
- Animal co-immunized with HIV-1 and IL-10 did not have any changes in the proliferative responses.
- Control chimpanzee demonstrated moderate increases in the proliferative responses to HIV-1 antigens.

---

**NHP.72 (9971763) Acute effects of pathogenic simian-human immunodeficiency virus challenge on vaccine-induced cellular and humoral immune responses to Gag in rhesus macaques**

**Authors**
Steger KK, Waterman PM, Pauza CD

**Journal**

**Objectives**
Challenge, Immunogenicity To test immunization with recombinant Salmonella typhimurium (expressing Gag) or soluble Gag in adjuvant, by challenge with SHIV89.6PD (macaques).

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
SIVhu
*Type:* Live Attenuated Virus
*Routes:* Intra gastric, Intramuscular

**Challenge**
SHIV89.6PD
*Route:* Intrarectal

**Main Findings**
- Virus infection accompanied by rapid losses of lymphoproliferative responses to Gag or phytohemagglutinin.
- 8 wpc mitogen responses recovered to near normal levels but antigen-specific immunity remained low or undetectable.
- Serum antibody levelselevated initially but soon dropped well below levels achieved by immunization.
- Rapid depletion of preexisting Gag-specific CD4(+) T cells prevent or limit subsequent antiviral cellular and humoral immune responses during acute SHIV infection.
**NHP.73** (10461832) Combined systemic and mucosal immunization with microsphere-encapsulated inactivated simian immunodeficiency virus elicits serum, vaginal, and tracheal antibody responses in female rhesus macaques  
*Authors* Israel ZR, Gettie A, Ishizaka ST, Mishkin EM, Staas J, Gilley R, Montefiori D, Marx PA, Eldridge JH  
*Objectives* Challenge, Immunogenicity To determine the efficacy of immunization with microsphere-encapsulated whole inactivated SIV by combined systemic and mucosal administration to protect female rhesus macaques against vaginal challenge.  
*Species/Subspecies* Macaca mulatta (Rhesus macaque)  
*Vaccine Name* SIVmac251. whole inactivated  
*Type:* Whole (killed) Inactivated Virus  
*Routes:* Intratracheal, Oral, Intramuscular  
*Challenge* SIVmac251  
*Routen:* Vaginal or perivaginal  
*Main Findings*  
- Intramuscular priming resulted in strong IgG and modest IgA response.  
- Intratracheal boosting following intramuscular priming resulted in high bronchial alveolar wash IgG and less pronounced IgA.  
- IgG was present in the animals immunized intramuscularly boosted either intramuscularly or intratracheally.  
- No neutralizing antibody to homologous SIVmac251 in response to the immunization with the whole inactivated SIV vaccine.  
- On vaginal challenge none of the immunized groups was infected at a lesser frequency than the unimmunized controls.

**NHP.74** (10438051) Induction of mucosal antibody responses by microsphere-encapsulated formalin-inactivated simian immunodeficiency virus in a male urethral challenge model  
*Authors* Ishizaka ST, Israel ZR, Gettie A, Mishkin EM, Staas JK, Gilley RM, Dailey PJ, Montefiori DC, Marx PA, Eldridge JH  
*Journal* Vaccine 1999 Jul 16;17(22):2817-25  
*Objectives* Challenge, Immunogenicity To test use of microsphere-encapsulated formalin-inactivated SIV particles against mucosal SIV challenge.  
*Species/Subspecies* Macaca mulatta (Rhesus macaque)  
*Vaccine Name* Whole inactivated SIVmac239 (encapsulated)  
*Type:* Whole (killed) Inactivated Virus  
*Routes:* Intratracheal, Intramuscular  
*Challenge* SIVmac251  
*Routen:* Urethral  
*Main Findings*  
- Macaques, primed intramuscularly, boosted tracheally, had strong Iga response to SIV vaccine.  
- The bulk of antibody response was against non-envelope epitopes.  
- No neutralizing antibody observed.  
- Intraurethral challenge with cell-free rhesus-grown virus showed no evidence of protection against challenge.  
- Microsphere-based immunization raises local and system responses, but does not provide sufficient immunity to protect against mucosal challenge.

**NHP.75** (10074183) Comparison of immunity generated by nucleic acid-, MF59-, and ISCOM-formulated human immunodeficiency virus type 1 vaccines in Rhesus macaques: evidence for viral clearance  
*Objectives* Challenge, Immunogenicity To compare the kinetics of T-helper immune responses in rhesus monkeys by 3 HIV vaccine strategies: a rgp120SF2 expressed in vivo by DNA immunization or when it was delivered as a subunit protein vaccine formulated with the MF59 adjuvant or by ISCOMs.  
*Species/Subspecies* Macaca mulatta (Rhesus macaque)  
*Vaccine Name* pUCgp120SF2-gold particle  
*Type:* DNA  
*Routen:* Intradermal (Gene Gun DNA-coated gold beads)  
*Vaccine Name* HIV-1SF2 rgp120  
*Type:* Recombinant Subunit Protein  
*Routen:* Intramuscular  
*Main Findings*  
- Virus-neutralizing antibodies against HIV-1SF2 reached similar titers in the two rgp120SF2 protein-immunized groups, with different kinetics, while nab were delayed and low in the DNA-immunized animals.
• rgp120/ISCOM-immunized animals rapidly developed marked IL-2, IFN-gamma (type 1-like), and IL-4 responses that peaked after the second immunization.
• Protection challenge with SHIV was observed in the two groups receiving the rgp120 subunit vaccines. Half of the animals in the ISCOM group were completely protected from infection.

NHP.76 (1708168) **Recombinant virus vaccine-induced SIV-specific CD8+ cytotoxic T lymphocytes**

**Authors** Shen L, Chen ZW, Miller MD, Stallard V, Mazzara GP, Panicali DL, Letvin NL

**Journal** Science 1991 Apr 19;252(5004):440-3

**Objectives** Immunogenicity To determine whether a genetically restricted live recombinant virus, the vaccinia-simian immunodeficiency virus of macaques (SIVmac) could generate a T lymphocyte-mediated antiviral response in a primate.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** rVaccinia-SIVmac-env.gagpol

**Type:** Recombinant Vector (virus/bacteria)  **Route:** Intradermal

**Main Findings**
• Vaccinia-SIVmac vaccination elicited an SIVmac Gag-specific, CD8+ CTL response in rhesus monkeys.
• The rhesus monkey major histocompatibility complex (MHC) class I gene product restricting this CTL response was defined.
• Both the vaccinated and control SIVmac-infected monkeys that shared this MHC class I gene product developed CTLs with the same Gag epitope specificity.
• The findings support the use of recombinant virus vaccines for the prevention of HIV infections in humans.

NHP.77 (10506654) **Accelerated clearance of SHIV in rhesus monkeys by virus-like particle vaccines is dependent on induction of neutralizing antibodies**

**Authors** Notka F, Stahl-Hennig C, Dittmer U, Wolf H, Wagner R

**Journal** Vaccine 1999 Sep;18(3-4):291-301

**Objectives** Challenge, Immunogenicity To investigate efficacy of recombinant, insect cell derived SIV Pr56(gag) virus-like particles modified either by inserting HIV-1 Gp160 derived peptides into the Pr56(gag) precursor or by integrating the complete HIV-1 gp120 in the particle membrane.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** SIV Pr56gag VLP-type II

**Type:** Virus-like Particle  **Route:** Intravenous

**Vaccine Name** SFV-Pr56gag VLP-type II

**Type:** Live Virus  **Route:** Intravenous

**Vaccine Name** SFV-SIV Pr56gag VLP-type I

**Type:** Virus-like Particle  **Route:** Intravenous

**Challenge** SHIV-4.vpu+

**Route:** Intravenous

**Main Findings**
• All vaccinated monkeys became infected upon challenge with SHIV-4, but animals vaccinated with VLPs presenting the complete gp120 cleared virus faster than nonimmunized controls.
• Observed virus elimination significantly correlated with an anamnestic antibody response and accelerated appearance of neutralizing antibodies postchallenge.

NHP.78 (10725402) **Vaccination with tat toxoid attenuates disease in simian/HIV-challenged macaques**


**Objectives** Challenge, Immunogenicity To study the role of tat by immunizing macaques with chemically inactivated tat toxoid and challenging animals intrarectally with SHIV89.6PD.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** inactivated Tat toxoid

**Type:** Other  **Routes:** Intradermal, Intramuscular

**Vaccine Name** rVaccinia-gp160

**Type:** Recombinant Vector (virus/bacteria)  **Route:** Intradermal

**Vaccine Name** soluble gp160

**Type:** Purified Viral Products  **Route:** Intramuscular

**Vaccine Name** biologically active Tat protein

**Type:** Purified Viral Products  **Routes:** Intradermal, Intramuscular
### Trial Summaries

#### SHIV89.6PD

**Challenge**: Intrarectal  
**Main Findings**

- Immune animals had significantly attenuated disease with lowered viral RNA, interferon-Alpha, and chemokine receptor expression (CXCR4 and CCR5) on CD4+ T cells, features linked to in vitro effects of Tat.
- Immunization with Tat toxoid inhibits key steps in viral pathogenesis.

#### NHP.79 (10936096)

**Evaluation of immune responses induced by HIV-1 gp120 in rhesus macaques: effect of vaccination on challenge with pathogenic strains of homologous and heterologous simian human immunodeficiency viruses**

**Authors**: Kumar A, Lifson JD, Silverstein PS, Jia F, Sheffer D, Li Z, Narayan O  
**Journal**: Virology 2000 Aug 15;274(1):149-64  
**Objectives**: Challenge, Immunogenicity  
**Species/Subspecies**: Macaca mulatta (Rhesus macaque)  
**Vaccine Name**: Monomeric rgp120  
**Type**: Recombinant Subunit Protein  
**Challenge**: SHIV-KU2, SHIV89.6P  
**Route**: Intradermal  
**Main Findings**

- All 8 vaccinated macaques developed high antibody titers against rgp120 that reacted efficiently with envelope proteins of homologous SHIVKU-2 and poorly with the SHIV89.6P envelope.  
- Vaccinated macaques showed anamnestic antibody and T-helper cell responses, but T-helper responses were short-lived.  
- After challenge, level of productive virus replication was indistinguishable between vaccine and control groups, suggesting that rgp120 did not confer protection against virus replication.

#### NHP.80 (10756013)

**Evidence for viral virulence as a predominant factor limiting human immunodeficiency virus vaccine efficacy**

**Authors**: Mooij P, Bogers WM, Oostermeijer H, Koornstra W, Ten Haaf P, Verstrepen BE, Van Der Auwera G, Heeney JL  
**Journal**: J Virol 2000 May;74(9):4017-27  
**Objectives**: Challenge, Immunogenicity  
**Species/Subspecies**: Macaca mulatta (Rhesus macaque)  
**Vaccine Name**: rgp120W6.1D  
**Type**: Recombinant Subunit Protein  
**Challenge**: SHIV.W6.1D, SHIV.SF13, SHIVHan2, SHIV89.6P  
**Route**: Intravenous  
**Main Findings**

- Protection from either of the divergent SHIVsf13 or SHIVhan2 challenges was demonstrated in the majority of the vaccinated animals.  
- Second challenge with the virulent SHIV89.6p achieved protection in only one of the previously protected vaccinees.  
- Immunization beneficial to viral load and CD4+ T-cell counts, but failed to protect from infection.

#### NHP.81 (11689887)

**Protection of rhesus macaques against disease progression from pathogenic SHIV-89.6PD by vaccination with phage-displayed HIV-1 epitopes**

**Objectives**: Challenge, Immunogenicity  
**Species/Subspecies**: Macaca mulatta (Rhesus macaque)  
**Vaccine Name**: gp120/gp41 mimotopes  
**Type**: Synthetic Protein/Peptide  
**Challenge**: SHIV89.6PD  
**Route**: Intravenous  
**Main Findings**

- Upon intravenous challenge with 60 MID50 of pathogenic SHIV-89.6PD, phage-borne epitopes elicit envelope-specific antibody responses.
• 4/5 mimotope-immunized monkeys had lower levels of peak viremia, followed by viral set points of undetectable or transient levels of viremia, mild decline of CD4+ T cells, protection from progression to AIDS-like illness.

**NHP.82.1** (10196297) Protection of Macaques against pathogenic simian/human immunodefi ciency virus 89.6PD by passive transfer of neutralizing antibodies


**Objectives** Challenge, Immunogenicity Used a chimeric SHIV based on the envelope of a primary isolate (HIV-89.6) to perform passive-transfer experiments and study the role of anti-envelope antibodies in protection (rhesus macaques).

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- Monoclonal antibody 2G12  Type: Passive Antibody  Route: Intravenous
- Monoclonal antibody 2F5  Type: Passive Antibody  Route: Intravenous
- HIVIG  Type: Passive Antibody  Route: Intravenous

**Challenge** SHIV89.6PD  Route: Intravenous

**Main Findings**
- 3/6 animals given HIVIG/2F5/2G12 were completely protected; the remaining 3 animals became SHIV infected but displayed reduced plasma viremia and near normal CD4(+)-cell counts.
- 1/3 monkeys given 2F5/2G12 exhibited only transient evidence of infection; 2/3 had marked reductions in viral load.
- All monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia.
- General correlation between in vitro neutralization and protection.

**NHP.82.2** (10196297) Protection of Macaques against pathogenic simian/human immunodefi ciency virus 89.6PD by passive transfer of neutralizing antibodies


**Objectives** Challenge, Immunogenicity, Passive Immunization Used a chimeric SHIV based on the envelope of a primary isolate (HIV-89.6) to perform passive-transfer experiments and study the role of anti-envelope antibodies in protection.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- Monoclonal antibody 2G12  Type: Passive Antibody  Route: Intravenous
- Monoclonal antibody 2F5  Type: Passive Antibody  Route: Intravenous
- HIVIG  Type: Passive Antibody  Route: Intravenous

**Challenge** SHIV89.6PD  Route: Intravenous

**Main Findings**
- 3/6 animals given HIVIG/2F5/2G12 were completely protected; the remaining 3 animals became SHIV infected but displayed reduced plasma viremia and near normal CD4(+)-cell counts.
- 1/3 monkeys given 2F5/2G12 exhibited only transient evidence of infection; 2/3 had marked reductions in viral load.
- All monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia.
- General correlation between in vitro neutralization and protection.

**NHP.83** (10772996) Passive infusion of immune serum into simian immunodeficiency virus-infected rhesus macaques undergoing a rapid disease course has minimal effect on plasma viremia

**Authors** Binley JM, Clas B, Gettie A, Vesanen M, Montefiori DC, Sawyer L, Booth J, Lewis M, Marx PA, Bonhoeffer S, Moore JP


**Objectives** Immunotherapy, Passive Immunization To investigate the role of passive immunization in controlling viremia and disease progression in infected macaques.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- SIVIG-1  Type: Passive Antibody  Route: Intravenous
- SIVIG-2  Type: Passive Antibody  Route: Intravenous

**Main Findings**
- Despite restoring anti-SIV titers to levels typical of macaques with a normal disease course, SIVIG had only a modest effect on plasma SIV RNA and cell-associated viral load.
- The kinetics of the viremia changes are inconsistent with neutralization of new cycles of infection. More likely, perhaps unexpectedly, is that infused antibodies killed SIV-infected cells, via an effector mechanism such as antibody-dependent cellular cytotoxicity.
### NHP.84 (10468614)

**Authors**

**Journal**
Proc Natl Acad Sci U S A 1999 Aug 31;96(18):10367-72

**Objectives**
Immunotherapy To evaluate neutralizing activity of mAb B4, a monoclonal antibody directed against HIV receptor complex.

**Species/Subspecies**
Pan Troglodytes (Chimpanzee)

**Vaccine Name**
mAb B4 Type: Passive Antibody

**Challenge**
HIV-1.DH12 Route: Intravenous

**Main Findings**
- mAb B4 preferentially neutralized primary HIV-1 isolates, including syncytium-inducing(si) and non-si phenotypes, for subtypes A-G and HIV-2, SIV, SHIV.
- Neutralization demonstrated in both pre- and postinfection models.
- Administration of mAb B4 after infectious challenge totally interrupted the infection of hu-PBL-severe combined immunodeficient mice by PBL-grown HIV-1 and the infection of chimpanzees by chimp-adapted HIV-1.

### NHP.85 (10655110)

**Authors**

**Journal**
Nat Med 2000 Feb;6(2):200-6

**Objectives**
Challenge, Passive Immunization To evaluate triple combination of the human IgG1 monoclonal antibodies F105, 2G12 and 2F5, which neutralize SHIV-vpu+, a chimeric simian-human virus that encodes the env gene of HIV-IIIB, to develop immunoprophylaxis against intrapartum HIV-1 transmission.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
F105/2G12/2F5 mab Type: Passive Antibody Route: Intravenous

**Challenge**
SHIV-vpu+ Route: Intravenous, Oral

**Main Findings**
- Four pregnant macaques treated with a triple combination of mab F105, 2G12 and 2F5 were protected from SHI-vpu+ challenge.
- Infants treated with the mab triple combination at birth and challenged orally: no evidence of infection in any infant during 6 months of follow-up.
- Epitopes recognized by the three monoclonal antibodies are important determinants for achieving substantial protection.

### NHP.86.1 (9930869)

**Authors**

**Journal**
Nat Med 1999 Feb;5(2):204-10

**Objectives**
Challenge, Passive Immunization To assess whether HIV-1 envelope-specific antibodies confer resistance against primate lentivirus infections (pigtailed macaques).

**Species/Subspecies**
Macaca nemestrina (pigtailed macaque)

**Vaccine Name**
- Anti-HIV-1 ch4750 Type: Passive Antibody Route: Intravenous
- Anti-HIV-1 ch1206 Type: Passive Antibody Route: Intravenous
- Anti-HIV-1 ch911 Type: Passive Antibody Route: Intravenous

**Challenge**
SHIV-MD14YE (DH12) Route: Intravenous

**Main Findings**
- In pigtailed macaques passively immunized with HIV-1 specific antibodies from chimpanzees, anti-SHIV neutralizing activity is the absolute requirement for antibody-mediated protection.
- Titers in plasma for complete protection of SHIV-challenged macaques in range of 1:5-1:8.
- HIV-1-specific nab studied are able to bind to native gp120 present on infectious virus particles.
- Administration of non-neutralizing anti-HIV IgG neither inhibited nor enhanced a subsequent SHIV infection.

### NHP.86.2 (9930869)
**Neutralizing antibody directed against the HIV-1 envelope glycoprotein can completely block HIV-1/SIV chimeric virus infections of macaque monkeys**

**Authors** Shibata R, Igarashi T, Haigwood N, Buckler-White A, Ogert R, Ross W, Willey R, Cho MW, Martin MA  
**Journal** Nat Med 1999 Feb;5(2):204-10  
**Objectives** Challenge, Immunogenicity, Passive Immunization  
**Species/Subspecies** Macaca nemestrina (pigtailed macaque)  
**Vaccine Name** Anti-HIV-1 ch1206  
**Type** Passive Antibody  
**Route** Intravenous

**Challenge** SHIV-MD14YE (DH12)  
**Route** Intravenous

### NHP.87 (10082123)
**Passively administered neutralizing serum that protected macaques against infection with parenterally inoculated pathogenic simian-human immunodeficiency virus failed to protect against mucosally inoculated virus**

**Objectives** Challenge, Immunogenicity, Passive Immunization  
To determine whether passive immunization with neutralizing serum would protect macaques against infection with pathogenic SHIV following oral inoculation of the virus.

**Species/Subspecies** Macaca nemestrina (pigtailed macaque)  
**Vaccine Name** Anti-SHIV Plasma  
**Type** Passive Antibody  
**Route** Intravenous

**Challenge** SHIV-KU1  
**Route** Oral

**Main Findings**  
- Ten pigtail macaques were inoculated orally with one animal infectious dose of SHIV(KU-1). Four of the 10 had been given pooled anti-SHIV plasma (15 ml/kg) 24 hr earlier, 4 others were given the same dose of anti-SHIV plasma 2 hr after virus challenge, and the 2 remaining animals were used as controls.  
- The neutralizing antibodies failed to protect macaques against infection after mucosal challenge with SHIV(KU-1).

### NHP.88 (11907251)
**Tat-vaccinated macaques do not control simian immunodeficiency virus SIVmac239 replication**

**Objectives** Challenge, Immunogenicity  
To assess the role of Tat-specific CTL in controlling pathogenic SIVmac239 replication after using a DNA-prime, vaccinia virus Ankara-boost vaccine regimen.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Vaccine Name** MVA-SIV239tat  
**Type** Recombinant Vector (virus/bacteria)  
**Route** Intradermal

**Vaccine Name** MVA-SIVSL8-tat28-35  
**Type** Recombinant Vector (virus/bacteria)  
**Route** Intradermal

**Vaccine Name** MVA-SIV251 32H tat  
**Type** Recombinant Vector (virus/bacteria)  
**Routes** Intrarectal, Intradermal

**Challenge** SIVmac239  
**Route** Intrarectal

**Main Findings**  
- Despite the induction of Tat-specific CTL, there was no significant reduction in either peak or viral set point in animals immunized with a DNA-prime, vaccinia virus Ankara-boost vaccine regimen and challenged with SIVmac239 compared to controls.

### NHP.89 (12021347)
**Critical role for Env as well as Gag-Pol in control of a simian-human immunodeficiency virus 89.6P challenge by a DNA prime/recombinant modified vaccinia virus Ankara vaccine**

**Authors** Amara RR, Smith JM, Staprans SI, Montefiori DC, Villinger F, Altman JD, O’Neil SP, Kozyr NL, Xu Y, Wyatt LS, Earl PL, Herndon JG, McNicholl JM, McClure HM, Moss B, Robinson HL
Vaccines

**Trial Summaries**

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Challenge, Immunogenicity To test Gag-Pol DNA priming and Gag-Pol rMVA boosting to evaluate the contribution of anti-Env immune responses to viral control.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species/Subspecies</td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>pGAL-gag-pol DNA vaccine Type: DNA Routes: Intradermal (Gene Gun DNA-coated gold beads), Intradermal</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>rMVA SIV239 gag-pol Type: Recombinant Vector (virus/bacteria) Routes: Intradermal, Intramuscular</td>
</tr>
<tr>
<td>Challenge</td>
<td>SHIV89.6P Route: Intrarectal</td>
</tr>
<tr>
<td>Main Findings</td>
<td>• Gag-specific T cell response to a gag-pol DNA vaccine was similar to those raised against the gag-pol-env vaccine and were capable of controlling challenge infection with SHIV89.6P.</td>
</tr>
<tr>
<td></td>
<td>• The control of the SHIV 89.6P challenge was delayed and inconsistent in the Gag-Pol-vaccinated group and all of the animals underwent severe and, in most cases, sustained loss of CD4(+) cells.</td>
</tr>
<tr>
<td></td>
<td>• Most of the lost CD4(+) cells in the Gag-Pol-vaccinated group were uninfected cells, suggesting that the rapid appearance of binding antibody for Env in Gag-Pol-Env-vaccinated animals helped protect uninfected CD4(+) cells from Env-induced apoptosis.</td>
</tr>
</tbody>
</table>

**NHP90.1** (12009868) **Comparison of vaccine strategies using recombinant env-gag-pol MVA with or without an oligomeric Env protein boost in the SHIV rhesus macaque model**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Earl PL, Wyatt LS, Montefiori DC, Bilksa M, Woodward R, Markham PD, Malley JD, Vogel TU, Allen TM, Watkins DI, Miller N, Moss B</th>
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<tbody>
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<td>Journal</td>
<td>Virology 2002 Mar 15;294(2):270-81</td>
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<td>Objectives</td>
<td>Challenge, Immunogenicity .</td>
</tr>
<tr>
<td>Species/Subspecies</td>
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</tr>
<tr>
<td>Vaccine Name</td>
<td>rMVASIV239gagpol.HIV89.6env Type: Recombinant Vector (virus/bacteria) Route: Intramuscular</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Oligomeric HIV-1.89.6 gp140 Type: Recombinant Subunit Protein Route: Intramuscular</td>
</tr>
<tr>
<td>Challenge</td>
<td>SHIV89.6 Route: Intravenous</td>
</tr>
<tr>
<td>Main Findings</td>
<td>• All control and vaccinated animals except one became infected. However, the levels of viremia were as follows: controls &gt; rMVA alone &gt; rMVA &gt; protein. The differences were statistically significant between immunized and control groups but not between the two immunized groups.</td>
</tr>
<tr>
<td></td>
<td>• A relationship between vaccine-induced antibody titers and reduction in virus burden was observed.</td>
</tr>
</tbody>
</table>

**NHP90.2** (12009868) **Comparison of vaccine strategies using recombinant env-gag-pol MVA with or without an oligomeric Env protein boost in the SHIV rhesus macaque model**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Earl PL, Wyatt LS, Montefiori DC, Bilksa M, Woodward R, Markham PD, Malley JD, Vogel TU, Allen TM, Watkins DI, Miller N, Moss B</th>
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<tr>
<td>Challenge</td>
<td>SHIV89.6P Route: Intravenous</td>
</tr>
<tr>
<td>Main Findings</td>
<td>• All animals became infected.</td>
</tr>
<tr>
<td></td>
<td>• The vaccinated group exhibited a 5-fold reduction in peak viremia and a 10-fold reduction in the postacute phase viremia in comparison to the controls.</td>
</tr>
<tr>
<td></td>
<td>• All of the controls required euthanasia by 10 mpc. A relationship between vaccine-induced antibody titers and reduction in virus burden was observed in both studies.</td>
</tr>
</tbody>
</table>
• Immunization with MVA/SHIV89.6 alone or with a protein boost stimulated both arms of the immune system and resulted in significant control of viremia and delayed progression to disease after challenge with SHIV-89.6P

NHP.92 (12111421) Characterization of simian and human immunodeficiency chimeric viruses re-isolated from vaccinated macaque monkeys after challenge infection

Authors Kwofie TB, Miura T, Ibuki K, Enose Y, Suzuki H, Ui M, Kuwata T, Hayami M

Objectives Challenge, Immunogenicity To examine the biological properties of circulating viruses whose replication has been suppressed in vaccinated monkeys.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings
• Monkeys vaccinated with nef-deleted SHIVs were either fully or partially protected against challenge with acute pathogenic SHIV-89.6P
• Though the vaccination did not completely prevent the replication of the challenge virus in the monkeys it did contain the challenge virus by suppressing the pathogenic variants.

NHP.93 (12100017) Spontaneous production of RANTES and antigen-specific IFN-gamma production in macaques vaccinated with SHIV-4 correlates with protection against SIVsm challenge


Objectives Challenge, Immunogenicity To investigate the production of beta-chemokines in eight cynomolgus macaques vaccinated with non-pathogenic SHIV-4 in relation to protection against pathogenic SIVsm challenge.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name SHIV-4  Type: Live Virus  Route: Intravenous

Challenge SIVsm  Route: Intrarectal

Main Findings
• 2/8 vaccinated monkeys were completely protected and one was partially protected against the challenge virus.
• The monkeys that resisted infectious SIVsm virus challenge showed higher spontaneous beta-chemokine production by peripheral blood mononuclear cells and had higher numbers of antigen-induced IFN-gamma secreting cells compared to the non-protected animals
• The genetic background of the host and/or environmental factors are involved in the chemokine production and beta-chemokines contribute to protection against HIV/SIV infection.

NHP.94 (1281660) Vaccination of macaques with SIV conserved envelope peptides suppressed infection and prevented disease progression and transmission

Authors Shafferman A, Lewis MG, McCutchan FE, Benveniste RE, Jahrling PB, Hickman RL, Lai CY, Burke DS, Eddy GA

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVenv-Bgal peptides  Type: Recombinant Subunit Protein  Route: Intramuscular

Challenge SIV(Mne) clone E11S  Route: Intravenous

Main Findings
• Vaccinated macaques became transiently viremic following challenge with SIVmne.
• Lymph nodes from all vaccinated macaques remain SIV-PCR positive.
• Lymph nodes and whole blood from vaccinated macaques challenged with SIV could not transmit SIV to naive macaques.

NHP.95.1 (1433263) Comparison of protection from homologous cell-free vs cell-associated SIV challenge afforded by inactivated whole SIV vaccines

Authors Heeney JL, de Vries P, Dubbes R, Koornstra W, Niphuis H, ten Haaft P, Boes J, Dings ME, Morein B, Osterhaus AD

Objectives Challenge, Immunogenicity To determine if SIV vaccines could protect against challenge with PBMCs from an SIV infected rhesus monkeys.
Trial Summaries

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings

100% SIV vaccinated animals challenged with the 11-88 cell-free stock of SIVmac32H were protected, whereas only 50% of the SIV vaccinated monkeys receiving the same infectious dose of the 1XC cell stock were protected.

NHP.95.2 (1466991) Comparison of protection afforded by whole virus ISCOM versus MDP adjuvanted formalin-inactivated SIV vaccines from IV cell-free or cell-associated homologous challenge

Authors: Osterhaus A, de Vries P, Morein B, Akerblom L, Heeney J

Objectives: Challenge, Immunogenicity
To test SIV-ISCOM and SIV-MDP adjuvanted vaccines for their potential to induce protection from intravenous homologous SIV challenge in rhesus monkeys.

Main Findings

7/7 monkeys vaccinated 4x over a 4-month period with the SIV-ISCOM or the SIV-MDP vaccine were protected from developing viremia during a three-month observation period since intravenous challenge with 10 MID50 cell-free SIVmac251(32H).

2/4 and 2/4 monkeys in 2 other groups of 4 monkeys vaccinated in the same way with either of these vaccines, then challenged (intravenously with 10 MID50 of SIVmac251(32H)-infected PBMC of a rhesus monkey) were protected.

All the control animals vaccinated with measles virus ISCOMs or MDP adjuvanted measles virus antigen were infected upon challenge.

Conclusion: vaccinated previously unchallenged nonhuman primates can be protected from infection with lentivirus-infected PBMC from another animal. Serological analysis indicated that SIV-specific serum antibody titers were considerably higher in SIV-ISCOM vaccinated animals than in the SIV-MDP vaccinated animals.

NHP.96 (1346285) Intrarectal challenge of macaques vaccinated with formalin-inactivated simian immunodeficiency virus

Authors: Cranage MP, Baskerville A, Ashworth LA, Dennis M, Cook N, Sharpe S, Farrar G, Rose J, Kitchin PA, Greenaway PJ
Journal: Lancet 1992 Feb 1;339(8788):273-4

Objectives: Challenge, Immunogenicity
To test the immunogenicity and efficacy of a formalin-inactivated SIV in rhesus macaques.

Main Findings

4 rhesus macaques vaccinated with a formalin-inactivated SIV given intramuscularly were protected from challenge up to 10 mpc.

NHP.97 (1466966) Immunization of rhesus monkeys with high- and low-dose Tween-ether-disrupted SIVMAC


Objectives: Challenge, Immunogenicity
To test the immunogenicity and protection from challenge induced by a low dose of tween-ether-disrupted SIVmac251.32H.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings

3/3 naive controls infected 14 dpc (increased neopterin levels correlated with infection).

4/7 protected from infection.

NHP.98 (10759543) Augmentation of immune responses to HIV-1 and simian immunodeficiency virus DNA vaccines by IL-2/Ig plasmid administration in rhesus monkeys


Vaccines

HIV Immunology and HIV/SIV Vaccine Databases 2003
### NHP.99.1  (11713828)

**Cytokine-induced augmentation of DNA vaccine-elicited SIV-specific immunity in rhesus monkeys**

**Authors**
Barouch DH, Letvin NL

**Journal**

**Objectives**
Immunogenicity To investigate the ability of an IL-2/lg cytokine fusion protein and a plasmid expressing IL-2/lg to augment immune responses in rhesus monkeys induced by DNA vaccines encoding SIV gag and HIV-1 env 89.6P.

**Main Findings**
- Both IL-2/lg protein and IL-2/lg plasmid augment DNA vaccine-elicited antibody and CTL responses.
- The most consistent and dramatic augmentation was observed using the IL-2/lg plasmid.

### NHP.99.2  (1466966)

**Immunization of rhesus monkeys with high- and low-dose Tween-ether-disrupted SIVMAC**

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity To test the immunogenicity and protection from challenge induced by a HIGH dose of tween-ether-disrupted SIVmac251.32H.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
SIVmac251/32H (Tween/Ether)  Type: Whole (killed) Inactivated Virus

**Challenge**
SIVmac251(32H)  Route:

**Main Findings**
- 3/3 naive historic controls infected 14 dpc.
- 4/5 protected from infection.

### NHP.100  (11085584)

**Maturation of envelope-specific antibody responses to linear determinants in monkeys inoculated with attenuated SIV**

**Authors**
Cole KS, Paliotti MJ, Murphey-Corb M, Montelaro RC

**Journal**

**Objectives**
Immunogenicity To characterize the evolution of antibody responses to define linear determinants of the SIV envelope protein.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
SIV 17E-CL  Type: Recombinant Live Attenuated Virus  Route: Intravenous

**Main Findings**
- Antibodies to certains envelope peptide domains have different patterns of antibody maturation to distinct linear envelope antigenic determinants.
- Potential for domain-specific serology to produce a high-resolution characterization of SIV-specific antibody responses that can be used to evaluate experimental vaccine responses and to identify potential immune correlates of protection.

### NHP.101  (10954580)

**Induction of mucosal homing virus-specific CD8(+) T lymphocytes by attenuated simian immunodeficiency virus**

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**Trial Summaries**

**Objectives**
Immunogenicity To investigate whether DNA vaccine-elicited immune responses in rhesus monkeys could be augmented by using either an IL-2/lg fusion protein or a plasmid expressing IL-2/lg.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
SIVmac239 gag DNA  Type: DNA  Route: Intramuscular

**Vaccine Name**
HIV-1.89.6P env DNA  Type: DNA  Route: Intramuscular

**Main Findings**
- The administration of both IL-2/lg protein and IL-2/lg plasmid induced a significant and sustained in vivo activation of peripheral T cells in the vaccinated monkeys.
- The monkeys that received IL-2/lg plasmid generated 30-fold higher Env-specific antibody titers and 5-fold higher Gag-specific, tetramer-positive CD8+ T cell levels than the monkeys receiving the DNA vaccines alone.
- IL-2/lg protein also augmented the vaccine-elicited immune responses, but less effectively than IL-2/lg plasmid.
- Augmentation of the immune responses by IL-2/lg was evident after the primary immunization and increased with subsequent boost immunizations.
Trial Summaries

**Authors** Cromwell MA, Veazey RS, Altman JD, Mansfield KG, Glickman R, Allen TM, Watkins DI, Lackner AA, Johnson RP

**Journal** J Virol 2000 Sep;74(18):8762-6

**Objectives** Immunogenicity To determine if virus-specific CD8+ lymphocytes induced in rhesus macaques by immunization with attenuated SIV express the mucosa-homing receptor α4β7 (and traffic to the intestinal mucosa).

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** SIVmac251ΔNef

**Type:** Live Attenuated Virus  **Route:** Intravenous

**Main Findings**
- Virus-specific CD8+ T cells are induced by immunization with attenuated SIV express α4β7 and home to mucosal sites, whereas those induced by a DNA-MVA vaccine lack expression of the intestinal homing receptor.
- SIV-specific CD8+ T lymphocytes expressing α4β7 by a vaccine approach that replicates in mucosal tissue suggest that induction of virus-specific lymphocytes that are able to home to mucosal sites may be an important characteristic of a successful AIDS vaccine.

**NHP.102** (10856795) *Anti-major histocompatibility complex antibody responses in macaques via intradermal DNA immunizations*

**Authors** Dela Cruz CS, MacDonald KS, Barber BH

**Journal** Vaccine 2000 Jul 15;18(27):3152-65

**Objectives** Immunogenicity To determine if DNA immunization with class I and class II MHC-encoding plasmids elicite xenogeneic and allogeneic antibody response against conformationally intact MHC molecules in rhesus macaques.

**Species/Subspecies** Macaca mulatta (Rhesus macaque), Macaca fascicularis (cynomolgus macaque)

**Main Findings**
- Intradermal immunizations of non-human primates with plasmid DNA encoding human MHC alleles can safely elicit xenogeneic anti-MHC antibody responses.
- DNA encoding a specific macaque allogeneic MHC induced anti-allogeneic MHC antibodies production.

**NHP.103** (10763887) *Control of viral replication and disease onset in cynomolgus monkeys by HIV-1 Tat vaccine*

**Authors** Ensoli B, Cafaro A


**Objectives** Challenge, Immunogenicity To test the hypothesis that humoral and cellular anti-Tat immunity have a protective role and may control disease progression.

**Main Findings**
- High titers of anti-Tat antibodies capable of neutralizing Tat activity and the in vitro infection with the SHIV89.6P, Tat-specific proliferation, CTLs, TNFalpha production and skin tests were detected in the vaccinated monkeys.
- Upon challenge with the highly pathogenic SHIV89.6P (10 MID50, i.v.), 5/7 of the vaccinated monkeys showed no signs of infection nor CD4+-T cell decline over 19 months of follow-up, whereas 3/3 controls were highly infected.

**NHP.104** (10729127) *Evidence for recombination of live, attenuated immunodeficiency virus vaccine with challenge virus to a more virulent strain*

**Authors** Gundlach BR, Lewis MG, Sopper S, Schnell T, Sodroski J, Stahl-Hennig C, Uberla K


**Objectives** Challenge, Immunogenicity To increase the immunogenicity of the vaccine virus with IL-2 and to investigate whether a recombination event between the vaccine and challenge viruses could explain the negative effect of vaccination with live, attenuated immunodeficiency viruses.

**Main Findings**
- Detection of recombination between a live attenuated vaccine and the challenge strain resulting in a more adverse clinical outcome in vaccinated animals.
- 3 of the vaccinated macaques developed higher set point viral load levels than unvaccinated control monkeys. 2 of these vaccinated monkeys developed AIDS, while the control monkeys infected in parallel remained asymptomatic.
- Emergence of more-virulent recombinants of live, attenuated viruses and less-aggressive wild-type viruses is an additional risk of live, attenuated immunodeficiency virus vaccines.
**NHP.105** (1173807)  
**DNA vaccine protection against challenge with simian/human immunodeficiency virus 89.6 in rhesus macaques**  
**Objectives** Challenge, Immunogenicity  
**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Main Findings**  
- 6/6 control monkeys became infected with challenge strain (SHIV89.6, 750 TCID50).  
- In monkeys immunized with DNA only: 5/6 had challenge virus recovered by co-cultivation; in the DNA-protein group 2/6 were culture positive.  
- Rechallenge using 600TCID50 of pathogenic SHIV-89.6P. A rapid CD4 cell count decline in the 4 control monkeys as well as in the monkey vaccinated with DNA only, but not 4 animals immunized with DNA + protein.  
- No virus was recovered from PBMC in two of these monkeys, and viral RNA loads in plasma were greatly reduced in three of them as compared with the controls. Absence of virus in PBMC was ascertained by whole blood transfusion to naive recipients. Altogether, this shows that the DNA prime-protein boost vaccine regimen could provide some protection against mucosal SHIV infection in rhesus monkeys, whereas DNA alone was ineffective.

**NHP.106** (10792505)  
**Up-regulation of beta-chemokines and down-modulation of CCR5 co-receptors inhibit simian immunodeficiency virus transmission in non-human primates**  
**Authors** Lehner T, Wang Y, Cranage M, Tao L, Mitchell E, Bravery C, Doyle C, Pratt K, Hall G, Dennis M, Villinger L, Bergmeier L  
**Journal** Immunology 2000 Apr;99(4):569-77  
**Objectives** Challenge, Immunogenicity  
To evaluate in vivo the mechanism of protection from SIV that involves up-regulation of chemokines, which bind and may down-modulate the CCR5 coreceptors, thereby preventing transmission.  
**Vaccine Name** rSIV-gp120 protein  
**Type:** Recombinant Subunit Protein  
**Route:** Subcutaneous  
**Vaccine Name** Recombinant p27  
**Type:** Recombinant Subunit Protein  
**Route:** Subcutaneous  
**Challenge** SIVmac220  
**Route:** Intrarectal  
**Main Findings**  
- Immunization induced significant increases in the concentrations of CD8 cell-derived suppressor factor (CD8SF), regulated on activation normal T cells expressed and secreted (RANTES), macrophage inflammatory protein (MIP)1 and MIP1, and down-modulation of the proportion of cells expressing CCR5 (r =0.737, P <0.05)  
- In vivo immunization up-regulates chemokines, which may down-modulate CCR5 coreceptors, and both functions are significantly correlated with the viral load.

**NHP.107** (12359422)  
**Immunization of Macaques with Live Simian Human Immunodeficiency Virus (SHIV) Vaccines Conferred Protection Against AIDS Induced by Homologous and Heterologous SHIVs and Simian Immunodeficiency Virus**  
**Journal** Virology 2002 Sep 30;301(2):189  
**Objectives** Challenge, Immunogenicity  
To evaluate the vaccine potential of SHIVs attenuated by deletion of viral accessory genes.  
**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Vaccine Name** DeltavpuDeltaNefSHIV-4  
**Type:** Live Attenuated Virus  
**Route:** Subcutaneous  
**Vaccine Name** DeltavpuSHIV-ppc  
**Type:** Live Attenuated Virus  
**Routes:** Oral, Subcutaneous  
**Challenge** SHIV-KU2, SIVmacR71, SHIV89.6P  
**Route:** Intrarectal  
**Main Findings**  
- No virological evidence of productive infection with the vaccine strains.  
- 7/7 animals developed binding as well as neutralizing antibodies.
Trial Summaries

- Virus-specific CTLs that recognized homologous as well as heterologous pathogenic SHIVs and SIV, and also soluble inhibitory factors that blocked the in vitro replication of the vaccine strains and different challenge viruses.
- 2/2 control animals were infected, succumbed to AIDS upon challenge.
- 7/7 vaccinees were also infected with challenge viruses, but peak VL were 2-5 lower than in the control and later plasma viral RNA became undetectable in vaccinees (in lymph nodes of 6/7 vaccinees, SHIV89.6P in 5/7, and SHIVKU in 3/7 animals).

NHP.108 (10839807) Effects of in vivo CD8(+) T cell depletion on virus replication in rhesus macaques immunized with a live, attenuated simian immunodeficiency virus vaccine

Authors: Metzner KJ, Jin X, Lee FV, Gettie A, Bauer DE, Di Mascio M, Perelson AS, Marx PA, Ho DD, Kostrakis LG, Connor RI


Objectives: Challenge, Immunogenicity

To investigate the role of CD8(+) T lymphocytes in controlling replication of live, attenuated simian immunodeficiency virus (SIV) as part of a vaccine study to examine the correlates of protection in the SIV/rhesus macaque model.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac251

Type: Live Attenuated Virus

Route: Intravenous

Challenge: SIVmac251

Route: Intravenous

Main Findings:
- CD8+ T cell depletion was associated with a 1-2 log increase in SIVmac239-nef plasma viremia.
- Control of SIVmac239-nef replication was temporally associated with the recovery of CD8+ T cells between days 8 and 10. The challenge virus, SIVmac251, was not detectable in either the plasma or lymph nodes after depletion of CD8+ T cells.
- CD8+ T cells play an important role in controlling replication of live, attenuated SIV in vivo.

NHP.109 (10612675) Simian immunodeficiency virus-specific cytotoxic T lymphocytes and protection against challenge in rhesus macaques immunized with a live attenuated simian immunodeficiency virus vaccine

Authors: Nixon DF, Donahoe SM, Kakimoto WM, Samuel RV, Metzner KJ, Gettie A, Hanke T, Marx PA, Connor RI

Journal: Virology 2000 Jan 5;266(1):203-10

Objectives: Challenge, Immunogenicity

To examine the role of SIV-specific CTLs in macaques immunized with an attenuated strain of simian immunodeficiency virus (SIVmac239Deltanef) in protection against pathogenic challenge with SIVmac251.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVmac239-Δnef

Type: Live Attenuated Virus

Route: Intravenous

Challenge: SIVmac251

Route: Intravenous

Main Findings:
- Attenuated SIVmac239Deltanef can elicit specific CTL precursor cells (CTLp), but no correlation was observed between breadth or strength of CTLp response to structural proteins SIV-Env, -Gamg or -Pol and protection against infection.
- The low level of Mamu-A*01/p11C, C-M-specific CTLs induced through attenuated SIVmac239Deltanef vaccination increased in the absence of detectable SIVmac251 or SIVmac239Deltanef proviral DNA.

NHP.110 (9371609) Identification of the V1 region as a linear neutralizing epitope of the simian immunodeficiency virus SIVmac envelope glycoprotein


Objectives: Immunogenicity

To investigate the role of the V1 in neutralization.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

NHP.111 (10644340) Antiretroviral therapy during primary immunodeficiency virus infection can induce persistent suppression of virus load and protection from heterologous challenge in rhesus macaques

Authors: Rosenwirth B, ten Haaf P, Bogers WM, Nieuwenhuis IG, Niphuis H, Kuhn EM, Bischofberger N, Heeney JL, Uberla K
Objectives
Challenge, Immunogenicity To study rhesus macaques with the pathogenic simian/human immunodeficiency virus RT-SHIV and treat them with the antiretroviral drug (R)-9-(2-phosphonylmethoxypropyl)adenine (PMPA) for 8 weeks starting 7 or 14 days postinfection.

Species/Subspecies
Macaca mulatta (Rhesus macaque)

Vaccine Name
RT-SHIV Type: Live Virus Route: Intravenous

Main Findings
• Rhesus macaques inoculated with the pathogenic RT-SHIV then treated with the antiretroviral drug (R)-9-(2-phosphonylmethoxypropyl)adenine (PMPA) for 8 weeks starting 7 or 14 days postinfection, showed suppressed viral replication efficiently.
• Suppression of viral replication was transient in 4/6 monkeys.
• The challenge of the monkeys with better outcome with SIV(8980) shows that both monkeys proved to be protected against the heterologous virus.

NHP.112 (9765452)
Oral immunization of macaques with attenuated vaccine virus induces protection against vaginally transmitted AIDS

Authors

Objectives
Challenge, Immunogenicity.

Species/Subspecies
Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name
DeltavpuDeltanefSHIV-4 Type: Live Attenuated Virus Route: Subcutaneous

Vaccine Name
DeltavpuSHIV-ppc Type: Live Attenuated Virus Route: Oral

Challenge
SHIV-KU1 Route: Oral, Vaginal or perivaginal

Main Findings
• 4/4 controls developed low CD4+ T-cell counts (<200/µl) and AIDS.
• 12/12 vaccinees became infected with SHIVKU-1, and two in group 1 developed a persistent productive infection followed by development of AIDS in one. The other 10 maintained almost complete control over virus replication
• First demonstration of protection against virulent SHIV administered by the intravaginal route. Thus, sexually transmitted HIV disease can be prevented by parenteral or oral immunization.

NHP.113 (11054270)
Characterization of immune escape viruses from a macaque immunized with live-virus vaccine and challenged with pathogenic SHIVKU-1

Authors
Stipp HL, Kumar A, Narayan O

Objectives
Challenge To characterize immune escape viruses (SHIV(KU-1/105w52) and SHIV(KU-1/105w98)) from a macaque immunized with DeltavpuDeltanef SHIV-4 and challenged with pathogenic SHIV(KU-1).

Main Findings
• The two newly identified escape variant viruses could not be neutralized by anti-SHV(KU-1)-specific neutralizing antibodies and were poorly recognized by challenge virus-specific CTLs.
• Sequence analysis of the gene encoding gp120 revealed several mutations in the protein that might have contributed to the development of the immune-escape viruses.

NHP.114 (10888354)
Protective immune responses induced by a non-pathogenic simian/human immunodeficiency virus (SHIV) against a challenge of a pathogenic SHIV in monkeys

Authors
Yoshino N, Ami Y, Someya K, Ando S, Shinohara K, Tashiro F, Lu Y, Honda M

Objectives
Challenge, Immunogenicity.

Species/Subspecies
Macaca fascicularis (cynomolgus macaque)

Vaccine Name
SHIV-NM3n Type: Live Attenuated Virus

Challenge
SHIV89.6 Route: Intravenous
Main Findings

- After the heterologous virus challenge, all of the vaccinees were completely protected from SHIV challenge.
- The inhibition of CD4+ cell depletion was associated with maintaining the proliferative response of helper T-cells against SIV p27 in the vaccinated animals following the pathogenic virus challenge.
- Decline of CD28+ cells, the increase in CD95+ cells, and the enhancement of in vitro apoptosis in PBMC were inhibited in the non-pathogenic virus-inoculated animals.

NHP.115  (11348720) **Enhanced simian immunodeficiency virus-specific immune responses in macaques induced by priming with recombinant Semliki Forest virus and boosting with modified vaccinia virus Ankara**


**Objectives** Challenge, Immunogenicity

To investigate the the immunogenicity and protection from challenge of two vector-based vaccines, either given alone or in a prime-boost regimen.

**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)

**Main Findings**

- Generally, antibody responses, T-cell proliferative responses and cytotoxic T-cell responses remained low or undetectable in vaccinees receiving MVA-SIVmac or SFV-SIVmac alone, in contrast with monkeys who first received SFV-SIVmac twice and then were boosted with MVA-SIVmac.
- No evidence of protection was seen against an intrarectal heterologous SIVsm challenge given 3 months after the last immunization.

NHP.116  (11514733) **In situ hybridization and immunolabelling study of the early replication of simian immunodeficiency virus (SIVmacJ5) in vivo**


**Journal** J Gen Virol 2001 Sep;82(Pt 9):2225-34

**Objectives** Pathogenicity

To determine the distribution of virus-infected cells in cynomolgus macaques following intravenous challenge with 1000 TCID50 of the wild-type simian immunodeficiency virus SIVmacJ5 (stock J5C).

**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)

**Challenge** SIVmac251(32H)  **Route**: Intravenous

**Main Findings**

- Following intravenous inoculation with SIVmacJ5, all macaques became infected, as determined by virus isolation and/or DNA PCR.
- At day 4 post-infection detection of the virus was sporadic. By 7 dpc significant SIV loads were detected in the blood and lymphoid tissues by DNA PCR and virus co-cultivation. Large numbers of cells expressing SIV RNA were detected in mesenteric lymph nodes by ISH and significantly fewer (P<0.05) in the spleen.
- A major site of the initial replication of SIV is gut-associated lymphoid tissue.

NHP.117  (11983253) **Passive immunization with human neutralizing monoclonal antibodies: correlates of protective immunity against HIV**

**Authors** Xu W, Hofmann-Lehmann R, McClure HM, Ruprecht RM

**Journal** Vaccine 2002 May 6;20(15):1956-60

**Objectives** Challenge, Immunogenicity, Passive Immunization

To determine the value of passive immunization to protect rhesus macaque against SHIV challenge.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** F105/2G12/2F5 mab **Type**: Passive Antibody

**Challenge** SHIV89.6P, SHIV-vpu+  **Route**: Intravenous, Oral

**Main Findings**

- Passive immunization with synergistic combinations of human monoclonal antibodies (mAbs) directed against conserved epitopes of the HIV envelope completely protected 13/16 rhesus monkeys challenged intravenously or orally with chimeric simian-humanimmunodeficiency virus (SHIV) strains; partial protection was seen in another 2.
- A high degree of protection was seen among orally challenged neonates.
<table>
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<tr>
<th>NHP.118</th>
<th>A DNA/MVA-based candidate human immunodeficiency virus vaccine for Kenya induces multi-specific T cell responses in rhesus macaques</th>
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<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Wee EG, Patel S, McMichael AJ, Hanke T</td>
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<tr>
<td><strong>Journal</strong></td>
<td>J Gen Virol 2002 Jan;83(Pt 1):75-80</td>
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<tr>
<td><strong>Objectives</strong></td>
<td>Immunogenicity</td>
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<tr>
<td><strong>Species/Subspecies</strong></td>
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<tr>
<td><strong>Vaccine Name</strong></td>
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<tr>
<td><strong>Type</strong></td>
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<tr>
<td><strong>Routes</strong></td>
<td>Intradermal, Intramuscular</td>
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<tr>
<td><strong>Main Findings</strong></td>
<td>The very same vaccines that had entered clinical trials in Oxford and Nairobi (plasmid pTHr.HIVA DNA and recombinant modified vaccinia virus Ankara MVA.HIVA in a prime-boost protocol) induced cellular immune responses specific for multiple HIV-derived epitopes in rhesus macaques.</td>
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<tr>
<th>NHP.119</th>
<th>Induction of anti-simian immunodeficiency virus cellular and humoral immune responses in rhesus macaques by peptide immunogens: correlation of CTL activity and reduction of cell-associated but not plasma virus load following challenge</th>
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<td><strong>Journal</strong></td>
<td>J Gen Virol 2002 Jan;83(Pt 1):81-91</td>
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<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity</td>
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<tr>
<td><strong>Species/Subspecies</strong></td>
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<td><strong>Vaccine Name</strong></td>
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<td><strong>Type</strong></td>
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<td><strong>Vaccine Name</strong></td>
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<td><strong>Type</strong></td>
<td>Synthetic Protein/Peptide</td>
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<td><strong>Route</strong></td>
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<td><strong>Vaccine Name</strong></td>
<td>V2-MAP</td>
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<td><strong>Type</strong></td>
<td>Synthetic Protein/Peptide</td>
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<td><strong>Routes</strong></td>
<td>Subcutaneous, Intramuscular</td>
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<td><strong>Vaccine Name</strong></td>
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<td><strong>Type</strong></td>
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<td><strong>Routes</strong></td>
<td>Subcutaneous, Intramuscular</td>
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<tr>
<td><strong>Challenge</strong></td>
<td>SIV mac251 (European) stock 5</td>
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<td><strong>Route</strong></td>
<td>Intravenous</td>
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<tr>
<td><strong>Main Findings</strong></td>
<td>Although none of the monkeys were protected from infection, most demonstrated an anamnestic CTL response with epitope-specific CTL precursor frequencies reaching as high as 1 in 20 total PBMC as measured by limiting dilution CTL assay or 25% of all CD8+ T-cells using tetrameric MHC-I/peptide complexes. A significant inverse correlation between the levels of CTLp and the number of infected cells in circulation. However, no such correlation with the plasma viral load (RNA copies/ml) was evident</td>
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<tr>
<th>NHP.120</th>
<th>Evaluation of SIV library vaccines with genetic cytokines in a macaque challenge</th>
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<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Sykes KF, Lewis MG, Squires B, Johnston SA</td>
</tr>
<tr>
<td><strong>Journal</strong></td>
<td>Vaccine 2002 May 22;20(17-18):2382-95</td>
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<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity</td>
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<tr>
<td><strong>Species/Subspecies</strong></td>
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<td><strong>Vaccine Name</strong></td>
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<td><strong>Type</strong></td>
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<td><strong>Type</strong></td>
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<td><strong>Routes</strong></td>
<td>Intradermal, Intramuscular</td>
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<tr>
<td><strong>Challenge</strong></td>
<td>SIVmac251</td>
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<tr>
<td><strong>Route</strong></td>
<td>Intravenous</td>
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<tr>
<td><strong>Main Findings</strong></td>
<td>8/12 animals in the three test groups showed some anti-SIV immune response, whereas the controls did not. Six months after priming, monkeys were intravenously challenged with virulent SIVmac251: All were infected but animals in two groups vaccinated with SIV libraries showed a trend toward lower viral-loads, mitigated clinical disease, and higher survival rates than controls.</td>
</tr>
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</table>
• Significantly, co-administering the GMCSF and IL-12-encoding plasmids worsened the measures of protection.

**NHP.121** (11907220) **Outcome of simian-human immunodeficiency virus strain 89.6p challenge following vaccination of rhesus macaques with human immunodeficiency virus Tat protein**

**Authors** Silvera P, Richardson MW, Greenhouse J, Valyey-Ogunro J, Shaw N, Mirchandani J, Khalili K, Zagury JF, Lewis MG, Rappaport J


**Objectives** Challenge, Immunogenicity To investigate whether vaccination with biologically active Tat or inactive Tat toxoid derived from HIV-1(IIIB) and SHIV strain 89.6p would induce protective immunity in rhesus macaques.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- HIV-1 HXBc2 Tat Toxoid Type: Other Route: Intramuscular
- SHIV89.6P tat toxoid Type: Other Route: Intramuscular
- HIV-1 HXBc2 Tat Type: Purified Viral Products Route: Intramuscular
- SHIV89.6P tat Type: Purified Viral Products Route: Intramuscular

**Challenge** SHIV89.6P Route: Intravenous

**Main Findings**
- Vaccination induced high titers of anti-Tat immunoglobulin G in all immunized animals by week 7, but titers were somewhat lower in the 89.6p Tat group.
- Tat-specific T-helper responses were detected in 50% of immunized animals.
- T-cell epitopes appeared to map within amino acids (aa) 1 to 24 and aa 37 to 66.
- Tat-specific gamma interferon responses were detected in CD4+ and/or CD8+ T lymphocytes in 11/16 immunized animals on the day of challenge.
- All animals became infected upon intravenous challenge with 30 AID50 of SHIV 89.6p, and there were no significant differences in viral loads or CD4+ T-cell counts between immunized and control animals

**NHP.123** (11823518) **Recombinant canarypox vaccine-elicited CTL specific for dominant and subdominant simian immunodeficiency virus epitopes in rhesus monkeys**


**Objectives** Challenge, Immunogenicity

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- ALVAC-SIV-gpe (vcp180) Type: Recombinant Vector (virus/bacteria)
- SIVmac251 Route: Intrarectal

**Challenge** SIVmac251 Route: Intrarectal

**Main Findings**
- Following a series of five immunizations, memory gag-specific (not pol) CTL responses specific were demonstrated in vaccinated monkeys.
- Following challenge with SIVmac251, the vaccinated animals developed high frequency CTL responses specific for the dominant Gag epitope, associated with the early containment of viral replication.
- The vaccinees, but not the control animals, developed CTL responses to the subdominant Pol epitope that were detectable only after containment of early viremia.

**NHP.124** (12076047) **DNA prime/protein boost vaccine strategy in neonatal macaques against simian human immunodeficiency virus**


**Objectives** Challenge, Immunogenicity

**Main Findings**
- Following SHIV-vpu+ challenge, containment of infection was observed in 4/15 animals given DNA priming/protein boost vaccination and in 3/4 animals given gp160 boosts only.
- Rechallenge with homologous virus of 6 animals that contained the first challenge virus resulted in rapid viral clearance or low viral loads.
Upon additional rechallenge with heterologous, pathogenic SHIV89.6P, 4/6 animals maintained normal CD4+ T-cell counts with no or limited SHIV89.6P infection.

Humoral and cellular immune mechanisms may have contributed to the containment of SHIV89.6P; however, viral interference with SHIV-vpu+ could also have played a role.

Immunogenicity and efficacy of candidate AIDS vaccines are not affected when vaccination is initiated during infancy as compared with later in life.

### NHP.125  (11907330) Immunization with recombinant modified vaccinia virus Ankara can modify mucosal simian immunodeficiency virus infection and delay disease progression in macaques


**Journal** J Gen Virol 2002 Apr;83(Pt 4):807-18

**Objectives** Challenge, Immunogenicity

**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**
- rMVA (SIVsm) gagpolenv  **Type:** Recombinant Vector (virus/bacteria)  **Route:** Intramuscular
- Native SIV gp148 env  **Type:** Purified Viral Products  **Route:** Intramuscular
- SIVmac251 p27  **Type:** Purified Viral Products  **Route:** Intramuscular

**Challenge** SIVsm  **Route:** Intrarectal

**Main Findings**
- At the time of challenge, antibody titers to SIV Env and lymphocyte proliferation responses to whole viral antigen were highest in vaccinees receiving MVA-SIVsm with protein immunizations.
- One immunized animal was completely protected from intrarectal challenge SIVsm.
- A prolonged survival time was observed in 2/4 monkeys in each of the groups immunized with MVA-SIVsm, in 2 monkeys given MVA-SIVsm followed by protein and in 3/4 monkeys given wild-type MVA, compared with naive controls.
- Immunization with MVA-SIVsm, as well as wild-type MVA alone, seemed to delay disease progression after mucosal SIV infection in a proportion of the monkeys.

### NHP.126  (11751978) Vaccine protection against functional CTL abnormalities in simian human immunodeficiency virus-infected rhesus monkeys

**Authors** McKay PF, Schmitz JE, Barouch DH, Kuroda MJ, Lifton MA, Nickerson CE, Gorgone DA, Letvin NL

**Journal** J Immunol 2002 Jan 1;168(1):332-7

**Objectives** Challenge, Immunogenicity To assess cytokine production by virus-specific CTL in the rhesus monkey model for AIDS to determine its contribution to the functional impairment of CTL.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- HIV-1.89.6P env DNA  **Type:** DNA  **Route:** Intramuscular
- SIVmac239 gag DNA  **Type:** DNA  **Route:** Intramuscular
- SIVmac251 (J5), SHIV89.6, SHIV89.6P  **Route:** Intravenous

**Challenge** SIVmac251 (J5), SHIV89.6, SHIV89.6P

**Main Findings**
- CTL from monkeys infected with nonpathogenic isolates of simian and simian-human immunodeficiency virus expressed high levels of IFN-gamma, TNF-alpha, and IL-2 after in vitro exposure to a nonspecific mitogen or the optimal peptide representing a dominant virus-specific CTL epitope.
- CTL from vaccinated monkeys that effectively controlled the replication of a highly pathogenic simian-human immunodeficiency virus isolate following challenge demonstrated a preserved capacity to produce these cytokines.

### NHP.127  (12743287) Comparative immunogenicity in rhesus monkeys of DNA plasmid, recombinant vaccinia virus, and replication-defective adenovirus vectors expressing a human immunodeficiency virus type 1 gag gene

### Trial Summaries

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<tr>
<td><strong>Objectives</strong></td>
<td>Immunogenicity To evaluate an MVA vector and a replication-defective adenovirus serotype 5 (Ad5) vector, each expressing the same codon-optimized HIV-1 gag gene for immunogenicity in rhesus monkeys.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
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</table>
| **Main Findings** | • The Ad5-gag vector was the most effective in eliciting anti-Gag CTL; the vaccine produced both CD4(+) and CD8(+) T-cell responses, with the latter consistently being the dominant component.  
• Of the formulations tested, the DNA-CRL1005 vaccine primed T-cell responses most effectively and provided the best overall immune responses after boosting with Ad5-gag.  
• Conclusion: An immunization strategy for humans that is based on the adenovirusvector and in which existing adenovirus immunity may be overcome by combined immunization with adjuvanted DNA and adenovirus vector boosting |

#### NHP.128 (11751749)

**Prime-boost immunization generates a high frequency, high-avidity CD8(+) cytotoxic T lymphocyte population**

| **Objectives** | Challenge, Immunogenicity To study a ‘prime-boost’ immunization with DNA vaccines and recombinant poxvirus vectors that generates high frequencies of CTL. |
| **Main Findings** | • The ‘prime-boost’ immunization with DNA vaccines and recombinant poxvirus vectors generated high frequencies of cytotoxic T lymphocytes (CTL) that recognize target cells expressing very low levels of specific antigen; these cells persist for at least 6 months at levels representing approximately 10% of the CD8(+) T cell population.  
• Prime-boost immunized animals were capable of eliminating target cells expressing 10- to 100-fold less immunogenic peptide than mice given either vector alone.  
• Viral challenge led to rapid expansion of CTL effectors in prime-boost groups, to levels representing >30% of total CD8(+) T cell numbers |

#### NHP.129 (12208982)

**Sustained Peptide-Specific Gamma Interferon T-Cell Response in Rhesus Macaques Immunized with Human Immunodeficiency Virus gag DNA Vaccines**

| **Objectives** | Immunogenicity To examine the influence of dose and method of antigen delivery on the dynamics and durability of T-cell responses to candidate human immunodeficiency virus (HIV) vaccines. |
| **Main Findings** | • Cell-mediated immune (CMI) response in rhesus macaques persisted for at least 18 months following a four-dose vaccination regimen.  
• The plasmid vaccine, with or without CRL8623, was immunogenic in macaques; however, the form coadministered with adjuvant exhibited improved T-cell responses, with a bias toward more antigen-specific CD8(+) T cells.  
• Broad and durable CMI response to HIV DNA vaccines can be induced in a relevant nonhuman primate model. |

#### NHP.131 (12127792)

**Protection by intranasal immunization of a nef-deleted, nonpathogenic SHIV against intravaginal challenge with a heterologous pathogenic SHIV**

| Journal | Virology 2002 Jul 5;298(2):306-16 |
| **Objectives** | Challenge, Immunogenicity To examine the possibility of using an attenuated virus for mucosal immunization, four female macaques were intranasally or intravenously administered with a chimeric simian-human immunodeficiency virus with a deleted nef gene (SHIV-dn). |
| **Species/Subspecies** | Macaca mulatta (Rhesus macaque) |
| **Vaccine Name** | SHIV-dn  
**Type:** Live Attenuated Virus  
**Routes:** Intravenous, Intranasal |
| **Challenge** | SHIV89.6P  
**Route:** Vaginal or perivaginal |
### Trial Summaries

**Main Findings**

- Although all the monkeys had anti-HIV-1 antibodies with neutralizing activity in the plasma, the intranasally immunized monkeys had much higher levels of HIV-1 Env-specific IgG and IgA antibodies in mucosal secretions compared with the intravenously immunized monkeys.
- 3/4 intranasally immunized monkeys were completely protected from intravaginal challenge with a pathogenic virus, SHIV-89.6P, whereas only 1 intravenously immunized monkey was protected.
- Intranasal immunization of an attenuated virus can induce the protective efficacy against intravaginal infection.

<table>
<thead>
<tr>
<th>NHP.132</th>
<th>Different patterns of immune responses but similar control of a simian-human immunodeficiency virus 89.6P mucosal challenge by modified vaccinia virus Ankara (MVA) and DNA/MVA vaccines</th>
</tr>
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<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Amara RR, Villinger F, Staprans SI, Altman JD, Montefiori DC, Kozyr NL, Xu Y, Wyatt LS, Earl PL, Herndon JG, McClure HM, Moss B, Robinson HL</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To evaluate the ability of the MVA component of this vaccine to serve as both a prime and a boost for an AIDS vaccine.</td>
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<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
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<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIV-HIV89.6 DNA vaccine Type: DNA Route: Intradermal</td>
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<tr>
<td><strong>Vaccine Name</strong></td>
<td>rMV A 89.6 Type: Recombinant Vector (virus/bacteria) Routes: Intravenous, Intramuscular</td>
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<tr>
<td><strong>Challenge</strong></td>
<td>SHIV89.6P Route: Intrarectal</td>
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<tr>
<td><strong>Main Findings</strong></td>
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</table>
- Compared to the DNA/MVA vaccine, the MVA-only vaccine raised less than one-tenth the number of vaccine-specific T cells but 10-fold-higher titers of binding antibody for Env.
- Postchallenge, the animals vaccinated with MVA alone increased their CD8 cell numbers to levels that were similar to those seen in DNA/MVA-vaccinated animals.
- By 5 wpc, the MVA-only-vaccinated animals had achieved as good control of the viral infection as the DNA/MVA group. |

### NHP.133 (11085582) SHIV89.6P pathogenicity in cynomolgus monkeys and control of viral replication and disease onset by human immunodeficiency virus type 1 Tat vaccine

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity

**Main Findings**
- A vaccine based on the Tat protein of HIV blocks primary infection with SHIV89.6P and prevents the CD4 T cell decline and disease onset in cynomolgus monkeys.
- No signs of virus replication were found in five out of seven vaccinated macaques for almost 1 year of follow-up.
- Since the inoculated virus is shown to be highly pathogenic in cynomolgus macaques, the results indicate efficacy of Tat vaccination in protection against highly pathogenic virus challenge.
- There was a correlation of protection with a cytotoxic T cell response.

### NHP.134 (10482571) Role of immune responses against the envelope and the core antigens of simian immunodeficiency virus SIVmne in protection against homologous cloned and uncloned virus challenge in Macaques

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity To examine (i) the effect of priming by recombinant vaccinia virus; (ii) the role of surface antigen gp130; and (iii) the role of core antigens (Gag and Pol) in eliciting protective immunity.

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**
Recombinant vaccinia virus vac-gp160 (v-SE5) Type: Recombinant Vector (virus/bacteria) Route: Scarification
### Trial Summaries

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
<th>Challenge</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recombinant vaccinia gp130 (v-SE6)</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Scarification</td>
<td></td>
<td>- Priming with recombinant vaccinia virus was more effective than subunit antigen in eliciting protective responses.</td>
</tr>
<tr>
<td>Recombinant vaccinia gagpol (v-SG11)</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Scarification</td>
<td></td>
<td>- While both gp130 and gp160 elicited similar levels of SIV-specific antibodies, gp130 was not as effective as gp160 in protection, indicating a possible role for the transmembrane protein in presenting functionally important epitopes.</td>
</tr>
<tr>
<td>Recombinant vaccinia gagpolenv (v-SGE14)</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Scarification</td>
<td></td>
<td>- Although animals immunized with core antigens failed to generate any neutralizing antibody and were infected upon challenge, their virus load was 50- to 100-fold lower than that of the controls.</td>
</tr>
<tr>
<td>rgp160</td>
<td>Recombinant Subunit Protein</td>
<td>Intramuscular</td>
<td>SIV(Mne) clone E11S</td>
<td>Complete protection against intravenous infection by the pathogenic uncloned SIVmne was achieved by immunization with both the envelope and the core antigens.</td>
</tr>
<tr>
<td>Recombinant gp130</td>
<td>Recombinant Subunit Protein</td>
<td>Intramuscular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recombinant gagpol particles</td>
<td>Recombinant Subunit Protein</td>
<td>Intramuscular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recombinant gagpolenv particles</td>
<td>Recombinant Subunit Protein</td>
<td>Intramuscular</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### NHP.135 (10203053) Protection from pathogenic SIV challenge using multigenic DNA vaccines

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity

**Main Findings**
- Humoral immune responses were stronger in the macaques receiving subunit boosts.
- Significant Nab titters to SIVmne detected in one of the subunit-boosted animals and in none of the DNA-only animals prior to challenge.
- T-cell proliferative responses to gp160 and to Gag were detected in all immunized animals after three immunizations, and these responses increased after four immunizations.

#### NHP.136 (9930869) Neutralizing antibody directed against the HIV-1 envelope glycoprotein can completely block HIV-1/SIV chimeric virus infections of macaque monkeys

**Authors**

**Journal**
Nat Med 1999 Feb;5(2):204-10

**Objectives**
Challenge, Immunogenicity, Passive Immunization

**Main Findings**
- Passive immunization of pig-tailed macaques with IgG purified from multiply infected HIV-1+ chimpanzees followed by intravenous challenge with a SHIV (env derived form HIV-1DH12).
- Anti-SHIV neutralizing activity is the absolute requirement for antibody-mediated protection in vivo.
- Administration of non-neutralizing anti-HIV IgG neither inhibited nor enhanced a subsequent SHIV infection.

#### NHP.137 (9863867) Live attenuated simian immunodeficiency virus (SIV)mac in macaques can induce protection against mucosal infection with SIVsm

**Authors**

**Journal**
AIDS 1998 Dec 3;12(17):2261-70

**Objectives**
Challenge, Immunogenicity

**Main Findings**
- Live attenuation of simian immunodeficiency virus (SIV)macC8 could induce long-term protective immunity against rectal exposure to SIVsm and intravenous exposure to the more divergent HIV-2.
Main Findings

- At the time of challenge, 8/10 vaccinees were PCR-positive for SIVmacC8 DNA but no virus could be isolated from peripheral blood mononuclear cells.
- After SIVsm challenge, 3/6 vaccinees were repeatedly SIVsm PCR-negative. In 1/3 infected monkeys, the challenge virus was initially suppressed but the monkey ultimately developed AIDS after increased replication of the pathogenic virus. Monkeys protected from initial challenge remained uninfected after rechallenge.
- Infection with SIV did not protect from challenge with HIV-2.
- All controls became infected with either SIVsm or HIV-2.
- At the time of challenge the vaccinees had neutralizing antibodies to SIVmac but no demonstrable cross-neutralizing antibodies to SIVsm or HIV-2.
- Titers of antigen-binding or neutralizing antibodies did not correlate with protection.
- Cytotoxic T-cell responses to SIV Gag/Pol and virus-specific T-cell proliferative responses were low.

NHP.138 (9747945) Presence of circulating CTL induced by infection with wild-type or attenuated SIV and their correlation with protection from pathogenic SHIV challenge

Authors Vogel TU, Fournier J, Sherring A, Ko D, Parenteau M, Bogdanovic D, Mihowich J, Rud EW


Objectives Challenge, Immunogenicity To evaluate the role of CTLs in the protection from challenge with pathogenic SHIV in macaques vaccinated with attenuated virus.

Main Findings

- SIVmacC8-vaccinated monkeys demonstrated a broader CTL response than the SIVmacJ5-infected animals.
- CTL against some proteins in SIVmacC8-vaccinated monkeys became progressively more difficult to detect through the day of challenge.
- Neither the presence of circulating CTL nor the CTL precursor frequency against any of the tested proteins correlated with the outcome of the challenge when SIVmacJ5- and SIVmacC8-infected animals were analyzed together.
- Only the protected animal had detectable CTL precursors with moderate frequencies against all three tested proteins at the day of challenge.

NHP.139 (9814958) Prime-boost immunization strategies against HIV

Authors Barnett SW, Klinger JM, Doe B, Walker CM, Hansen L, Duliege AM, Sinangil FM


Objectives Passive immunotherapy .
### Vaccine Name

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD5-gp160(MN)</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intranasal</td>
</tr>
<tr>
<td>AD7-gp160(MN)</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intranasal</td>
</tr>
<tr>
<td>CHO cell-expressed HIV-1SF2 gp120</td>
<td>Recombinant Subunit Protein</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

### Challenge

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Type</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1.SF2, HIV-1.5016</td>
<td></td>
<td>Intravenous</td>
</tr>
</tbody>
</table>

### Main Findings

- Following challenge with HIV-1.5016, complete protection in 1/3 chimpanzees previously protected against low- and high-dose HIV-1SF2 exposures after immunization with an adenovirus-HIV-1MN gp160 priming-HIV-1SF2 gp120 boosting regimen.
- At challenge, the protected chimpanzee exhibited broad humoral immunity, including neutralizing antibody activity.

### NHP.142 (9811759)

**Enhanced T-cell immunogenicity and protective efficacy of a human immunodeficiency virus type 1 vaccine regimen consisting of consecutive priming with DNA and boosting with recombinant fowlpox virus**

**Authors**

Kent SJ, Zhao A, Best SJ, Chandler JD, Boyle DB, Ramshaw IA

**Journal**

J Virol 1998 Dec;72(12):10180-8

**Objectives**

Challenge, Immunogenicity To evaluate a consecutive immunization strategy involving priming with DNA and boosting with rFPV vaccines encoding common HIV-1 antigens.

**Main Findings**

- A dramatic boosting effect on DNA vaccine-primed HIV-1-specific helper and cytotoxic T-lymphocyte responses, but a decline in HIV-1 antibody titers, was observed following rFPV immunization.
- The vaccine regimen protected macaques from an intravenous HIV-1 challenge, with the resistance most likely mediated by T-cell responses.

### NHP.143 (9765452)

**Oral immunization of macaques with attenuated vaccine virus induces protection against vaginally transmitted AIDS**

**Authors**


**Journal**


**Objectives**

Challenge, Immunogenicity

**Species/Subspecies**

Macaca (sp)

**Main Findings**

- Six adult macaques immunized subcutaneously with DeltavpuDeltaneSHIV-4 (vaccine 1), and six were immunized orally with DeltavpuSHIVPPc (vaccine 2). Both viruses caused infection in all inoculated animals, but whereas vaccine 1 virus caused only a nonproductive type of infection, vaccine 2 virus replicated productively but transiently for a 6- to 10-week period.
- The 12/12 vaccinated animals became infected with the challenge virus SHIVKU-1, and two in group 1 developed a persistent productive infection followed by development of AIDS in one. The other 10 have maintained almost complete control over virus replication even though spliced viral RNA was detected in lymph nodes.

### NHP.144 (1466990)

**Inactivated whole SIV vaccine in macaques: evaluation of protective efficacy against challenge with cell-free virus or infected cells**

**Authors**


**Journal**


**Objectives**

Challenge, Immunogenicity To evaluate the protective efficacy against challenge with cell-free virus or infected cells.

### NHP.146 (1466992)

**Prevention of HIV-2 and SIVSM infection in cynomolgus monkeys by active or passive immunization**

**Authors**

Biberfield G, Putkonen P, Thorstensson R, Norrby E

**Journal**


**Objectives**

Challenge, Immunogenicity, Passive Immunization

**Main Findings**

- Protection against homologous HIV-2 infection was demonstrated in 2/2 monkeys immunized with a Triton-X100-treated whole HIV-2SBL-6669 vaccine in incomplete Freund’s adjuvant and in 2/4 monkeys immunized with a formalin-inactivated whole HIV-2 vaccine in RIBI adjuvant.
Monkeys preinfected with a live poorly replicating HIV-2 strain were shown to develop cross-protection against SIV-induced disease.

### NHP.147 (1470916)
**Cellular proteins bound to immunodeficiency viruses: implications for pathogenesis and vaccines**

**Authors**

**Journal**
Science 1992 Dec 18;258(5090):1935-8

**Main Findings**
- Retracted from public display.

### NHP.148 (1470917)
**Protective effects of a live attenuated SIV vaccine with a deletion in the nef gene**

**Authors**
Daniel MD, Kirchhoff F, Czajak SC, Sehgal PK, Desrosiers RC

**Journal**
Science 1992 Dec 18;258(5090):1938-41

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Challenge**
SIVmac239, SIVmac251  
Route: Intravenous

**Main Findings**
- Rhesus monkeys vaccinated with live SIV deleted in nef were completely protected against challenge by intravenous inoculation of live, pathogenic SIV.
- 2/2 naive controls infected 14 dpc and dead of SAIDS 252 dpc.
- 2/2 vaccinees protected from increased viral load and disease and remain healthy >208 wpc (>4 years).
- 2/2 vaccinees protected from infection >208 wpc (>4 years).

### NHP.149.1 (1677743)
**Prevention of HIV-2 and SIVsm infection by passive immunization in cynomolgus monkeys**

**Authors**

**Journal**
Nature 1991 Aug 1;352(6334):436-8

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Challenge**
HIV-2.SBL6669  
Route: Intravenous

**Main Findings**
- All 6 control animals treated with normal monkey serum or no serum (n = 39) became infected by the challenge virus.
- 5/7 animals pretreated with antibody-containing serum at a dose of 9 ml kg-1 resisted infection.
- Conclusion: passively transferred antibodies can protect against a low-dose lentivirus challenge in a nonhuman primate.

### NHP.149.2 (1677743)
**Prevention of HIV-2 and SIVsm infection by passive immunization in cynomolgus monkeys**

**Authors**

**Journal**
Nature 1991 Aug 1;352(6334):436-8

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Challenge**
DNA Vaccine pNL432-ZF1  
Type: DNA  
Route: Intravenous

**Main Findings**
- Antibody titers declined to undetectable level after challenge.
- Active infection did not occur during 6-10 months of follow up in 3/4 passively immunized monkeys.
### NHP.150.1 (8986737)

**Resistance of neonatal monkeys to live attenuated vaccine strains of simian immunodeficiency virus**

**Authors**
Wyand MS, Manson KH, Lackner AA, Desrosiers RC

**Journal**
Nat Med 1997 Jan;3(1):32-6

**Objectives**
Challenge, Immunogenicity, Passive Immunization.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Main Findings**
- High viral loads and disease were observed in only 2 of 18 neonatal monkeys infected with gene-deleted vaccine strains of simian immunodeficiency virus.
- Pathogenicity was restricted to neonates born to unvaccinated mothers and that received extremely high doses of vaccine virus orally.
- No in utero transmission of vaccine virus was observed in 4 neonates born to mothers vaccinated during the second trimester.
- Conclusion: Live attenuated vaccine approach should remain a viable option for preventing HIV infection and disease in high-risk human populations.

### NHP.150.2 (8986737)

**Resistance of neonatal monkeys to live attenuated vaccine strains of simian immunodeficiency virus**

**Authors**
Wyand MS, Manson KH, Lackner AA, Desrosiers RC

**Journal**
Nat Med 1997 Jan;3(1):32-6

**Objectives**
Challenge, Passive Immunization.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
SIVmac239Δ3

**Type:** Live Attenuated Virus  **Routes:** Oral, Intraplacental

**Main Findings**
- 0/4 cases of vertical transmission of SIVmac239Δ3.
- Maternal antibody did not prevent transmission of the autologous challenge in 3/4 neonates.

### NHP.151 (1733103)

**Immunization with tween-ether-treated SIV adsorbed onto aluminum hydroxide protects monkeys against experimental SIV infection**

**Authors**

**Journal**
Virology 1992 Feb;186(2):588-96

**Objectives**
Challenge, Immunogenicity To study immunogenicity and protective values of tween-ether-disrupted SIVmac251/32H adsorbed onto aluminum hydroxide immunization in monkeys.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
SIVmac251/32H (Tween/Ether)

**Type:** Whole (killed) Inactivated Virus  **Route:** Intravenous

**Challenge**
SIVmac251(32H)

**Route:** Intravenous

**Main Findings**
- 4/7 immunized animals did not show any signs of virus replication and therefore appeared to be protected.
- Nonvaccinated control animals and the vaccine failures showed a rise in their urinary neopterin concentrations 1 to 2 weeks after infection.
- After the challenge, control animals and infected vaccinees showed a primary or secondary antibody response while antibody titers declined in virus-negative animals.
- Specific cytotoxic T-lymphocytes were not present prior to challenge.

### NHP.152.1 (1741059)

**Prevention of HIV-1 infection in chimpanzees by gp120 V3 domain-specific monoclonal antibody**

**Authors**

**Journal**

**Objectives**
Challenge, Passive Immunization To demonstrate the protective efficacy of anti-V3 domain antibody in vivo.

**Species/Subspecies**
Pan Troglodytes (Chimpanzee)

**Vaccine Name**
Cβ1 anti-V3

**Type:** Passive Antibody  **Route:** Intravenous

**Challenge**
SIVmac251(32H)

**Route:** Intravenous

**Main Findings**
- 1/1 control chimpanzee infected.
<table>
<thead>
<tr>
<th>NHP.152.2</th>
<th>Prevention of HIV-1 infection in chimpanzees by gp120 V3 domain-specific monoclonal antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objectives</td>
<td>Challenge, Immunotherapy To demonstrate the protective efficacy of anti-V3 post challenge with live virus.</td>
</tr>
<tr>
<td>Species/Subspecies</td>
<td>Pan Troglodytes (Chimpanzee)</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>Cβ1 anti-V3                                      Type: Passive Antibody Route: Intravenous</td>
</tr>
<tr>
<td>Challenge</td>
<td>SIVmac251(32H)                                   Route: Intravenous</td>
</tr>
<tr>
<td>Main Findings</td>
<td>• 1/1 protected from infection &gt;336 dpc.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NHP.153</th>
<th>Passive immunization of newborn rhesus macaques prevents oral simian immunodeficiency virus infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Authors</td>
<td>Van Rompay KK, Berardi CJ, Dillard-Telm S, Tarara RP, Canfield DR, Valverde CR, Montefiori DC, Cole KS, Montelaro RC, Miller CJ, Marthas ML</td>
</tr>
<tr>
<td>Objectives</td>
<td>Challenge, Passive Immunization To determine if passively acquired antiviral antibodies modulate virus transmission and disease progression in human pediatric AIDS.</td>
</tr>
<tr>
<td>Species/Subspecies</td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td>Main Findings</td>
<td>• Untreated neonates became infected after oral SIV inoculation and had high viremia, and most animals developed fatal AIDS within 3 months.</td>
</tr>
<tr>
<td></td>
<td>• In contrast, SIV hyperimmune serum given subcutaneously prior to oral SIV inoculation protected 6 newborns against infection.</td>
</tr>
<tr>
<td></td>
<td>• When SIV hyperimmune serum was given to 3 newborns 3 weeks after oral SIV inoculation, viremia was not reduced, and all 3 infants died within 3 months of age due to AIDS and immune-complex disease.</td>
</tr>
<tr>
<td></td>
<td>• Conclusion: passively acquired anti-HIV IgG may decrease perinatal HIV transmission</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NHP.154</th>
<th>Protection of macaques with a simian immunodeficiency virus envelope peptide vaccine based on conserved human immunodeficiency virus type 1 sequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Authors</td>
<td>Shafferman A, Jahrling PB, Benveniste RE, Lewis MG, Phipps TJ, Eden-McCutchan F, Sadoff J, Eddy GA, Burke DS</td>
</tr>
<tr>
<td>Objectives</td>
<td>Challenge, Immunogenicity To evaluate envelope peptide vaccine based on conserved HIV-1 sequences.</td>
</tr>
<tr>
<td>Species/Subspecies</td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td>Vaccine Name</td>
<td>SIVenv-Bgal peptides                                      Type: Recombinant Subunit Protein Route: Intramuscular</td>
</tr>
<tr>
<td>Challenge</td>
<td>SIV(Mne) clone E11S                                      Route: Intravenous</td>
</tr>
<tr>
<td>Main Findings</td>
<td>• After challenge with virulent virus, controls became virus positive and developed gradually rising antibody titers to SIV over 63 weeks.</td>
</tr>
<tr>
<td></td>
<td>• Immunized macaques developed a postchallenge anamnestic response to SIVenv antigens within 3-6 weeks followed bya gradual, fluctuating decline in SIV antibody titers and partial or total suppression of detectable SIV.</td>
</tr>
<tr>
<td></td>
<td>• Virus suppression correlated with prechallenge neutralizing antibody titers.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NHP.155</th>
<th>Efficacy of SIV/deltaB670 glycoprotein-enriched and glycoprotein-depleted subunit vaccines in protecting against infection and disease in rhesus monkeys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objectives</td>
<td>Challenge, Immunogenicity To define the role of virion components in the induction of protective immunity.</td>
</tr>
</tbody>
</table>
### Trial Summaries

#### Macaca mulatta (Rhesus macaque)

**Main Findings**
- Immunization with the glycoprotein-enriched preparation prevented infection in 2/4 monkeys, whereas the glycoprotein-depleted vaccine failed to prevent infection in all 4 vaccinates tested.
- Glycoprotein-depleted vaccine appeared to moderate the progression of SIV-induced disease compared with non-immunized infected control monkeys inoculated with the same challenge dose.
- Conclusion: subunit vaccines containing sufficient quantities of viral glycoproteins can protect against SIV infection, whereas subunit vaccines composed predominantly of viral core proteins cannot.

#### Prevention of HIV-1 IIIB infection in chimpanzees by CD4 immunoadhesin

**Authors** Ward RH, Capon DJ, Jett CM, Murthy KK, Mordenti J, Lucas C, Frie SW, Prince AM, Green JD, Eichberg JW

**Journal** Nature 1991 Aug 1;352(6334):434-6

**Objectives** Challenge, Passive Immunization To evaluate the CD4 immunoadhesin (CD4-IgG) in the protection against HIV-1 infection in chimpanzees.

**Species/Subspecies** Pan Troglodytes (Chimpanzee)

**Vaccine Name** CD4 Immunoadhesin (CD4-IgG) **Type:** Other **Routes:** Intravenous, Intramuscular

**Main Findings**
- Pretreatment with CD4-IgG can prevent the infection of chimpanzees with HIV-1.

#### Preliminary report: protection of cynomolgus macaques against simian immunodeficiency virus by fixed infected-cell vaccine

**Authors** Stott EJ, Chan WL, Mills KH, Page M, Taffs F, Cranage M, Greenaway P, Kitchin P

**Journal** Lancet 1990 Dec 22-29;336(8730):1538-41

**Objectives** Challenge, Immunogenicity see experiment 1 (except the challenge was carried out at week 18).

**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)

**Vaccine Name** Fixed inactivated SIVmac251 infected cells **Type:** Whole (killed) Inactivated Virus **Route:** Subcutaneous

**Challenge** SIVmac251 **Route:** –

**Main Findings**
- Upon challenged with 10 MID50 of SIVmac251, virus and proviral DNA were not found in any of the vaccinated cynomolgus macaques immunized with inactivated SIV-infected cells and 'Quil-A' as adjuvant.
- Virus was repeatedly isolated from unvaccinated animals on at least 5 separate occasions and proviral DNA was detected in circulating lymphocytes by polymerase chain reaction amplification (Trials 1,2).
- In animals previously infected, vaccination regimen did not eliminate virus (Trial 3).

#### Preliminary report: protection of cynomolgus macaques against simian immunodeficiency virus by fixed infected-cell vaccine

**Authors** Stott EJ, Chan WL, Mills KH, Page M, Taffs F, Cranage M, Greenaway P, Kitchin P

**Journal** Lancet 1990 Dec 22-29;336(8730):1538-41

**Objectives** Challenge, Immunogenicity see experiment 1 (except the challenge was carried out at week 18).

**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)

**Vaccine Name** Fixed inactivated SIVmac251 infected cells **Type:** Whole (killed) Inactivated Virus **Route:** Subcutaneous

**Challenge** SIVmac251 **Route:** Subcutaneous

**Main Findings**
- See Experiment 1.
Trial Summaries

**Vaccines**


**Objectives**

Immunotherapy To evaluate whether a vaccine would reduce the course of SIV infection in animals already infected with the live virus and have active progressive infection.

**Species/Subspecies**

Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**

Fixed inactivated SIVmac251 infected cells  
Type: Whole (killed) Inactivated Virus  
Route: Subcutaneous

**Challenge**

SHIV.DH12R-PS1  
Route: –

**Main Findings**

- The vaccine that protected from challenge in Trial 1 and 2, did little to eliminate the virus in already infected animals

**NHP.158**  (1979745)  
**Infection of cynomolgus monkeys with HIV-2 protects against pathogenic consequences of a subsequent simian immunodeficiency virus infection**

**Authors**


**Journal**


**Objectives**

Challenge, Immunogenicity

**Species/Subspecies**

Macaca fascicularis (cynomolgus macaque)

**Main Findings**

- At the time of SIV challenge the HIV-2-infected monkeys had neutralizing antibodies against HIV-2, but virus could no longer be recovered from their PBMCs and no clinical symptoms or decrease in CD4+ lymphocytes were observed.
- Protection from challenge with SIVsm including SIV-induced immunodeficiency (no decrease of CD4+ lymphocytes) and lymphadenopathy was observed in HIV-2-infected monkeys for 9 months post challenge.
- 4 naive control monkeys that were inoculated with the same dose of SIV became persistently infected and developed a decrease of the absolute numbers of CD4+ cells and showed a marked lymphadenopathy

**NHP.159**  (1988952)  
**Immunization of chimpanzees confers protection against challenge with human immunodeficiency virus**

**Authors**


**Journal**


**Objectives**

Challenge, Immunogenicity To evaluate protection against challenge with human immunodeficiency virus in immunized chimpanzees.

**Species/Subspecies**

Pan Troglodytes (Chimpanzee)

**Main Findings**

- After 6 months of follow-up, immunized chimpanzees appeared uninfected by serologic and virologic criteria, including polymerase chain reaction analysis and failure to isolate virus from peripheral blood lymphocytes, bone marrow, and lymph node tissue.
- Of 2 chimpanzees monitored for 1 yr, virus was isolated initially from 1 animal at 32 weeks, but the second chimpanzee was virus negative by all assays through 12 mo; the third animal has remained virus negative through 9 mo of follow-up.

**NHP.160**  (2078406)  
**Vaccine protection of rhesus macaques against simian immunodeficiency virus infection**

**Authors**


**Journal**


**Objectives**

Challenge, Immunogenicity

**Species/Subspecies**

Macaca mulatta (Rhesus macaque), Macaca (sp)

**Main Findings**

- Method: Rhesus macaques were immunized with an inactivated whole SIVmac vaccine and muramyl dipeptide (MDP), incomplete Freund's adjuvant (IFA), or aqueous suspension were challenged intravenously with 0.1 TCID50 of cell-free SIVmac.
- Virus was readily recovered from the PBMCs of 10/10 controls.
- 3/3 animals that received the vaccine with MDP were protected from challenge.
- 1/2 animals that received the vaccine with IFA were protected from challenge.
- 1/3 animals that received the aqueous vaccine were protected from challenge.
### NHP.161 (2127681)
**Title**: Yeast-expressed p55 precursor core protein of human immunodeficiency virus type 1 does not elicit protective immunity in chimpanzees

**Authors**: Eminni EA, Schleif WA, Quintero JC, Conard PG, Eichberg JW, Vlasuk GP, Lehman ED, Polokoff MA, Schaeffer TF, Schultz LD, et al.


**Objectives**: Challenge, Immunogenicity.

### NHP.162 (11282197)
**Title**: Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P)


**Journal**: Vaccine 2001 Apr 6;19(20-22):2862-77

**Objectives**: Challenge, Immunogenicity.

**Species/Subspecies**: Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**: pCV-tat

**Type**: DNA

**Route**: Intramuscular

**Main Findings**: A Tat-expressing vector (pCV-tat), expressing the HIV-1 BH10 isolate Tat gene, and containing unmethylated CpG dinucleotides, induced an anti-Tat CTL response that was protective in containing primary infection with SHIV89.6P.

### NHP.163 (11282197)
**Title**: Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P)


**Journal**: Vaccine 2001 Apr 6;19(20-22):2862-77

**Objectives**: Challenge, Immunogenicity.

**Main Findings**: Intramuscular inoculation of the pCV-tat contained primary infection with the highly pathogenic SHIV89.6P virus preventing the CD4+ T cell decline in all the vaccinated monkeys.

- Undetectable virus replication and negative virus isolation correlated in all cases with the presence of anti-Tat CTLs.
- CD8-mediated non-cytolytic antiviral activity was present in all protected animals.
- CpG-rich tat DNA vaccine may represent a promising candidate for preventive and therapeutic vaccination against AIDS.

### NHP.164 (9747943)
**Title**: The role of type-1 and type-2 T-helper immune responses in HIV-1 vaccine protection

**Authors**: Heeney JL, van Gils ME, van der Meide P, de Giuli Morghen C, Ghioni C, Gimelli M, Raddelli A, Davis D, Akerblom L, Morein B


**Species/Subspecies**: Macaca mulatta (Rhesus macaque)

**Vaccine Name**: HIV-1.SF2 gp120/p24 Recombinant

**Type**: Recombinant Subunit Protein

**Route**: Intramuscular

**Vaccine Name**: V2.V3.HIV-1.SF2 Synth.peptides

**Type**: Synthetic Protein/Peptide

**Route**: Intramuscular

**Challenge**: SHIV.SF13

**Route**: Intravenous

### NHP.165 (9733821)
**Title**: Env-independent protection induced by live, attenuated simian immunodeficiency virus vaccines


**Objectives**: Challenge, Immunogenicity.

**Main Findings**
• In contrast to the results with naive control monkeys, no challenge virus could be isolated from the SIV-IL2- and SIVNU-infected macaques.
• Challenge virus sequences detected by nested PCR in some of the vaccinated macaques.
• 4 vaccinated macaques were rechallenged with an SIV-murine leukemia virus (MLV) hybrid were protected from productive infection with the SIV-MLV hybrid in the absence of measurable Nab, while 2 naive control monkeys were readily infected.
• Chemokine inhibition and receptor interference phenomena were not involved in protection.
• Conclusion: protective responses induced by live attenuated SIV vaccines can be independent of host immune reactions directed against Env

NHP.166 (9718118) **Neutralizing antibodies administered before, but not after, virulent SHIV prevent infection in macaques**  
**Authors** Foreman L, Jia F, Li Z, Wang C, Stephens EB, Sahni M, Narayan O, Joag SV  
**Objectives** Challenge, Immunogenicity  
**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Main Findings**  
• 3/6 macaques inoculated with anti-SHIV plasma and challenged 24 hr later with approximately 300 AID of SHIV(KU-2), completely resisted infection with SHIV(KU-2). A fourth animal failed to yield infectious virus, but DNA extracted from its peripheral blood mononuclear cells (PBMC) and lymph nodes had viral sequences.  
• 2/6 vaccinees had partial control of infection.  
• 6/6 macaques given the same dose of anti-SHIV plasma 18 hr after exposure to virus became infected.  
• 2/2 macaques given anti-SHIV plasma only 2 hr after exposure to virus became infected.

NHP.167 (9718117) **Fine specificity of anti-V3 antibodies induced in chimpanzees by HIV candidate vaccines**  
**Authors** Coeffier E, Girard M, Barre-Sinoussi F, Meignier B, Muchmore E, Fultz PN, LeClerc C  
**Objectives** Challenge, Immunogenicity  
**Species/Subspecies** Pan Troglodytes (Chimpanzee)  
**Main Findings**  
To assess the specificity of the anti-V3 antibody responses induced in chimpanzees immunized by various human immunodeficiency type 1 (HIV-1) candidate vaccines and challenged by heterologous strains of HIV-1.

NHP.168 (8896498) **Immunogenicity and protective efficacy of a human immunodeficiency virus type 2 recombinant canarypox (ALVAC) vaccine candidate in cynomolgus monkeys**  
**Authors** Andersson S, Makitalo B, Thorstensson R, Franchini G, Tartaglia J, Limbach K, Polletti E, Putkonen P, Biberfeld G  
**Objectives** Challenge, Immunogenicity  
**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)  
**Main Findings**  
• High antibody titers to HIV-2 gp125 and significant lymphocyte proliferative responses to killed HIV-2 virions demonstrated in monkeys given booster immunizations with gp125.  
• Neutralizing antibody titers were low.  
• 3/12 monkeys generated HIV-2-specific cytotoxic T lymphocytes prior to viral challenge.  
• 4/10 monkeys immunized with ALVAC HIV-2 plus HIV-2 gp125 or V3 peptides were protected.

NHP.169 (9714241) **In vivo resistance to simian immunodeficiency virus superinfection depends on attenuated virus dose**  
**Authors** Cranage MP, Sharpe SA, Whatmore AM, Polyanskaya N, Norley S, Cook N, Leech S, Dennis MJ, Hall GA  
NHP.170  (8892959)  Failure of a human immunodeficiency virus type 1 (HIV-1) subtype B-derived vaccine to prevent infection of chimpanzees by an HIV-1 subtype E strain  
Authors Girard M, Yue L, Barre-Sinoussi F, van der Ryst E, Meignier B, Muchmore E, Fultz PN  

NHP.171  (8892046)  In vivo protective anti-HIV immune responses in non-human primates through DNA immunization  

NHP.172  (9696847)  Temporal analyses of virus replication, immune responses, and efficacy in rhesus macaques immunized with a live, attenuated simian immunodeficiency virus vaccine  
Authors Connor RI, Montefiori DC, Binley JM, Moore JP, Bonhoeffer S, Gettie A, Fenamore EA, Sheridan KE, Ho DD, Dailey PJ, Marx PA  

NHP.173  (8827215)  Protection against mucosal SIVsm challenge in macaques infected with a chimeric SIV that expresses HIV type 1 envelope  
Authors Quesada-Rolander M, Makitalo B, Thorstensson R, Zhang YJ, Castanos-Velez E, Biberfeld G, Putkonen P  

NHP.174  (8827214)  Multiple immunizations with attenuated poxvirus HIV type 2 recombinants and subunit boosts required for protection of rhesus macaques  
Authors Myagkikh M, Aliapanah S, Markham PD, Tartaglia J, Paoletti E, Gallo RC, Franchini G, Robert-Guroff M  

Main Findings

- 4/4 immunized monkeys were infected with the vaccine virus.
- All monkeys developed neutralizing antibodies to HIV-1 and high antibody titers to HIV-1 env glycoproteins, but no Nabs to SIVsm.
- After a follow-up period of 1 year, 2/4 SHIV-infected monkeys were completely protected against SIVsm infection.
- 2/2 SHIV-immunized and infected with the challenge virus, but were able to control this infection.
- CTL in 1/4 of the immunized animals.
- All 6 control animals yielded virus repeatedly after SIVsm challenge and 3 of them showed declining CD4 cell counts.

- Macaques primed with ALV AC recombinant exhibited sporadic T cell proliferative activity, and all but one failed to develop neutralizing antibodies.
- In contrast, macaques primed with NYVAC recombinants had no T cell proliferative activity but exhibited neutralizing antibody titers (highest in the three recombinant group) that declined by the time of challenge.
- None of the macaques exhibited significant CTL activity.
- Following challenge at 32 weeks with HIV-2.SBL6669 all macaques became infected. Thus, immunization regimen was not sufficient to confer protective immunity in the HIV-2 rhesus macaque model.
- Delayed infection in macaques immunized with the NYVAC-HIV-2 recombinant may have been associated with the development of memory B cells capable of providing a neutralizing antibody response on challenge.
<table>
<thead>
<tr>
<th>NHP.175</th>
<th>(9614868)</th>
<th>Cytotoxic T cells and neutralizing antibodies induced in rhesus monkeys by virus-like particle HIV vaccines in the absence of protection from SHIV infection</th>
</tr>
</thead>
</table>

<table>
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<tr>
<th>NHP.176</th>
<th>(8811357)</th>
<th>Attenuated SIV imparts immunity to challenge with pathogenic spleen-derived SIV but cannot prevent repair of the nef deletion</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Authors</em></td>
<td>Stahl-Hennig C, Dittmer U, Nisslein T, Pekrun K, Petry H, Jurkiewicz E, Fuchs D, Wachtler H, Rud EW, Hunsmann G</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NHP.177</th>
<th>(8811354)</th>
<th>Recombinant subunit vaccines as an approach to study correlates of protection against primate lentivirus infection</th>
</tr>
</thead>
</table>

**Objectives**
- Challenge.
- Immunogenicity.

<table>
<thead>
<tr>
<th>NHP.178</th>
<th>(8806509)</th>
<th>Passive immune globulin therapy in the SIV/macaque model: early intervention can alter disease profile</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Authors</em></td>
<td>Conley AJ, Kessler JA II, Boots LJ, McKenna PM, Schleif WA, Emini EA, Mark GE III, Katinger H, Cobb EK, Lunceford SM, Rouse SR, Murthy KK, Lane HC, Martin MA</td>
<td></td>
</tr>
</tbody>
</table>

**Objective**
- A clinically relevant HIV-I subunit vaccine protects rhesus macaques from in vivo passaged simian-human immunodeficiency virus infection

<table>
<thead>
<tr>
<th>NHP.179</th>
<th>(8794312)</th>
<th>Reduction in SIV replication in rhesus macaques infected with autologous lymphocytes engineered with antiviral genes</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Authors</em></td>
<td>Conley AJ, Kessler JA II, Boots LJ, McKenna PM, Schleif WA, Emini EA, Mark GE III, Katinger H, Cobb EK, Lunceford SM, Rouse SR, Murthy KK</td>
<td></td>
</tr>
</tbody>
</table>

**Objective**
- The consequence of passive administration of an anti-human immunodeficiency virus type 1 neutralizing monoclonal antibody before challenge of chimpanzees with a primary virus isolate

<table>
<thead>
<tr>
<th>NHP.180</th>
<th>(8794330)</th>
<th>Intrarectal transmission of simian immunodeficiency virus in rhesus macaques: selective amplification and host responses to transient or persistent viremia</th>
</tr>
</thead>
</table>

**Objective**
- Resistance of previously infected chimpanzees to successive challenges with a heterologous intraclade B strain of human immunodeficiency virus type 1
NHP.185.1 (8673922)  Protective mucosal immunity elicited by targeted iliac lymph node immunization with a subunit SIV envelope and core vaccine in macaques
Objectives Challenge, Immunogenicity To evaluate a novel route of immunization (the targeted iliac lymph node-TILN) aiming close to the iliac lymph nodes draining the genitoreal mucosa.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name rSIV-gp120 protein  Type: Recombinant Subunit Protein  Route: Targeted Lymph node immunization
Vaccine Name Recombinant p27  Type: Recombinant Subunit Protein  Route: Targeted Lymph node immunization
Challenge SIVmac251(32H)  Route: Intrarectal
Main Findings • Rectal challenge with the SIVmac 32H J5 molecular clone induced total protection in 4/7 macaques immunized by targeted iliac lymph node (TILN), compared with infection in 13/14 unimmunized macaques or immunized by other routes (P = 0.025)(experiment 1 and experiment 2).
• Protection was associated with significant increase in the iliac lymph nodes of IgA antibody-secreting cells to p27 (P < 0.02), CD8-suppressor factor (P < 0.01), and the chemokines RANTES and MIP-1 beta (P < 0.01)

NHP.185.2 (8680896)  Protective mucosal immunity elicited by targeted iliac lymph node immunization with a subunit SIV envelope and core vaccine in macaques
Objectives Challenge, Immunogenicity To evaluate a novel route of immunization (the targeted iliac lymph node-TILN) aiming close to the iliac lymph nodes draining the genitoreal mucosa.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name rSIV-gp120 protein  Type: Recombinant Subunit Protein  Routes: Intrarectal, Targeted Lymph node immunization, Intradermal, Intramuscular
Vaccine Name Recombinant p27  Type: Recombinant Subunit Protein  Routes: Intrarectal, Targeted Lymph node immunization, Intradermal, Intramuscular
Challenge SIVmac251 (J5)  Route: Intrarectal
Main Findings • Rectal challenge with the SIVmac 32H J5 molecular clone induced total protection in 4/7 macaques immunized by targeted iliac lymph node (TILN), compared with infection in 13/14 unimmunized macaques or immunized by other routes (P = 0.025)(experiment 1 and experiment 2).
• Protection was associated with significant increase in the iliac lymph nodes of IgA antibody-secreting cells to p27 (P < 0.02), CD8-suppressor factor (P < 0.01), and the chemokines RANTES and MIP-1 beta (P < 0.01)

NHP.186 (8648707)  Vaccine protection by a triple deletion mutant of simian immunodeficiency virus
Authors Wyand MS, Manson KH, Garcia-Moll M, Montefiori D, Desrosiers RC
Objectives Challenge, Immunogenicity

NHP.187 (9445041)  Selection of virus variants and emergence of virus escape mutants after immunization with an epitope vaccine
Authors Mortara L, Letourneau F, Gras-Masse H, Venet A, Guillet JG, Bourgault-Villada I

NHP.188 (9449524)  Vaccine evaluation studies of replication-defective SIVsmB7

NHP.189 (8648735)  Simian immunodeficiency virus DNA vaccine trial in macaques
### Trial Summaries

**Authors** Lu S, Arthos J, Montefiori DC, Yasutomi Y, Manson K, Mustafa F, Johnson E, Santoro JC, Wissink J, Mullins JI, Haynes JR, Letvin NL, Wyand M, Robinson HL  

**NHP.190** (8648204) **Vaccination of pregnant macaques protects newborns against mucosal simian immunodeficiency virus infection**  
**Authors** Van Rompay KK, Otsyula MG, Tarara RP, Canfield DR, Berardi CJ, McChesney MB, Marthas ML  

**Objectives**  
- Challenge, Immunogenicity

**Species/Subspecies** Pan Troglodytes (Chimpanzee)  
**Vaccine Name** CHO cell-expressed HIV-1SF2 gp120  
**Type:** Recombinant Subunit Protein  
**Route:** Intramuscular

**Challenge** HIV-1.SF2  
**Route:** Intravenous

**Main Findings**  
- 1/2 vaccinated animals showed no serologic or virologic evidence of infection suggesting a complete sterilizing protection from challenge in 1 animal and a transient infection in the other animal.
- Both control animals showed evidence of seroconversion in ELISA and Western blot assays; virus was detected in the early, acute phase of infection of both control animals by plasma RNA PCR, virus culture and PBMC DNA PCR assays.

**NHP.191** (8642649) **Construction and characterization of replication-competent simian immunodeficiency virus vectors that express gamma interferon**  
**Authors** Giavedoni LD, Yilma T  

**Objectives** Challenge, Immunogenicity

**Species/Subspecies** Pan Troglodytes (Chimpanzee)  
**Vaccine Name** SIVmac251, 32H, (C8)  
**Type:** Live Attenuated Virus  
**Route:** Intravenous

**Challenge** SIVmac251(32H)  
**Route:** Intravenous

**Main Findings**  
- 3/4 monkeys challenged at 10 weeks and 3/4 challenged at 20 weeks were protected from productive superinfection.
- No apparent correlation between the levels of binding or neutralizing antibodies on the day of challenge and subsequent protection.
Trial Summaries

Objectives
Challenge, Immunogenicity
To determine the breadth of protection afforded by immunization with live attenuated virus.

Species/Subspecies
Macaca mulatta (Rhesus macaque)

Vaccine Name
SIVmac251
Type: Live Virus
Route: Intravenous

Vaccine Name
SIVmac251, 32H, (C8)
Type: Live Attenuated Virus
Route: Intravenous

Main Findings
- Animals previously immunized with live attenuated SIVmac251 then with the wild type SIVmac251 were protected from infection with SIVsm.
- The virus load was 2-3 orders of magnitude lower than the control animals.

NHP.195 (8680896) Utility of SHIV for testing HIV-1 vaccine candidates in macaques
Authors
Journal

NHP.196 (8605046) Protection from HIV-1 envelope-bearing chimeric simian immunodeficiency virus (SHIV) in rhesus macaques infected with attenuated SIV: consequences of challenge
Authors
Bogers WM, Niphuis H, ten Haaf P, Laman JD, Koornstra W, Heeney JL
Journal
AIDS 1995 Dec;9(12):F13-8

NHP.197 (9444999) Induction of neutralizing antibodies to T-cell line-adapted and primary human immunodeficiency virus type 1 isolates with a prime-boost vaccine regimen in chimpanzees
Authors
Journal

NHP.198 (8537682) Protection of MN-rgp120-immunized chimpanzees from heterologous infection with a primary isolate of human immunodeficiency virus type 1
Authors
Berman PW, Murthy KK, Wrin T, Vennari JC, Cobb EK, Eastman DJ, Champe M, Nakamura GR, Davison D, Powell MF, Bussiere J, Francis DP, Matthews T, Gregory TJ, Obijeski JF
Journal

NHP.199 (9420212) Administration of an anti-CD8 monoclonal antibody interferes with the clearance of chimeric simian/human immunodeficiency virus during primary infections of rhesus macaques
Authors
Matano T, Shibata R, Siemon C, Connors M, Lane HC, Martin MA
Journal
**Trial Summaries**

**NHP.200** (8493576)  
**Protection against vaginal SIV transmission with microencapsulated vaccine**  
**Authors** Marx PA, Compans RW, Gettie A, Staas JK, Gilley RM, Mulligan MJ, Yamshchikov GV, Chen D, Eldridge JH  
**Journal** Science 1993 May 28;260(5112):1323-7  
**Objectives** Challenge, Immunogenicity  
To study the immunogenicity and protection conferred by formalin inactivated SIV macaques.  
**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Vaccine Name**  
SIVmac251 (encapsulated)  
**Type:** Whole (killed) Inactivated Virus  
**Routes:** Intratracheal, Oral, Intramuscular  
**Challenge** SIVmac251  
**Route:** Vaginal or perivaginal  
**Main Findings**  
- 5/6 macaques immunized with formalin-treated SIV in biodegradable microspheres by the intramuscular plus oral or plus intratracheal route were protected against vaginal challenge.  
- Oral immunization alone did not protect.  
- After a second vaginal challenge, 3/4 intramuscularly primed and mucosally boosted macaques remained protected.

**NHP.201.1** (9419166)  
**Induction of Th2 cytokine expression for p27-specific IgA B cell responses after targeted lymph node immunization with simian immunodeficiency virus antigens in rhesus macaques**  
**Objectives** Immunogenicity  
To determine if there is an association between the isotype of SIV-specific B cell responses and the profile of Th1 and Th2 cytokine expression.  
**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Vaccine Name**  
rSIV-gp120 protein  
**Type:** Recombinant Subunit Protein  
**Route:** Targeted Lymph node immunization  
**Vaccine Name**  
Whole inactivated SIVmac251  
**Type:** Whole (killed) Inactivated Virus  
**Route:** Targeted Lymph node immunization  
**Vaccine Name**  
Recombinant p27  
**Type:** Recombinant Subunit Protein  
**Route:** Targeted Lymph node immunization  
**Main Findings**  
- In rhesus macaques immunized with SIV antigens, when CD4+ T cells purified from antigen-stimulated PBMCs were analyzed, the levels of Th2 cytokine production were gradually increased after the second and third immunizations with no change of interferon-gamma.  
- The main isotype following the second and third immunization was IgG.  
- Induction of Th2 type responses in TLN-immunized rhesus macaques reflects the sequence of initial induction of SIV-specific IgG-producing cells followed by IgA-secreting cells.

**NHP.201.2** (9456249)  
**Targeted lymph-node immunization with whole inactivated simian immunodeficiency virus (SIV) or envelope and core subunit antigen vaccines does not reliably protect rhesus macaques from vaginal challenge with SIVmac251**  
**Objectives** Challenge, Immunogenicity  
To investigate protection from challenge by recombinant subunit protein inoculation targeting iliac lymph node.  
**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Vaccine Name**  
rSIV-gp120 protein  
**Type:** Recombinant Subunit Protein  
**Route:** Targeted Lymph node immunization  
**Vaccine Name**  
Whole inactivated SIVmac251  
**Type:** Whole (killed) Inactivated Virus  
**Route:** Targeted Lymph node immunization  
**Vaccine Name**  
Recombinant p27  
**Type:** Recombinant Subunit Protein  
**Route:** Targeted Lymph node immunization  
**Challenge** SIVmac251  
**Route:** Vaginal or perivaginal  
**Main Findings**  
- High-titer SIV-specific IgG antibodies in serum in all animals immunized with recombinant subunit proteins inoculated by (targeted) iliac lymph node immunization.  
- Upon intravaginal challenge with SIVmac251, all animals became virus isolation-positive, except 1 animal immunized with SIV p27 and gp120.
### NHP.202 (9395361)
**DNA vaccination as anti-human immunodeficiency virus immunotherapy in infected chimpanzees**

**Authors**

**Journal**
J Infect Dis 1997 Dec;176(6):1501-9

**Objectives**
Immunogenicity, Immunotherapy To evaluate the role of DNA vaccine as anti-HIV immunotherapy in infected chimpanzees.

**Species/Subspecies**
Pan Troglodytes (Chimpanzee)

**Vaccine Name**
- pCMN160 HIV-1.MN.env-rev
- HIV-1 IIIB

**Type**
- DNA
- Intramuscular

**Challenge**
- HIV-1 IIIB
- Intravenous

**Main Findings**
- Two HIV-1-infected chimpanzees were vaccinated with plasmid pCMN160-HIV-1.MN.env-rev demonstrated enhanced humoral responses, decrease in viral load to background levels from week 20.
- The control chimpanzee was subsequently vaccinated with pCMN160 following the inoculation with a control sham plasmid, had the antibody responses increased and, as in the first animal, and the virus load decreased.
- Conclusion: the immune response has a direct impact on HIV-1 replication in chimpanzees.

### NHP.203 (8427714)
**Studies on the specificity of the vaccine effect elicited by inactivated simian immunodeficiency virus**

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- SIVmac251, 32H, (C8)
- HIV-1 GB8
- HIV-1 GB8
- SIVmac251(32H)
- HIV-1 GB8
- SIVsmB670
- SIVmac251(32H)

**Type**
- Whole (killed) Inactivated Virus
- Intramuscular

**Route**
- Intramuscular
- Intramuscular
- Intravenous
- Intramuscular
- Intramuscular

**Challenge**
- SIVsmB670, SIVmac251(32H)
- Intravenous

**Main Findings**
- Partially purified SIVmac protected macaques from intravenous challenge with homologous and heterologous SIV grown on human cells but not on monkey grown cells.
- HIV-1 grown on human C8166 T cell line protected macaques against challenge with human cell-grown SIVmac.
- All vaccinated macaques had anti-cell antibodies.

### NHP.204 (8427039)
**Immune response of chimpanzees after immunization with the inactivated whole immunodeficiency virus (HIV-1), three different adjuvants and challenge**

**Authors**
Niedrig M, Gregersen JP, Fultz PN, Broker M, Mehdi S, Hilfenhaus J

**Journal**
Vaccine 1993;11(1):67-74

**Objectives**
Challenge, Immunogenicity

**Species/Subspecies**
Pan troglodytes troglodytes (chimpanzee)

**Vaccine Name**
- Whole inactivated HIV-1 IIIB
- Recombinant HIV-1 gag core (p24,p15) antigen
- Recombinant HIV-1 env gp160 antigen
- HIV-1.LAI

**Type**
- Whole (killed) Inactivated Virus
- Recombinant Subunit Protein
- Recombinant Subunit Protein
- Intramuscular

**Route**
- Intramuscular
- Subcutaneous
- Intramuscular
- Intravenous

**Main Findings**
- Weak and inconsistent responses were observed in animals that received HIV-1 formulated with alum as adjuvant, whereas HIV-1 formulated with incomplete Freund’s adjuvant or an experimental adjuvant (BWZL) induced good humoral and cellular immune responses to the virus.
- The 3 animals that received HIV-1 with the BWZL adjuvant generated overall the best immune responses.
Upon challenge with infectious HIV-1, despite good humoral and cell-mediated immunity, all 3 immunized animals and a control animal became infected within 4 weeks.

### NHP.205.1 (9343211)

**An adenovirus-simian immunodeficiency virus env vaccine elicits humoral, cellular, and mucosal immune responses in rhesus macaques and decreases viral burden following vaginal challenge**

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity To investigate the immunogenicity of an adenovirus expressing SIV env and its ability to protect rhesus macaques against vaginal challenge.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
Ad5hr-SIVenv  Type: Recombinant Vector (virus/bacteria)  Routes: Intratracheal, Oral, Intranasal

**Vaccine Name**
Native SIV gp120  Type: Purified Viral Products  Route: Intratracheal

**Challenge**
SIVmac251  Route: Vaginal or perivaginal

**Main Findings**
- The vaccine induced SIV-specific neutralizing antibodies and HIV gp120 binding IgG and IgA detected in nasal and rectal secretions.
- SIV-specific IgGs were also observed in vaginal secretions and saliva.
- T-cell proliferative responses to SIV gp140 and T-helper epitopes were sporadically detected in all immunized macaques.
- Following vaginal challenge with SIVmac251, transient or persistent infection resulted in both immunized and control monkeys.
- Conclusion: Ad5hr-SIV env recombinant and gp120 subunit induces strong humoral, cellular, and mucosal immunity in rhesus macaques.

### NHP.205.2 (12021334)

**Rhesus macaque resistance to mucosal simian immunodeficiency virus infection is associated with a postentry block in viral replication**

**Authors**

**Journal**

**Objectives**
Challenge To investigate the mechanism of resistance to challenge of an unvaccinated control rhesus macaque.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Challenge**
SIVmac251(32H), SIVmac251  Route: Intrarectal, Vaginal or perivaginal

**Main Findings**
- Rhesus macaque 359, a vaccine control animal, resisted 2 successive intravaginal challenges with SIVmac251 (and failed to seroconvert) an additional intrarectal SIVmac32H challenge.
- Resistance of this macaque to SIV infection was not due to a high-level of CD8+ suppressor activity but to an inherent resistance of its CD4+ T cells.
- Resistance is due to a postentry block in viral replication and implicates a cellular inhibitory mechanism in its CD4+ T cells.

### NHP.205.3 (10438833)

**Factors associated with slow disease progression in macaques immunized with an adenovirus-simian immunodeficiency virus (SIV) envelope priming-gp120 boosting regimen and challenged vaginally with SIVmac251**

**Authors**

**Journal**
J Virol 1999 Sep;73(9):7430-40

**Objectives**
Challenge .

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
Ad5hr-SIVenv  Type: Recombinant Vector (virus/bacteria)  Routes: Intratracheal, Oral, Intranasal

**Vaccine Name**
Native SIV gp120  Type: Purified Viral Products  Route: Intratracheal

**Challenge**
SIVmac251  Route: Vaginal or perivaginal

**Main Findings**
- Reboosting and re-challenge of macaques vaccinated and challenged in trials 205.1 and 205.2 again resulted in partial protection from pathogenicity of challenge.
### NHP.206 (8411103)
**Immunization of Macaca fascicularis with inactivated SIV preparations: challenge with human- or monkey-derived SIV and the effects of a longer immunization schedule**

**Authors**

**Journal**
J Med Primatol 1993 Feb-May;22(2-3):110-8

**Objectives**
Challenge, Immunogenicity To compare two human-derived SIVmac251 whole virus vaccines, a long vs short immunization schedule, and two different challenge viruses.

**Main Findings**
- Both vaccines induced protection after challenge with human-derived SIVmac251/32H.
- No difference between the 2 schedules of immunization.
- 5/7 were protected following the first challenge (human-derived).
- No protection was observed in monkeys that were boosted and rechallenged with monkey-derived SIVmac251.

### NHP.207 (9343164)
**Live, attenuated simian immunodeficiency virus vaccines elicit potent resistance against a challenge with a human immunodeficiency virus type 1 chimeric virus**

**Authors**
Shibata R, Siemon C, Czajak SC, Desrosiers RC, Martin MA

**Journal**

**Objectives**
Challenge, Immunogenicity To ask what protection live attenuated vaccines can provide against SHIVdh12 challenge. A long term follow up.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- SIMmac239Δ2 *Type*: Live Attenuated Virus *Route*: Intravenous
- SIVmac239Δ3 *Type*: Live Attenuated Virus *Route*: Intravenous

**Challenge**
SHIV.MD1 *Route*: Intravenous

**Main Findings**
- 3 rhesus macaques, previously immunized with SIVΔ3 or SIVΔ2, then challenged with 30,000 TCID50 dose of SHIV.DH12 controlled the SHIV infection by reducing the viral load to barely detectable levels.
- Only SIV sequences, derived from the vaccine, could be amplified from numerous tissue samples collected at the conclusion of the experiment, 60 weeks postchallenge, but SHIV-specific sequences (viz., HIV-1 env) could not.
- Live attenuated SIV vaccines provide strong long-term protection even against challenge strains with highly divergent envelope sequences.

### NHP.208 (8363756)
**Protection of monkeys by a split vaccine against SIVmac depends upon biological properties of the challenge virus**

**Authors**

**Journal**
AIDS 1993 Jun;7(6):787-95

**Objectives**
Challenge, Immunogenicity To investigate the role of the anti-cellular immune response in the protection of rhesus macaques against infection with SIVmac and to determine the biological differences between SIV challenge stocks grown either on human T-cell lines or on monkey PBMC.

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Main Findings**
- Protection from virus challenge with C8166-grown SIVmac251/32H or SIVmac251/MPBMC did not correlate with anti-cellular antibodies or proliferative T-cell reactivities.
- Control animals infected with SIVmac251/MPBMC showed high persistent antigenaemia and high plasma virus titres.
- Neither the antibody nor the proliferative T-cell response to SIVmac correlates with protection from virus challenge. In contrast to SIVmac251/32H grown on C8166 cells, the MPBMC-grown challenge virus SIVmac251 appears to belong to the 'rapid-high' phenotype, possibly explaining the lack of protection against this SIV.

### NHP.209 (9333153)
**Superinfection with human immunodeficiency virus type 2 can reactivate virus production in baboons but is contained by a CD8 T cell antiviral response**

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1272 HIV Immunology and HIV/SIV Vaccine Databases 2003
**Authors** Locher CP, Blackbourn DJ, Barnett SW, Murthy KK, Cobb EK, Rouse S, Greco G, Reyes-Teran G, Brasky KM, Carey KD, Levy JA  
**Objectives** Challenge, Immunogenicity To assess resistance to superinfection by human immunodeficiency virus.  
**Main Findings**  
- Background: Asymptomatic baboons previously infected with HIV-2, were first challenged with homologous virus (HIV-2UC2 or HIV-2UC14) and later with heterologous virus (HIV-2UC12).  
- After both virus inoculations, either resistance to viral infection or a transient viremia was observed.  
- The original virus was recovered in 3 baboons, suggesting that reactivation of a latent infection occurred on heterologous challenge and that HIV-2 superinfection is blocked by processes established during prior infection.  
- Low antibody titers and low levels of virus neutralization.  
- Suppression of HIV-1 replication was observed attributed to CD8 T cells.

**NHP.210** (8312055)  

*In vitro spontaneous production of anti-SIV antibodies is a reliable tool in the follow-up of protection of SIV-vaccinated monkeys*  
**Authors** Zamarchi R, Veronese ML, Titti F, Geraci A, Verani P, Rossi GB, Amadori A, Chieco-Bianchi L  
**Objectives** Challenge, Immunogenicity To assess the reliability of the spontaneous in vitro synthesis of simian immunodeficiency virus (SIV)-specific antibodies as a marker in the monitoring of protection in SIV-vaccinated animals.  
**Main Findings**  
- Background: Macaca fascicularis monkeys were immunized with formalin-inactivated SIVmac251 or SIVmac251/32H, and challenged with human-derived (SIVmac251/32H) or monkey-derived live SIV.  
- Immunized animals were protected against human-derived SIV challenge.  
- No spontaneous in vitro synthesis of anti-SIV antibody was observed in nonstimulated PBMC cultures over a 4-month follow-up.  
- Human cell-grown SIVmac251 immunization did not afford protection against monkey-derived SIV, and all the animals became infected and showed spontaneous in vitro synthesis of anti-SIV antibodies.

**NHP.211** (9315483)  

*Gene gun-based nucleic acid immunization alone or in combination with recombinant vaccinia vectors suppresses virus burden in rhesus macaques challenged with a heterologous SIV*  
**Authors** Fuller DH, Simpson L, Cole KS, Clements JE, Panicali DL, Montelaro RC, Murphey-Corb M, Haynes JR  
**Objectives** Challenge, Immunogenicity To evaluate the ability of gene gun-based DNA immunization alone or in combination with recombinant vaccinia vectors to elicit protective immune responses in rhesus macaques challenged with a pathogenic heterologous SIV.  
**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Main Findings**  
- Geometric mean end-point IgG titres in the DNA + VAC and VAC + DNA groups were substantially higher than the responses seen in the VAC + VAC and DNA + DNA groups, demonstrating a synergistic relationship between DNA-based vaccines and recombinant vacciniavirus-based vaccines.  
- The vaccines did not prevent infection.  
- All vaccine groups showed significant virus load reductions from 7 to 56 days post challenge when compared to controls.  
- DNA + DNA group developed the lowest prechallenge antibody responses and the most significant reduction (200-fold) in virus load was associated with this group. In addition, a significant delay in CD4+ T cell loss relative to controls was observed in the DNA + DNA group.

**NHP.212** (9271187)  

*Mechanisms of protection induced by attenuated simian immunodeficiency virus. IV. Protection against challenge with virus grown in autologous simian cells*  
**Objectives** Challenge, Immunogenicity To test the mechanism of protection provided by live attenuated SIV.
Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Main Findings:

- Background: 8 animals infected with live attenuated SIV then challenged with wild-type grown in autologous and heterologous cells.
- Animals infected with attenuated SIV are protected against wild-type SIV grown in autologous or heterologous cells.
- Live attenuated SIV protects by the induction of allogeic antibodies is not tenable.

NHP.213 (8217348) Lymphoproliferative responses in macaques immunized with inactivated SIV vaccine

Authors: Teng XC, Ashworth LA, Sharpe SA, Dennis MJ, Cranage MP


Objectives: Challenge, Immunogenicity

To examine the lymphoproliferative response of macaques immunized with inactivated, partially purified SIVmac32H grown in C8166 cells.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- Animals vaccinated with partially purified C8166 cell-grown SIVmac32H in alum adjuvant (Group 1) were protected from initial challenge with SIVmac32H but became infected when rechallenged with SIVmac251.
- No association could be demonstrated between protection from challenge and lymphoproliferative response to one particular antigen tested against.

NHP.214 (9266989) Macaques infected with attenuated simian immunodeficiency virus resist superinfection with virulence-revertant virus

Authors: Sharpe SA, Whatmore AM, Hall GA, Cranage MP


Objectives: Challenge, Immunogenicity

To examine the protective values of live attenuated virus vaccine to protect against revertant autologous strains.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:

- 3 macaques already infected with the attenuated molecular clone SIVmacC8 were resistant to superinfection with virulent virus that arose in vivo following repair of a 12 bp attenuating lesion in the nef/3’ LTR.
- 4 naive animals became infected following inoculation with blood taken from the macaque in which virulent virus arose.

NHP.215 (9266988) Mechanisms of protection induced by attenuated simian immunodeficiency virus. I. Protection cannot be transferred with immune serum


Objectives: Challenge, Passive Immunization

To evaluate the role in protection induced by live attenuated SIVmacC8 against SIVmaj5 challenge.

Species/Subspecies: Macaca fascicularis (cynomolgus macaque)

Vaccine Name: Anti-SIVmacC8  Type: Passive Antibody  Route: Intraperitoneal

Challenge: SIVmacJ5M  Route: ND

Main Findings:

- 4/4 control animals were infected as indicated by the test at 14 dpc.
- 2 of passively immunized animals were protected from infection at 14 dpc but were shown to be infected thereafter.
- The failure of passive immunization to transfer protection indicates that serum components alone are not sufficient to mediate the potent protection obtained using live attenuated vaccines.

NHP.216 (8198872) Reduced virus load in rhesus macaques immunized with recombinant gp160 and challenged with simian immunodeficiency virus

Authors: Ahmad S, Lohman B, Marthas M, Giavedoni L, el-Amad Z, Haigwood NL, Scandella CJ, Gardner MB, Luciw PA, Yilma T


Objectives: Challenge, Immunogenicity

To evaluate the potential of SIVmac239 gp160 expressed by recombinant vaccinia virus (vSIVgp160) and baculovirus (bSIVgp160) to protectively immunize rhesus macaques against intravenous infection with pathogenic SIVmac isolates.
Trial Summaries

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Binding antibodies to gp130 were induced in all animals following immunization with SIVgp160.
- Immunization did not induce neutralizing antibodies up to 1 week prior to virus challenge.
- No protection from challenge: All animals became infected after i.v. inoculation with 1-10 AID50 of either challenge virus.

NHP.217 (8198871) Passive immunization of cynomolgus macaques with immune sera or a pool of neutralizing monoclonal antibodies failed to protect against challenge with SIVmac251

Objectives: Passive Immunization

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- HIV-1 Env protein as a boosting immunogen generates a high titer neutralizing antibody response in rhesus macaques.
- HIV-1 env DNA (multiple doses) followed by a final immunization with HIV-1 env DNA plus HIV-1 Env protein (env gene from HXBc2 clone of HIV IIIB; Env protein from parental HIV IIIB) completely protects monkeys from infection after i.v. challenge with a chimeric virus expressing HIV-1 env (HXBc2) on a simian immunodeficiency virusmac backbone (SHIV-HXBc2).

NHP.218 (9256490) Potent, protective anti-HIV immune responses generated by bimodal HIV envelope DNA plus protein vaccination
Authors: Letvin NL, Montefiori DC, Yasutomi Y, Perry HC, Davies ME, Lekutis C, Alroy M, Freed DC, Lord CI, Handt LK, Liu MA, Shiver JW

Objectives: Challenge, Immunogenicity
To study prime-boost regimen using HIV-1 env DNA and synthetic protein and neutralizing antibodies in nonhuman primate species.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- HIV-1 Env protein as a boosting immunogen generates a high titer neutralizing antibody response in rhesus macaques.
- HIV-1 env DNA (multiple doses) followed by a final immunization with HIV-1 env DNA plus HIV-1 Env protein (env gene from HXBc2 clone of HIV IIIB; Env protein from parental HIV IIIB) completely protects monkeys from infection after i.v. challenge with a chimeric virus expressing HIV-1 env (HXBc2) on a simian immunodeficiency virusmac backbone (SHIV-HXBc2).

NHP.219 (8179961) Immune responses induced by prototype vaccines for AIDS in rhesus monkeys
Authors: Ohkawa S, Wilson LA, Larosa G, Javaherian K, Martin LN, Murphey-Corb M

Objectives: Challenge, Immunogenicity
To profile humoral and cell mediated immune response induced by immunization with candidate vaccines consisting of recombinant SIV gp110 with SAF-M adjuvant or rgp140+FA adjuvant.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- All the monkeys were infected after intravenous challenge.
- 16 days following infection, viral antigenemia was reduced in both groups of vaccinates compared to controls.
- After 23 days antigenemia in the gp110 +/- SAF-M group remained at the same level as on day 16, whereas antigenemia in the gp140 + FA group was significantly reduced further than the level observed on day 16.
- Both vaccines induced high ELISA titers of IgG antibody against rgp140.
- gp110 +/- SAF-M (not gp140 + FA) induced high titers of neutralizing antibody.

NHP.220 (9223408) Anti-major histocompatibility complex antibody responses to simian B cells do not protect macaques against SIVmac infection
Authors: Polyanskaya N, Sharpe S, Cook N, Leech S, Banks J, Dennis M, Hall G, Stott J, Cranage M

Objectives: Challenge, Immunogenicity
To investigate the efficacy of alloimmunization with simian B cells expressing high level of MHC class I and class II molecules to confer protection against systemic challenge with SIVmac.

Species/Subspecies: Macaca mulatta (Rhesus macaque)
- Antibody responses to allogeneic MHC molecules do not protect against infection with immunodeficiency lentiviruses.

### NHP.221 (8176640)
**Long-standing protection of macaques against cell-free HIV-2 with a HIV-2 iscom vaccine**


**Objectives** Challenge, Immunogenicity To investigate the capacity of two immunostimulating-complex (iscom) formulations including inactivated native HIV-2 viral proteins and selected peptides to induce protective immunity against HIV-2 in a nonhuman primate.

**Species/Subspecies** Macaca fascicularis (cynomolgus macaque)

**Main Findings**
- 3/4 immunized macaques were protected from challenge.
- 4/4 control macaques became readily infected with challenge virus.
- 1/3 protected animals showed an anamnestic antibody response to a dominating antigenic site.
- The vaccine-protected monkeys were subsequently resistant to rechallenge infection at 12, 15, and 18 months after the first challenge, suggesting that a reasonable duration of protective immunity had been induced by the vaccine.

### NHP.222 (9188572)
**Evolution of envelope-specific antibody responses in monkeys experimentally infected or immunized with simian immunodeficiency virus and its association with the development of protective immunity**

**Authors** Cole KS, Rowles JL, Jagerski BA, Murphey-Corb M, Unangst T, Clements JE, Robinson J, Wyand MS, Desrosiers RC, Montelaro RC


**Objectives** Challenge, Immunogenicity

**Main Findings**
- The establishment of long-term protective immunity in general parallels the absence of further detectable changes in antibody responses and a maintenance of relatively constant antibody titer, avidity, conformational dependence, and the presence of neutralizing antibody for at least 2 years postinoculation.
- Attenuated SIV vaccine and whole virus elicited mature antibody response.
- Envelope subunit vaccines elicited in general immature antibody response characterized by poor reactivity with native envelope proteins, low avidity, low conformational dependence, and the absence of neutralization activity against the challenge strain.

### NHP.223 (8107246)
**Incomplete protection, but suppression of virus burden, elicited by subunit simian immunodeficiency virus vaccines**

**Authors** Israel ZR, Edmonson PF, Maul DH, O’Neil SP, Mossman SP, Thiriart C, Fabry L, Van Opstal O, Bruck C, Bex F, et al.


**Objectives** Challenge, Immunogenicity To compare the efficacy of immunization with either SIVEnv glycoprotein, Gag-Env, or whole inactivated virus, with or without recombinant live vaccinia vector priming, in protecting rhesus macaques from challenge with SIVmac251 clone BK28.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Main Findings**
- Sterilizing immunity was induced only by whole inactivated vaccine.
- Abortive infection (strong immunity) was observed in 2 animals (one VV-Env and one Gag-Env).
- Suppression of infection (incomplete or partial immunity) occurred in the 8/12 of subunit-vaccinated animals.
- Active infection developed in all controls and 2/3 VV-Gag-Env-immunized animals.

### NHP.224 (8046353)
**Major histocompatibility complex class I-associated vaccine protection from simian immunodeficiency virus-infected peripheral blood cells**


**Objectives** Challenge, Immunogenicity To evaluate the effectiveness of vaccine protection from infected cells from another individual of the same species.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)
• 50% of the SIV-vaccinated animals were protected from challenge.
• 50% SIV-vaccinees were unprotected and rapidly progressed to AIDS.
• Protection was unrelated to either total antibody titers to human cells, used in the production of the vaccine, to HLA antibodies, or to virus neutralizing activity.
• All animals protected against cell-associated virus challenge were those which were SIV vaccinated and which shared the MHC class I allele (Mamu-A26) with the donor of the infected cells.
• CTL specific for SIV envelope protein were detected in 3/4 protected animals vs. 1/4 unprotected animals, suggesting a possible role of MHC class I-restricted CTL in protection from infected blood cells.

**NHP.225 (9185593)**

**Challenge of chimpanzees immunized with a recombinant canarypox-HIV-1 virus**

**Authors**

**Journal**
Virology 1997 May 26;232(1):98-104

**Objectives**
Challenge, Immunogenicity To evaluate the potential protective efficacy of a live recombinant HIV-1 canarypox vaccine candidate.

**Species/Subspecies**
Pan Troglodytes (Chimpanzee)

**Main Findings**
• Vaccination against HIV-1(IIIB(LAI)) or HIV-1(MN) did not protect animals from challenge with heterologous cell-free HIV-1(DH12).
• 1/2 chimpanzees vaccinated 5 times with ALVAC-HIV-1 vCP250 and challenged by iv injection of PBMC from an HIV-1(IIIB(LAI))-infected chimpanzee were protected.
• After booster inoculation 5 months post-challenge, both animals were re-challenged with HIV-1(DH12) and neither animal had neutralizing antibodies to HIV-1(DH12) and neither was protected from infection.
• ALVAC-HIV-1 vCP250 expresses HIV-1(IIIB(LAI))gp120/TM, gag and protease gene products.

**NHP.226 (9142121)**

**Protection of chimpanzees from high-dose heterologous HIV-1 challenge by DNA vaccination**

**Authors**

**Journal**
Nat Med 1997 May;3(5):526-32

**Objectives**
Challenge, Immunogenicity To examine the immunogenicity and efficacy of of an HIV-1 DNA vaccine encoding env, rev, gag/pol in a chimpanzee model system.

**Species/Subspecies**
Pan Troglodytes (Chimpanzee)

**Main Findings**
• The immunized animals developed specific cellular and humoral immune responses.
• The DNA constructs induced protection from the establishment of infection with a heterologous challenge (HIV-1 SF2).
• Control animal was infected.

**NHP.227 (9135877)**

**Live attenuated SIV vaccines are not effective in a postexposure vaccination model**

**Authors**

**Journal**
AIDS Res Hum Retroviruses 1997 May 1;13(7):593-9

**Objectives**
Challenge, Immunogenicity, Immunotherapy To evaluate the value of live attenuated vaccine therapeutic immunization.

**Species/Subspecies**

**Main Findings**
• 4/4 controls (vaccinated with delta nef only - i.e., without the SIV IL-2 construct) were infected.
• 0/4 vaccinees protected from increased viral loads.
• 0/4 vaccinees protected from infection.
• All coinfected macaques had a high viral load, and some of them developed AIDS-like symptoms and pathological alterations rapidly.
• In the presence of pathogenic SIV, both live attenuated SIV vaccines did not protect from disease in this postexposure vaccination model.
**NHP.228 (7986590)**

**Induction of antigen-specific killer T lymphocyte responses using subunit SIVmac251 gag and env vaccines containing QS-21 saponin adjuvant**

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity To increase the immunogenicity of recombinant subunit vaccine (SIVmac251 gag and env) with QS-21 adjuvant.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Main Findings**
- Antigen-specific killer cell responses could be induced by a subunit vaccine formulated with the QS-21 saponin adjuvant that was detected was mediated by both CD4+ and CD8+ lymphocytes.
- Despite the presence of these killer cells, all of the animals became infected with the SIVmac251 on experimental challenge.
- The characteristics of the responses suggested that the effector cells were T lymphocytes, expressing either CD4 or CD8.

**NHP.229 (9123856)**

**Macaques infected with live attenuated SIVmac are protected against superinfection via the rectal mucosa**

**Authors**
Cranage MP, Whatmore AM, Sharpe SA, Cook N, Polyanskaya N, Leech S, Smith JD, Rud EW, Dennis MJ, Hall GA

**Journal**
Virology 1997 Mar 3;229(1):143-54

**Objectives**
Challenge, Immunogenicity To determine if protection against systemic challenge in the SIVmac model of AIDS extends to intrarectal mucosal challenge.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Main Findings**
- 4 macaques previously infected with the attenuated SIVmacC8 resisted superinfection with SIVmacJ5, following intrarectal inoculation.
- Immunization with live attenuated SIV protected 4 macaques from intrarectal challenge with SHIV (composed of SIVmac239 expressing the HXBc2 env, tat, and rev genes).
- In protected animals, SIV-specific CTL were detected in gut-associated lymph nodes and may have a role in limiting superinfection following mucosal exposure.

**NHP.230.1 (7986589)**

**High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection**

**Authors**
Daniel MD, Mazzara GP, Simon MA, Sehgal PK, Kodama T, Panicali DL, Desrosiers RC

**Journal**

**Objectives**
Challenge, Immunogenicity To evaluate the ability of two different vaccinia virus recombinant to elicit immune response and to protect macaques against challenge.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Main Findings**
- Method: Monkeys primed with a recombinant vaccinia virus expressing SIV Gag, Pol, and Env polypeptides +/- SIV particles boost in adjuvant.
- Despite the induction of vigorous immune responses, 17/18 rhesus monkeys became infected on challenge with a low dose of virulent SIVmac.
- Vaccination may have diminished SIV burdens and rates of CD4+ cell declines in some of the animals.
- Vaccinated/challenged/infected animals eventually developed fatal disease similar to control animals.

**NHP.230.2 (7986589)**

**High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection**

**Authors**
Daniel MD, Mazzara GP, Simon MA, Sehgal PK, Kodama T, Panicali DL, Desrosiers RC

**Journal**

**Objectives**
Challenge, Immunogenicity To evaluate the ability of two different vaccinia virus recombinant to elicit immune response and to protect macaques against challenge.

**NHP.230.3 (7986589)**

**High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection**
Vaccines

**NHP.231 (7966239)**  Efficacy of inactivated whole HIV-2 vaccines with various adjuvants in cynomolgus monkeys


*Species/Subspecies* Macaca mulatta (Rhesus macaque)

**Objectives** Challenge, Immunogenicity

**Main Findings**
- Preinoculated African green monkeys showed drastic decreases in virus load or were protected from challenge.
- Vaccine protection occurred in the absence of detectable vaccine virus replication and humoral immune response, suggesting a protective cellular immune response similar to that associated with subinfectious or abortive infections.
- SIVagm3(delta)nef replication was delayed marginally in vitro, but highly attenuated in vivo.

**NHP.232 (9108105)**  Vaccine effect using a live attenuated nef-deficient simian immunodeficiency virus of African green monkeys in the absence of detectable vaccine virus replication in vivo

*Authors* Beer B, Baier M, zur Megede J, Norley S, Kurth R

*Journal* Proc Natl Acad Sci U S A 1997 Apr 15;94(8):4062-7

*Species/Subspecies* Cercopithecus aetiops (African Green monkeys)

**Objectives** Challenge, Immunogenicity

**Main Findings**
- Two groups of animals were vaccinated then challenged with either SIV-Human or SIV-Macaque virus.
- All SIV-Human vaccinees were protected from infection, and all SIV-Macaque vaccinees became infected.
- Difference between the two groups is due to cellular proteins in the virus preparation rather than the pathogenic or genetic properties of the virus
- Immune responses of all vaccinees were indistinguishable from one another.
- No virus was isolated from PBMC of macaques challenged with SIV-Human during the course of the study.

**NHP.233 (7966237)**  Immunization with whole inactivated vaccine protects from infection by SIV grown in human but not macaque cells


*Journal* J Med Primatol 1994 Feb-May;23(2-3):75-82

*Species/Subspecies* Macaca (sp)

**Objectives** Challenge, Passive Immunization

**Main Findings**
- Plasma from a monkey that had been protected by an inactivated-whole SIV(mac) vaccine conferred protection to animals challenged iv 4-18 hours later with 10 AID50 of homologous cell-free virus.
- Plasma or purified immunoglobulin (Ig) from SIVmac infected asymptomatic monkeys failed to protect any recipients, and may have enhanced infection and accelerated disease.
**Trial Summaries**

- Anti-SIV Ig administered 24 hours post challenge may have enhanced infection

### NHP.235 (7966226)

**Cellular immune responses in rhesus macaques infected rectally with low dose simian immunodeficiency virus**

**Authors**
Salvato MS, Emau P, Malkovsky M, Schultz KT, Johnson E, Pauza CD

**Journal**

**Main Findings**
- Monkeys infected rectally with low dose of SIV were resistant to high dose challenge with SIV.
- PBMC from 2/4 challenged monkeys were unable to support SIV replication in vitro unless cultures were depleted of CD8+ lymphocytes.
- Monkeys that survived high dose rectal infection with SIV also suppressed virus replication in cultured PBMC.
- Virus-suppressive activity of PBMC may be an important correlate of protective immunity in AIDS.

### NHP.236 (7887023)

**Protection of rhesus macaques from SIV infection by immunization with different experimental SIV vaccines**

**Authors**

**Journal**
Vaccine 1994 Nov;12(15):1443-52

**Main Findings**
- Higher SIV-specific serum antibody titres were found in the SIV-MDP-immunized monkeys than in the SIV-ISCOM-immunized ones.
- 4/4 SIV-MDP- and 4/4 SIV-ISCOM-immunized monkeys were protected against intravenous challenge.
- 2/2 in each control group were infected with the challenge virus.
- 0/4 in each vaccinee group were protected after reboost and rechallenge with 10 MID50 of the same virus produced in PBMC from a rhesus macaque.
- SIV-ISCOM-immunized animals of PBMC-only (Group B) did not develop clinical symptoms during observation period, unlike most other animals in this trial.
- Both SIV preparations induced low VN antibody titres, possibly caused by denatured form of gp120 after formaldehyde or acid treatment in both vaccine preparations.

### NHP.237 (9032322)

**Rhesus macaques previously infected with simian/human immunodeficiency virus are protected from vaginal challenge with pathogenic SIV-mac239**

**Authors**

**Journal**

**Main Findings**
- 5 Rhesus macaques infected intravaginally with SHIV89.6 then challenged intravaginally with pathogenic SIV-mac239 had low or undetectable viral RNA levels in plasma compared to control animals.
- 3/5 of the SHIV-immunized animals remained virus isolation negative for more than 8 months, while 2 became virus isolation positive.
- The presence of SIV Gag-specific cytotoxic T lymphocytes in peripheral blood mononuclear cells and SIV-specific antibodies in cervicovaginal secretions at the time of challenge was associated with resistance to pathogenic SIV infection after vaginal challenge.

### NHP.238 (9000087)

**Rapid development of vaccine protection in macaques by live-attenuated simian immunodeficiency virus**

**Authors**
**NHP.239 (2157886)**  
**Inactivated simian immunodeficiency virus vaccine failed to protect rhesus macaques from intravenous or genital mucosal infection but delayed disease in intravenously exposed animals**

**Authors**  
Sutjipto S, Pedersen NC, Miller CJ, Gardner MB, Hanson CV, Gettie A, Jennings M, Higgins J, Marx PA

**Journal**  
J Virol 1990 May;64(5):2290-7

**Objectives**  
Challenge, Immunogenicity To test efficacy of a whole-virus vaccine inactivated with psoralen and UV light.

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Vaccine Name**  
SIVmac HUT-78 ((Psoralem-UV)

**Type:** Whole (killed) Inactivated Virus

**Challenge**  
SIVmac (not determined)  
**Route:** Urethral, Vaginal or perivaginal, Mucosal

**Main Findings**

- The vaccine elicited humoral immune response prior to challenge.
- All immunized animals became infected after challenge, but their clinical course was delayed compared with controls.
- Route of infection affected disease course, with animals infected by the iv route more likely to develop acute form of SIV than those infected by the genital mucosal route.
- Concentration of challenge did not affect outcome; vaccinated animals did not fare any better following minimal mucosal challenge than a much greater iv infection.

**NHP.240 (2164591)**  
**Immunization with a live, attenuated simian immunodeficiency virus (SIV) prevents early disease but not infection in rhesus macaques challenged with pathogenic SIV**

**Authors**  
Marthas ML, Sutjipto S, Higgins J, Lohman B, Torten J, Luciw PA, Marx PA, Pedersen NC

**Journal**  

**Objectives**  
Challenge, Immunogenicity To test the potential of virulence-attenuated virus to protect against iv challenge with a pathogenic SIV(MAC) strain.

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Vaccine Name**  
SIVmac1A11

**Type:** Live Attenuated Virus  
**Route:** Intravenous

**Challenge**  
SIVmac (not determined)  
**Route:** Intravenous

**Main Findings**

- Live SIVmac1A11 is immunogenic, did not induce disease, but failed to protect against moderately high dose of pathogenic virus.
- Immunization prevented severe, early disease and prolonged the lives of monkeys subsequently infected with pathogenic SIV.
- Within 1-6 weeks iv inoculated animals developed transient viremia without clinical disease and persistent humoral antibody response.
- Time until severe clinical symptoms: 267-304 days in immunized monkeys, 38-227 days PC in naive controls.

**NHP.241 (2370678)**  
**Antibody-mediated in vitro neutralization of human immunodeficiency virus type 1 abolishes infectivity for chimpanzees**  

**Authors**  
Vaccines

Trial Summaries


**Objectives**

Challenge, Immunogenicity

To determine whether antibody against the HIV-1 V3 loop can abolish infectivity of HIV-1 in chimpanzees.

**Species/Subspecies**

Pan Troglodytes (Chimpanzee)

**Main Findings**

- Antibody to the gp120 principal neutralization determinant (V3 loop) prevented HIV-1 infection in vitro and inhibited infection in vivo.

NHP.242 (2455898)

**Authors**


**Journal**

Proc Natl Acad Sci U S A 1988 Jul;85(14):5200-4

**Objectives**

Challenge, Immunogenicity

**Species/Subspecies**

Pan troglodytes troglodytes (chimpanzee)

**Vaccine Name**

rgp120

**Type:** Recombinant Subunit Protein

**Route:** Intramuscular

**Challenge**

HIV-1 IIIB

**Route:** Intravenous

**Main Findings**

- The recombinant gp120 was effective in eliciting cellular and humoral immunity as well as immunologic memory.
- Anti-ggp120 antibodies reacted with authentic viral gp120 in immunological blot assays and were able to neutralize HIV-1 infectivity in vitro.
- Sera from the rgp120-immunized animals were able to neutralize HIV-1 pseudotypes of vesicular stomatitis virus prepared from the IIIB isolate, from which the gene encoding rgp120 was derived, as well as two heterologous isolates, ARV-2 and RF.
- The immune response elicited against the rgp120 was not effective in preventing viral infection after intravenous challenge with HIV-1.

NHP.243 (2370678)

**Authors**


**Journal**


**Objectives**

Immunogenicity

To compare proliferative responses to HIV and to vaccinia virus antigens of lymphocytes taken at various times from chimpanzees vaccinated with recombinant vaccinia virus expressing different HIV genes.

**Species/Subspecies**

Pan Troglodytes (Chimpanzee)

**Main Findings**

- Irrespective of the HIV gene utilized, lymphocyte proliferation to HIV was usually weak and rapidly decreased after each inoculation, contrasting with strong and sustained responses to vaccinia virus.
- IL-2-producing VV did not lead to increased responsiveness.
- Reactivity to soluble purified gp160, but not to p25, could be detected in PBL from animals that had received both VV160 and VV25, while immunization with VVF resulted in a significant response to this protein in 1/2 animals.

NHP.245.1 (2548210)

**Authors**

Desrosiers RC, Wyand MS, Kodama T, Ringler DJ, Arthur LO, Sehgal PK, Letvin NL, King NW, Daniel MD

**Journal**


**Objectives**

Challenge, Immunogenicity

**Main Findings**

- Vaccine protection against simian immunodeficiency virus infection
**Trial Summaries**

**Vaccines**

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
Whole inactivated SIVmac251

**Type**
Whole (killed) Inactivated Virus

**Route**
Intramuscular

**Challenge**
SIVmac251

**Route**
Intravenous

**Main Findings**

- 2/6 vaccinated monkeys showed no evidence of infection following the live virus challenge.
- Transfusion of 10 ml of whole blood from these 2 into uninfected, naive rhesus monkeys did not result in infection of the recipients, providing further support for the lack of infection in the 2 previously vaccinated animals.
- 4/4 unvaccinated control monkeys inoculated with live SIV became infected and 3 of these died with AIDS 118-258 days after infection (in contrast with 1/6 vaccinated monkeys).
- 4/4 naive controls infected and developed SAIDS.
- 0/4 vaccinees protected from infection.
- 1/4 protected from increased viral load and disease to 930 dpc.

**NHP.245.2 (2548210)**

**Vaccine protection against simian immunodeficiency virus infection**

**Authors**
Desrosiers RC, Wyand MS, Kodama T, Ringler DJ, Arthur LO, Sehgal PK, Letvin NL, King NW, Daniel MD

**Journal**

**Objectives**
Challenge, Immunogenicity.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
Whole inactivated SIVmac251

**Type**
Whole (killed) Inactivated Virus

**Route**
Intramuscular

**Challenge**
SIVmac251

**Route**
Intravenous

**Main Findings**

- 2/2 animals became infected with HIV, indicating that the immune response elicited by immunization with gp120 formulated in alum was not effective in preventing infection with HIV-1.

**NHP.247 (2555541)**

**Challenge of chimpanzees (Pan troglodytes) immunized with human immunodeficiency virus envelope glycoprotein gp120**

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity. To determine the efficacy of the immunization of a gp120 immunization to prevent infection from homologous HIV-1 IIIB challenge in chimpanzees.

**Species/Subspecies**
Pan troglodytes troglodytes (chimpanzee)

**Vaccine Name**
HIV-1 IIIB gp120

**Type**
Purified Viral Products

**Route**
Intravenous

**Main Findings**

- 2/2 animals became infected with HIV, indicating that the immune response elicited by immunization with gp120 formulated in alum was not effective in preventing infection with HIV-1.

**NHP.248 (2555923)**

**A formalin-inactivated whole SIV vaccine confers protection in macaques**

**Authors**

**Journal**
Science 1989 Dec 8;246(4935):1293-7

HIV Immunology and HIV/SIV Vaccine Databases 2003 1283
**Vaccines**

**Trial Summaries**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Species/Subspecies</th>
<th>Vaccine Name</th>
<th>Challenge</th>
<th>Challenge Route</th>
<th>Main Findings</th>
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<tbody>
<tr>
<td><strong>SIV/DeltaB670</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
<td>SIV/DeltaB670</td>
<td>Route: Intramuscular</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SIVDeltaB670</strong></td>
<td></td>
<td></td>
<td>Route: Intravenous</td>
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</tbody>
</table>

**Objectives**
- Challenge, Immunotherapy
- Evaluate capacity of formalin-inactivated whole virus vaccine to prevent infection and/or block development of SIV.

**Main Findings**
- Immunization with formalin-inactivated whole SIV potentiated with either MDP or MDP combined with alum protected 9/9 juvenile rhesus monkeys against disease for at least 1 year after challenge.
- A high dose of highly purified material was used for all immunizations.
- The vaccine contained all major virion proteins.
- A rest period sufficient to establish appropriate memory cells was allowed before exposure to live virus.

**NHP.249**

**Authors**

**Journal**

**Objectives**
- Challenge, Immunogenicity

**Main Findings**
- Although HIV-specific antibody and T-cell responses were elicited by immunization, virus was isolated from lymphocytes of all challenged chimpanzees, indicating that immunization did not prevent infection by HIV.
- Among the animals that received a higher dose of LAV-1, 1/2 control chimpanzees, but none of the 4 v-env5-immunized chimpanzees developed substantial and persistent lymphadenopathy.

**NHP.250**

**Authors**

**Journal**

**Objectives**
- Challenge, Immunogenicity
- To evaluate potential of subunit vaccine (nef) to elicit protection with nef-specific CTLs.

**Main Findings**
- Strong CTL responses substantially reduce viral load and appear to clear infection.
- Early decline in viraemia, observed in both vaccinated and unvaccinated control animals was associated with the development of virus-specific CTL activity and not with the presence of virus-specific neutralizing antibodies.

**NHP.251**

**Authors**

**Journal**

**Objectives**
- Challenge, Immunogenicity

**Main Findings**
- Background: Rhesus macaques immunized with attenuated vaccinia or canarypox HIV-1 recombinants and boosted with HIV-1 protein subunits formulated in alum, then challenged with HIV-2.SBL6669.
- Following challenge with HIV-2SBL6669, 3/8 immunized macaques resisted infection for 6 months and another exhibited significantly delayed infection, whereas all 3 naïve controls became infected.
- Immunizations elicited both humoral and cellular immune responses with no clear correlation with protection.

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**1284 HIV Immunology and HIV/SIV Vaccine Databases 2003**
<table>
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<tr>
<th>NHP.252 (7585217)</th>
<th>Long-term protection against SIV-induced disease in macaques vaccinated with a live attenuated HIV-2 vaccine</th>
</tr>
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<tbody>
<tr>
<td><strong>Journal</strong></td>
<td>Nat Med 1995 Sep;1(9):914-8</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To test the ability of a live attenuated human immunodeficiency virus type 2 (HIV-2) vaccine to protect cynomolgus monkeys against superinfection with a pathogenic simian immunodeficiency virus (SIVsm).</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td>3/4 monkeys vaccinated with live HIV-2 were protected against immunosuppression and SIV-induced disease during more than 5 years of follow-up.</td>
</tr>
<tr>
<td></td>
<td>The quality of the immunity was permissive for infection, but monkeys that survived showed restricted viral replication in peripheral blood and lymph nodes.</td>
</tr>
<tr>
<td></td>
<td>Protection against a pathogenic heterologous primate lentivirus is possible.</td>
</tr>
<tr>
<td></td>
<td>Vaccine can prevent disease in vaccinated monkeys even if infection is not prevented.</td>
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</tbody>
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<table>
<thead>
<tr>
<th>NHP.253 (7625117)</th>
<th>Heterologous HIV-2 challenge of rhesus monkeys immunized with recombinant vaccinia viruses and purified recombinant HIV-2 proteins</th>
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</thead>
<tbody>
<tr>
<td><strong>Journal</strong></td>
<td>Vaccine 1995 Feb;13(2):202-8</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To analyze the role of anti-envelope immunity in the protection of rhesus monkeys against an HIV-2 intravenous challenge.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td>None of the animals was protected in spite of high humoral immune responses on day of challenge as determined by ELISA and Western Blot assays.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>NHP.254 (7521918)</th>
<th>Vaccine-induced neutralizing antibodies directed in part to the simian immunodeficiency virus (SIV) V2 domain were unable to protect rhesus monkeys from SIV experimental challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Schlienger K, Montefiori DC, Mancini M, Riviere Y, Tiollais P, Michel ML</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To analyze the role of an SIV V2 vaccine as an effective region to boost SIV-neutralizing antibodies and to protect against live SIV challenge.</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td>2 rhesus macaques primed with vaccinia virus recombinants expressing the surface glycoprotein gp140 of SIVmac then given booster with the SIVmac V2 domain: The 2 vaccinated macaques exhibited SIV-neutralizing antibodies (part of which directed specifically to the V2 region) after primer injections that were enhanced by the V2/HBsAg injections.</td>
</tr>
<tr>
<td></td>
<td>Animals not protected against homologous challenge with SIVmac251.BK28.</td>
</tr>
<tr>
<td></td>
<td>Vaccinees had higher viral loads than control animals after challenge.</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>NHP.255 (7632466)</th>
<th>In vivo administration of CD4-specific monoclonal antibody: effect on provirus load in rhesus monkeys chronically infected with the simian immunodeficiency virus of macaques</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Reimann KA, Cate RL, Wu Y, Palmer L, Olson D, Waite BC, Letvin NL, Burkly LC</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Immunotherapy, Passive Immunization To study the potential role of monoclonal antibodies specific for CD4 as an AIDS therapy.</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td>6 infected monkeys treated with anti-CD4 MAb demonstrated a significant decrease in SIVmac provirus level after 9 days (3 had &gt;800 CD4 cell/microliter and developed strong antimouse Ig response that prevented further treatment; the remaining 3 monkeys had &lt;800 CD4 cell/microliter and failed to develop antimouse Ig antibody response).</td>
</tr>
</tbody>
</table>
|  | 4 control monkeys that received a control MAb of irrelevant specificity for 9-22 days showed either no significant change or a transient increase in SIVmac provirus.
<table>
<thead>
<tr>
<th>NHP.256</th>
<th>Vaccine-induced protection of chimpanzees against infection by a heterologous human immunodeficiency virus type 1</th>
</tr>
</thead>
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<tr>
<th>NHP.257</th>
<th>Vaccine-induced virus-neutralizing antibodies and cytotoxic T cells do not protect macaques from experimental infection with simian immunodeficiency virus SIVmac32H (15)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Hulskotte EG, Geretti AM, Siebelink KH, van Amerongen G, Cranage MP, Rud EW, Norley SG, de Vries P, Osterhaus AD</td>
</tr>
</tbody>
</table>

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<tr>
<th>NHP.258</th>
<th>Cross-protective immune responses induced in rhesus macaques by immunization with attenuated macrophage-tropic simian immunodeficiency virus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Clements JE, Montelaro RC, Zink MC, Amedee AM, Miller S, Trichel AM, Jagerski B, Hauer D, Martin LN, Bohm RP, et al.</td>
</tr>
</tbody>
</table>

**Objectives**
- Immunogenicity

**Species/Subspecies**
- Macaca mulatta (Rhesus macaque)

**Main Findings**
- Rhesus macaques inoculated with an attenuated macrophage-tropic recombinant of SIVmac239 (SIV/17E-CI) exhibited vigorous type-specific nab responses restricted to SIV/17E-CI by 2 weeks postinfection.
- Cross-reactive neutralizing antibodies emerged by 7 months, which neutralized not only SIV/17E-CI but also the heterologous primary isolate SIV/DeltaB670.
- Challenge of SIV/17E-CI-infected monkeys with SIV/DeltaB670: protective responses associated with cross-reactive neutralizing antibodies.
- Passive transfer of sera from SIV/17E-CI-infected animals passively protected 2/4 naive recipients

<table>
<thead>
<tr>
<th>NHP.259</th>
<th>Macaques immunized with HLA-DR are protected from challenge with simian immunodeficiency virus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Arthur LO, Bess JW Jr, Urban RG, Strominger JL, Morton WR, Mann DL, Henderson LE, Benveniste RE</td>
</tr>
</tbody>
</table>
**Objectives**
Challenge, Immunogenicity To identify the potential antigens involved in protection induced by the immunization with uninfected human cells against the challenge with SIV propagated in human cells.

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Main Findings**
- All macaques immunized with beta 2M and HLA class I developed high antibody titers to beta 2M, BUT were not protected from a subsequent challenge with infectious SIV grown in human cells.
- The macaques immunized with class II protein (HLA-DR) and mock virus developed antibodies to class II protein and were protected from the intravenous infectious virus challenge.
- The protection seen with human class II protein did not extend to protection from infection with SIV containing macaque class II proteins.
- Immunization with a purified cellular protein can protect from virus infection.

**NHP.260** (7752758) Protection by attenuated simian immunodeficiency virus in macaques against challenge with virus-infected cells

**Authors**
Almond N, Kent K, Cranage M, Rud E, Clarke B, Stott EJ

**Journal**
Lancet 1995 May 27;345(8961):1342-4

**NHP.261** (7865285) Vaccine protection and reduced virus load from heterologous macaque-propagated SIV challenge

**Authors**

**Journal**
AIDS Res Hum Retroviruses 1994;10 Suppl 2:S117-21

**NHP.262** (7884874) A vaccine-elicted, single viral epitope-specific cytotoxic T lymphocyte response does not protect against intravenous, cell-free simian immunodeficiency virus challenge

**Authors**

**Journal**

**NHP.263** (7818809) T-cell proliferation to subinfectious SIV correlates with lack of infection after challenge of macaques

**Authors**
Clerici M, Clark EA, Polacino P, Axberg I, Kuller L, Casey N, Morton WR, Shearer GM, Benveniste RE

**Journal**

**NHP.265** (11090194) Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity To use molecular clones (that express nucleocapsid deletion mutant SIVs that are replication defective but capable of completing virtually all of the steps of a single viral infection cycle) in a vaccine challenge study.

**Species/Subspecies**
Macaca nemestrina (pigtailed macaque)

**Vaccine Name**
SIV(Mne)NC

**Type**:
Live Attenuated Virus

**Routes**:
Subcutaneous, Intramuscular

**Challenge**
SIV(Mne) clone E11S

**Type**:
Live Attenuated Virus

**Routes**:
Intravenous

**Main Findings**
11/11 animals immunized with nucleocapsid mutant SIV DNA; immunized animals became infected following challenge but typically showed decreased initial peak plasma SIV RNA levels compared to those of control animals; all control animals became infected and 3/4 animals developed progressive SIV disease leading to death.

- Only modest and inconsistent humoral responses and no cellular immune responses were observed prior to challenge.
- Immunization of macaques with DNA that codes for replication-defective but structurally complete virions appears to protect from or at least delay the onset of AIDS after infection with a pathogenic immunodeficiency virus.
Protection by SIV VLP DNA prime/protein boost following mucosal SIV challenge is markedly enhanced by IL-12/GM-CSF co-administration

Authors

Journal

Objectives
Challenge, Immunogenicity To induce and enhance antiviral responses using a DNA prime/virus-like particles (VLP) protein boost strategy adjuvanted with interleukin (IL)-12/GM-CSF in rhesus macaques challenged with simian immunodeficiency virus (SIV).

Main Findings
• All except 1 immunized monkey became infected.
• All immunized monkeys showed a marked reduction of acute viral peaks.
• Reduction of viral load set points was only achieved in groups whose prime-boost immunizations were supplemented with IL-12/GM-CSF (prime) and/or with IL-12 (boost).
• Control of viremia correlated with lack of disease progression and survival.
• Detection of virus in rectal washes at 1 year post-challenge was only successful in monkeys whose immunizations did not include cytokine adjuvant, but these loads did not correlate with plasma viral loads.

Protection of chimpanzees from infection by HIV-1 after vaccination with recombinant glycoprotein gp120 but not gp160

Authors
Berman PW, Gregory TJ, Riddle L, Nakamura GR, Champe MA, Porter JP, Wurm FM, Hershberg RD, Cobb Ek, Eichberg JW

Journal

Objectives
Challenge, Immunogenicity To study chimpanzees that were immunized with recombinant forms of the HIV-1 glycoproteins gp120 and gp160 produced in Chinese hamster ovary cells, and then challenged with HIV-1.

Species/Subspecies
Pan Troglodytes (Chimpanzee)

Vaccine Name
gp120  Type: Recombinant Subunit Protein
rsgp160  Type: Recombinant Subunit Protein

Challenge
HIV-1 IIIB  Route: Intravenous

Main Findings
• The control and the 2 animals immunized with the gp160 variant became infected within 7 weeks of challenge.
• The 2 animals immunized with the gp120 variant have shown no signs of infection after more than 6 months.
• Conclusion: recombinant gp120, formulated in an adjuvant approved for human use, can elicit protective immunity against a homologous strain of HIV-1.

Minimization of chronic plasma viremia in rhesus macaques immunized with synthetic HIV-1 Tat peptides and infected with a chimeric simian/human immunodeficiency virus (SHIV33)

Authors
Goldstein G, Manson K, Tribbick G, Smith R

Journal
Vaccine 2000 Jun 15;18(25):2789-95

Objectives
Challenge, Immunogenicity To study the effect of Tat on HIV-1 replication in vivo during acute, chronic asymptomatic and AIDS stages of infection by comparisons of plasma viremia in Tat-immunized or control monkeys challenged with SHIV33 or SHIV33A.

Species/Subspecies
Macaca mulatta (Rhesus macaque)

Vaccine Name
Synthetic tat  Type: Synthetic Protein/Peptide  Route: Intramuscular

Challenge
SHIV33, SHIV33A  Route: Intravenous

Main Findings
• Immunization of monkeys with tat affected the outcome of challenge: chronic plasma viremia became undetectable or minimized in Tat-immunized asymptomatic SHIV33-infected monkeys while the high viral loads of acute infection or SHIV33A-induced simian AIDS were unaffected by Tat immunization.
• Active or passive immunotherapies targeting Tat provide potential approaches to controlling chronic HIV-1 viremia and preventing AIDS.
<table>
<thead>
<tr>
<th>NHP.268.2</th>
<th>Minimization of chronic plasma viremia in rhesus macaques immunized with synthetic HIV-1 Tat peptides and infected with a chimeric simian/human immunodeficiency virus (SHIV33)</th>
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<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Goldstein G, Manson K, Tribbick G, Smith R</td>
</tr>
<tr>
<td><strong>Journal</strong></td>
<td>Vaccine 2000 Jun 15;18(25):2789-95</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To study the effect of Tat on HIV-1 replication in vivo during acute, chronic asymptomatic and AIDS stages of infection by comparisons of plasma viremia in Tat-immunized or control monkeys challenged with SHIV33 or SHIV33A.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td>• See NHP.268.</td>
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<tr>
<th>NHP.269</th>
<th>Protection of macaques against intrarectal infection by a combination immunization regimen with recombinant simian immunodeficiency virus SIVmne gp160 vaccines</th>
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<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Polacino P, Stallard V, Montefiori DC, Brown CR, Richardson BA, Morton WR, Benveniste RE, Hu SL</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To examine the protective efficacy of recombinant simian immunodeficiency virus SIVmne envelope (gp160) vaccines against mucosal challenge by the cloned homologous virus E11S clone and the uncloned SIVmne.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca fascicularis (cynomolgus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>Recombinant vaccinia virus vac-gp160 (v-SE5) <strong>Type</strong>: Recombinant Vector (virus/bacteria) <strong>Route</strong>: Scarification</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>gp160/BSC-40 <strong>Type</strong>: Purified Viral Products <strong>Route</strong>: Intramuscular</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SIV(Mne) clone E11S, SIV(Mne) Cell-free <strong>Route</strong>: Intrarectal</td>
</tr>
<tr>
<td><strong>Main Findings</strong></td>
<td>• Protection correlates with high levels of SIV-specific antibodies.</td>
</tr>
<tr>
<td></td>
<td>• 4/4 vaccinees developed low levels of SIV-specific antibody responses after the recombinant vaccinia virus immunization; level increased 10-30 fold by boost envelop subunit.</td>
</tr>
<tr>
<td></td>
<td>• After intrarectal challenge with E11S, all 3 control animals became persistently infected, whereas 3/4 immunized macaques were completely protected.</td>
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<thead>
<tr>
<th>NHP.270.1</th>
<th>Induction of simian immunodeficiency virus (SIV)-specific CTL in rhesus macaques by vaccination with modified vaccinia virus Ankara expressing SIV transgenes: influence of pre-existing anti-vector immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Sharpe S, Polyansksaya N, Dennis M, Sutter G, Hanke T, Erfle V, Hirsch V, Cranage M</td>
</tr>
<tr>
<td><strong>Journal</strong></td>
<td>J Gen Virol 2001 Sep;82(Pt 9):2215-23</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity, Immunotherapy To compare the immunogenicity of two vaccine candidates, the canarypox-based ALVAC-SIV-gag-pol-env and the vaccinia-based NYVAC-SIV-gag-pol-env, in rhesus macaques infected with SIVmac251 and treated with ART by 2 weeks postinfection.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) <strong>Type</strong>: Recombinant Vector (virus/bacteria) <strong>Route</strong>: Intramuscular</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>ALVAC-SIV-gpe (vcp180) <strong>Type</strong>: Recombinant Vector (virus/bacteria) <strong>Route</strong>: Intramuscular</td>
</tr>
</tbody>
</table>

**HIV Immunology and HIV/SIV Vaccine Databases 2003**
Main Findings

- Both ALVAC-SIV-gpe and NYVAC-SIV-gpe vaccine candidates induced and/or enhanced a virus-specific CD8+ T cell response to a similar extent, as demonstrated by tetramer staining of Gag-specific CD8+ T cells.
- Both vaccines elicited comparable lymphoproliferative responses (LPRs) to the SIV p27 Gag and gp120 Env proteins.
- The vaccine was given after infection and initiation of HAART, as a therapeutic vaccine, not as protection from infection.

**NHP.275** (9234548) SIV DNA vaccine trial in macaques: post-challenge necropsy in vaccine and control groups

**Authors** Lu S, Manson K, Wyand M, Robinson HL


**Objectives** Challenge To study histopathologic findings from 9 macaques in a simian immunodeficiency virus (SIV) DNA vaccine trial evaluating the ability of a 5-plasmid DNA vaccine to protect against an uncloned SIVmac251 challenge (Lu et al., J. Virol. 1996, 70, 3978-3991).

**Species/Subspecies** Macaca (sp)

**Vaccine Name** DNA-SIV Type: DNA Routes: Intravenous, Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

**Main Findings**

- 3 vaccinated and 1 control macaques developed disease and were sacrificed in the first year following challenge.
- Diseased and clinically "normal" animals had developed typical SIV-related lymphoid changes, inflammatory disorders and opportunistic infections (all but 1 vaccinated animal and both controls).
- The ability to contain challenge was superior in animals immunized by 3 routes (iv,im and gene gun) as compared to those that received the control DNA or DNA vaccine by gene gun only.

**NHP.276** (12396607) Evaluation in rhesus macaques of Tat and rev-targeted immunization as a preventive vaccine against mucosal challenge with SHIV-BX08


**Journal** DNA Cell Biol 2002 Sep;21(9):653-8

**Objectives** Challenge, Immunogenicity To evaluate whether vaccination with Tat or Tat and Rev could significantly reduce viral load in nonhuman primates.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** SFV-tat Type: Recombinant Vector (virus/bacteria) Route: Subcutaneous

**Vaccine Name** SFV-rev Type: Recombinant Vector (virus/bacteria) Route: Subcutaneous

**Vaccine Name** MVA-tat Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

**Vaccine Name** MVA-rev Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

**Vaccine Name** DNA-pCI-tat Type: DNA Routes: Intradermal, Intramuscular

**Vaccine Name** DNA-pCI-rev Type: DNA Routes: Intradermal, Intramuscular

**Challenge** SHIV-BX08 Route: Intarrectal

**Main Findings**

- The immunization strategy by priming with either DNA or SFV seemed to be equivalent, but the additive or synergistic effect of a rev vaccine could not be clearly established.
- None of the animals was protected from infection.
- Peak viremia was reduced more than 200-fold compared to sham controls in one third (6/18) of vaccinated macaques.
- 4/6 protected animals did not seroconvert.

**NHP.277** (12396606) Immunogenicity of HIV-1 IIIB and SHIV 89.6P Tat and Tat toxoids in rhesus macaques: induction of humoral and cellular immune responses

**Authors** Richardson MW, Mirchandani J, Silvera P, Regulier EG, Capini C, Bojczuk PM, Hu J, Gracely EJ, Boyer JD, Khalili K, Zagury JF, Lewis MG, Rappaport J

**Journal** DNA Cell Biol 2002 Sep;21(9):637-51

**Objectives** Challenge, Immunogenicity To compare immune responses in rhesus macaques immunized with unmodified HIV-1 IIIB Tat, SHIV89.6P Tat, and carboxymethylated IIIB and 89.6P Tat toxoids.
Main Findings

- Immunization with either IIIB or 89.6P preparation induced high titer and broadly cross-reactive serum anti-Tat IgG that recognized HIV-1 subtype-E and SIVmac251 Tat.
- Proliferative responses to Tat toxoids corresponding to the immunogen were evident in vitro in both IIIB and 89.6P groups.
- All animals were infected upon intravenous challenge with 30 MID(50) of SHIV89.6P and outcome of vaccine groups was not different from controls.
- Tat specific CD8+ T-cell responses may not appropriately recognize infected cells in vivo in rhesus macaque model.

NHP.278 (12477432) Co-immunization of rhesus macaques with plasmid vectors expressing IFN-gamma, GM-CSF, and SIV antigens enhances anti-viral humoral immunity but does not affect viremia after challenge with highly pathogenic virus


Objectives Challenge, Immunogenicity To investigate the adjuvant capacity of.

Main Findings

- Proliferative responses significantly enhanced by co-immunization with the cytokines GM-CSF and interferon-γ.
- 12 immunized monkeys and 6 naive controls, were challenged by the oral mucosal route with the uncloned and highly pathogenic SIVmac251 and became infected.
- Plasma viremia set points were not different in co-immunized group and the non-immunized control group.
- Monkeys vaccinated with equivalent amounts of empty vector plasmid (i.e. no cytokine inserts) along with plasmids expressing viral antigens demonstrated a slight but significant decrease in acute viremia compared to non-immunized controls (P<0.02).
- Conclusion: results underscore the need for further testing of cytokines as vaccine adjuvants in relevant animal models.

NHP.279 (12396605) Potent, persistent cellular immune responses elicited by sequential immunization of rhesus macaques with Ad5 host range mutant recombinants encoding SIV Rev and SIV Nef

Authors Patterson LJ, Malkevitch N, Zhao J, Peng B, Robert-Guroff M
Journal DNA Cell Biol 2002 Sep;21(9):627-35

NHP.280 (12396604) Design and in vivo immunogenicity of a polyvalent vaccine based on SIVmac regulatory genes

Authors Hel Z, Tryniszewska E, Tsai WP, Johnson JM, Harrod R, Fullen J, Kalyanaraman VS, Altman JD, McNally J, Karpova T, Felber BK, Tartaglia J, Franchini G
Journal DNA Cell Biol 2002 Sep;21(9):619-26

NHP.281 (12391256) Vaccination of macaques with long-standing SIVmac251 infection lowers the viral set point after cessation of antiretroviral therapy

Authors Tryniszewska E, Nacsa J, Lewis MG, Silvera F, Montefiori D, Venzen D, Hel Z, Parks RW, Moniuszko M, Tartaglia J, Smith KA, Franchini G
Journal J Immunol 2002 Nov 1;169(9):5347-57

Objectives Immunotherapy, Chemotherapy Tested ART, ART plus therapeutic vaccine, ART plus therapeutic vaccine plus IL-2, ART plus IL-2.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Therapeutic vaccines reduced average viral load at set point, but not peak viral load following cessation of ART. Addition of IL-2 to therapeutic vaccine produced virus-specific proliferative resopnses lower than therapeutic vaccine alone.

NHP.282 (12391187) Containment of simian immunodeficiency virus infection in vaccinated macaques: correlation with the magnitude of virus-specific pre- and postchallenge CD4+ and CD8+ T cell responses

Authors Hel Z, Nacsa J, Tryniszewska E, Tsai WP, Parks RW, Montefiori DC, Felber BK, Tartaglia J, Pavlakis GN, Franchini G
Journal J Immunol 2002 Nov 1;169(9):4778-87
Both mucosal and systemic routes of immunization with the live, attenuated NYVAC/simian immunodeficiency virus SIV(gpe) recombinant vaccine result in gag-specific CD8(+) T-cell responses in mucosal tissues of macaques

Authors

Journal
J Virol 2002 Nov;76(22):11659-76

Elicitation of simian immunodeficiency virus-specific cytotoxic T lymphocytes in mucosal compartments of rhesus monkeys by systemic vaccination

Authors

Journal

Live, attenuated simian immunodeficiency virus SIVmac-M4, with point mutations in the Env transmembrane protein intracytoplasmic domain, provides partial protection from mucosal challenge with pathogenic SIVmac251

Authors
Shacklett BL, Shaw KE, Adamson LA, Wilkens DT, Cox CA, Montefiori DC, Gardner MB, Sonigo P, Luciwa PA

Journal
J Virol 2002 Nov;76(22):11365-78

Systemic infection and limited replication of SHIV vaccine virus in brains of macaques inoculated intracerebrally with infectious viral DNA

Authors

Journal
Virology 2002 Sep 15;301(1):130-5

A simian immunodeficiency virus nef peptide is a dominant cytotoxic T lymphocyte epitope in Indian-origin rhesus monkeys expressing the common MHC class I allele mamu-A*02

Authors

Journal
Virology 2002 Sep 30;301(2):365-73

Effects of cytotoxic T lymphocytes (CTL) directed against a single simian immunodeficiency virus (SIV) Gag CTL epitope on the course of SIVmac239 infection

Authors

Journal

Slowly declining levels of viral RNA and DNA in DNA/recombinant modified vaccinia virus Ankara-vaccinated macaques with controlled simian-human immunodeficiency virus SHIV-89.6P challenges

Authors
Tang Y, Villinger F, Staprans SI, Amara RR, Smith JM, Herndon JG, Robinson HL

Journal

Infection of macaques with chimeric simian and human immunodeficiency viruses containing Env from subtype F

Authors
Kuwata T, Takemura T, Takehisa J, Miura T, Hayami M

Journal
Arch Virol 2002 Jun;147(6):1121-32

Nonneutralizing antibodies to the CD4-binding site on the gp120 subunit of human immunodeficiency virus type 1 do not interfere with the activity of a neutralizing antibody against the same site

Authors
Herrera C, Spenlehauer C, Fung MS, Burton DR, Beddows S, Moore JP

Journal

Objectives
Passive Immunization To investigate whether nonneutralizing monoclonal antibodies to the gp120 subunit of env glycoprotein complex of HIV-1 can interfere with HIV-1 neutralization by another anti-gp120 MAb.

Main Findings
• REMOVE THIS.
**NHP.293** (1708168) Recombinant virus vaccine-induced SIV-specific CD8+ cytotoxic T lymphocytes

**Authors** Shen L, Chen ZW, Miller MD, Stallard V, Mazzara GP, Panicali DL, Letvin NL

**Journal** Science 1991 Apr 19;252(5004):440-3

**Main Findings**
- Upon challenge with virulent SIVmac251, all animals became infected.
- The immunized animals mounted better antiviral antibody responses, controlled virus levels more effectively, and had a longer disease-free survival than the unvaccinated infected monkeys.
- Maternal antibodies did not significantly reduce the efficacy of the MVA-SIVgpe vaccine.

**NHP.294** (12477823) Immunization of newborn rhesus macaques with simian immunodeficiency virus (SIV) vaccines prolongs survival after oral challenge with virulent SIVmac251.


**Objectives** Challenge, Immunogenicity To evaluate immunization of infant macaques at birth and 3 weeks of age with either MVA-SIV Gag, Pol, and Env or live-attenuated SIVmac1A11.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** rMV A SIVmac239 gagpolenv
- **Type**: Recombinant Vector (virus/bacteria)
- **Routes**: Intramuscular, Intranasal

**Vaccine Name** SIVmac1A11
- **Type**: Live Attenuated Virus
- **Routes**: Intravenous, Oral, Intranasal

**Vaccine Name** Anti-SIVmac251
- **Type**: Passive Antibody
- **Route**: Intraplacental

**Challenge** SIVmac251
- **Route**: Oral

**Main Findings**
- Following intravenous infection of macaques with SIVsmE543-3, the wide range in plasma viremia followed the same rank order as the relative susceptibility established by in vitro studies.
- Significant correlation between plasma viremia at 2-8 wpi and in vitro susceptibility (P < 0.05).
- Simian T-lymphotropic virus type 1 appears to enhance susceptibility to SIV infection.
- Intrinsic susceptibility of CD4+ target cells influences early virus replication patterns in vivo.

**NHP.295** (11000207) Intrinsic susceptibility of rhesus macaque peripheral CD4(+) T cells to simian immunodeficiency virus in vitro is predictive of in vivo viral replication

**Authors** Goldstein S, Brown CR, Dehghani H, Lifson JD, Hirsch VM


**Main Findings**
- Following intravenous infection of macaques with SIVsmE543-3, the wide range in plasma viremia followed the same rank order as the relative susceptibility established by in vitro studies.
- Significant correlation between plasma viremia at 2-8 wpi and in vitro susceptibility (P < 0.05).
- Simian T-lymphotropic virus type 1 appears to enhance susceptibility to SIV infection.
- Intrinsic susceptibility of CD4+ target cells influences early virus replication patterns in vivo.

**NHP.296** (12502820) Prevention of Disease Induced by a Partially Heterologous AIDS Virus in Rhesus Monkeys by Using an Adjuvanted Multicomponent Protein Vaccine

**Authors** Voss G, Manson K, Montefiori D, Watkins DI, Heeney J, Wyand M, Cohen J, Bruck C


**Objectives** Challenge To assess the efficacy of a recombinant human immunodeficiency virus type 1 (HIV-1) gp120, NefTat fusion protein, and simian immunodeficiency virus (SIV) Nef formulated in the clinically tested adjuvant AS02A.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)

**Vaccine Name** Recombinant gp120
- **Type**: Recombinant Subunit Protein
- **Route**: Intramuscular

**Vaccine Name** Nef-Tat
- **Type**: Recombinant Subunit Protein
- **Route**: Intramuscular

**Vaccine Name** SIV Nef
- **Type**: Recombinant Subunit Protein
- **Route**: Intramuscular

**Main Findings**
- Multiantigen subunit protein vaccine was able to prevent the development of disease induced in rhesus monkeys by a partially heterologous AIDS virus.
Trial Summaries

- Upon challenge of genetically unselected rhesus monkeys with the highly pathogenic and partially heterologous SIV/HIV strain SHIV89.6p, the vaccine was able to reduce virus load and protect the animals from a decline in CD4-positive cells.
- Vaccination prevented the development of AIDS for more than 2.5 years.

NHP.297 (12502815)  **Increased mucosal transmission but not enhanced pathogenicity of the CCR5-tropic, simian AIDS-inducing simian/human immunodeficiency virus SHIV(SF162P3) maps to envelope gp120**

**Authors** Hsu M, Harouse JM, Gettie A, Buckner C, Blanchard J, Cheng-Mayer C  
**Objectives** Pathogenicity To determine whether envelope glycoprotein gp120 is responsible for increased pathogenesis and transmissibility of the SHIV-SF162P3.

Main Findings

- See NHP.312.

NHP.298 (12477842)  **Importance of B-cell responses for immunological control of variant strains of simian immunodeficiency virus**

**Authors** Johnson WE, Lifson JD, Lang SM, Johnson RP, Desrosiers RC  
**Objectives** Immunogenicity, Pathogenicity To compare the pathogenicity of three variants of cloned simian immunodeficiency virus strain 239 (SIV239).

Main Findings

- All 3 cloned strains (M5, DeltaV1-V2 and 316) of SIVmac239 were capable of significant levels of fusion independent of CD4, and all 3 were considerably more sensitive to antibody-mediated neutralization than the parent strain from which they were derived.
- The 3 clones induce viral loads at peak height around day 14 that are indistinguishable from or only slightly less than those observed in monkeys infected with the parental SIV239 strain.
- Viral loads at the set point 20 to 50 weeks after infection, however, were more than 400- to 10,000-fold lower with the variant strains.
- Depletion of B cells around the time of infection with M5 resulted in less effective immunological control and much higher viral loads at the set point in 2/3 monkeys.

NHP.299 (12496959)  **Therapeutic dendritic-cell vaccine for simian AIDS**

**Authors** Lu W, Wu X, Lu Y, Guo W, Andrieu JM  
**Objectives** Immunogenicity, Immunotherapy To investigate the ability of a vaccination with chemically inactivated SIV-pulsed dendritic cells to induce cellular and humoral immunity in SIV infected rhesus monkey model.

Main Findings

- Chemically inactivated SIV-pulsed dendritic cells induced an effective and durable SIV-specific cellular and humoral immunity in SIV-infected rhesus monkeys.
- After 3 immunizations made at 2-week intervals, the animals exhibited a 50-fold decrease of SIV DNA and a 1,000-fold decrease of SIV RNA in peripheral blood with reduced viral load levels maintained over the remaining 34 weeks.

NHP.300 (12531331)  **A Gag-Pol/Env-Rev SIV239 DNA vaccine improves CD4 counts, and reduce viral loads after pathogenic intrarectal SIV(mac)251 challenge in Rhesus Macaques**

**Authors** Muthumani K, Bagarazzi M, Conway D, Hwang DS, Manson K, Ciccarelli R, Israel Z, Montefiori DC, Ugen K, Miller N, Kim J, Boyer J, Weiner DB  
**Journal** Vaccine 2003 Jan 30;21(7-8):629-37  
**Objectives** Challenge, Immunogenicity To study plasmid vaccines supplemented by IL-2 Ig cytokine gene adjuvants or boosted by recombinant MVA vectors expressing relevant SIV and HIV antigens.

Main Findings

Specie/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name | pGagpol/EnvRev SIV239 DNA | Type: DNA | Route: Intramuscular
---|---|---|---
Challenge | SIVmac251 | Route: Intrarectal
Main Findings
- The immunization strategy employed in this study prevented CD4(+) T-cell loss and lowered viral loads following pathogenic challenge.
- Using a pathogenic SIV251 rhesus mucosal challenge model, pGag/Pol+pEnv/Rev plasmid vaccines could not prevent SIV infection: vaccinated animals exhibited significant improvement in control of viral challenge and protection against CD4(+) T-cell loss compared to control animals.

**NHP.301** (12526038) Human and simian immunodeficiency virus-infected chimpanzees do not have increased intracellular levels of beta-chemokines in contrast to infected humans

Authors | Ondoa P, Vereecken C, Fransen K, Colebunders R, Van Der Groen G, Heeney JL, Kestens L
---|---
Objectives | Immunogenicity, Pathogenicity To explain why chimpanzees infected with HIV-1 or SIVcpz are relatively resistant to AIDS.
Species/Subspecies | Pan Troglodytes (Chimpanzee)
Main Findings
- In humans, the percentage of B-chemokine-positive cells was significantly higher in CD8+ T and natural killer (NK) cells than in CD4+ T cells in both uninfected and HIV-1-infected individuals.
- In the presence of HIV-1 infection, however, both CD8+ and CD4+ T cell subsets contained significantly more B-chemokine-positive cells than in the absence of infection.
- In chimpanzees, the percentage of B-chemokine-positive CD8+ T and NK cells was significantly higher than in uninfected humans.
- In contrast to humans, infection of chimpanzees with either HIV-1 or with SIVcpz was not associated with increased numbers of B-chemokine-positive cells.

**NHP.302** (12393472) Impact of simian immunodeficiency virus (SIV) infection on lymphocyte numbers and T-cell turnover in different organs of rhesus monkeys

---|---

**NHP.303** (12502833) Control of viremia and prevention of simian-human immunodeficiency virus-induced disease in rhesus macaques immunized with recombinant vaccinia viruses plus inactivated simian immunodeficiency virus and human immunodeficiency virus type 1 particles

---|---
Objectives | Challenge, Immunogenicity To evaluate the protective efficacy of a vaccine regimen that uses recombinant vaccinia viruses expressing SIV and HIV-1 structural proteins in combination with intact inactivated SIV and HIV-1 particles.
Species/Subspecies | Macaca mulatta (Rhesus macaque)
Vaccine Name | rVV-SIVmacgag/pol | Type: Recombinant Vector (virus/bacteria) | Route: Intradermal
---|---|---|---
Vaccine Name | rVV-HIV-1.DH12env | Type: Recombinant Vector (virus/bacteria) | Route: Intradermal
Vaccine Name | AT-2 rx SIVmac239 | Type: Live Attenuated Virus | Route: Intramuscular
Vaccine Name | AT-2 rx HIV-1.DH12 | Type: Live Attenuated Virus | Route: Intramuscular
Challenge | SHIV.DH12R-PS1 | Route: Intravenous
Main Findings
- Following virus challenge, control animals experienced a rapid and complete loss of CD4(+) T cells, sustained high viral loads, and developed clinical disease by 17 to 21 weeks.
- All the vaccinated monkeys became infected, displayed reduced post-peak viremia, had no significant loss of CD4(+) T cells, and have remained healthy for more than 15 mpc.
- CD8(+) T-cell and nab responses demonstrated in vaccinated animals following challenge.
- Immunologic control of infection was incomplete (no sterilizing protection) by 22 wpc.
<table>
<thead>
<tr>
<th>NHP.304 (12556683)</th>
<th>Post-exposure prophylaxis with human monoclonal antibodies prevented SHIV89.6P infection or disease in neonatal macaques</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Journal</strong></td>
<td>AIDS 2003 Feb 14;17(3):301-309</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunotherapy, Passive Immunization To develop passive immunization with human neutralizing monoclonal antibodies against mother-to-child transmission of HIV during delivery and through breastfeeding.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>Monoclonal antibody 2G12 Type: Passive Antibody Route: Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>Monoclonal antibody 2F5 Type: Passive Antibody Route: Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>Monoclonal antibody 4E10 Type: Passive Antibody Route: Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>IgG1 b12 Type: Passive Antibody Route: Intravenous</td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td>SHIV89.6P Route: Oral</td>
</tr>
</tbody>
</table>
| **Main Findings** | • 2/4 macaque infants treated with neutralizing mAbs showed no evidence of infection; the other 2 maintained normal CD4 T cell counts.  
• In contrast, all control animals became highly viremic and had profound CD4 T cell losses; 3/4 died from AIDS within 1.5-6 weeks of the challenge  
• Conclusions: Passive immunization with this quadruple neutralizing mAbs combination may represent a promising approach to prevent peri- and postnatal HIV transmission |

<table>
<thead>
<tr>
<th>NHP.305 (12545074)</th>
<th>Live attenuated, nef-deleted SIV is pathogenic in most adult macaques after prolonged observation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>Immunogenicity, Pathogenicity To demonstrate the pathogenicity of a live attenuated SIV (SIVmac239Δ3).</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIVmac239Δ3 (cell-infected) Type: Cell/Tissue Route: Intravenous</td>
</tr>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>SIVmac239Δ3 Type: Live Attenuated Virus Routes: Intravenous, Oral, Intra-amniotic</td>
</tr>
</tbody>
</table>
| **Main Findings** | • 11/11 rhesus macaques vaccinated with SIVmac239Δ3 developed signs of immune dysfunction.  
• 11/11 vaccinated animals had inverted CD4:CD8 ratio.  
• 7/11 (64%) had persistent recurrent viremia.  
• Other signs of immune dysfunction included decreased CD4, low CD4CD29 lymphocyte subsets, low anti-gag antibodies, etc  
• 2/11 (18%) vaccinees developed AIDS.  
• Conclusion: Live attenuated virus can cause immune dysfunction in vaccinees and similar live attenuated HIV seems contraindicated for mass vaccination of humans |

<table>
<thead>
<tr>
<th>NHP.306.1 (11797011)</th>
<th>Replication-incompetent adenoviral vaccine vector elicits effective anti-immunodeficiency-virus immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Journal</strong></td>
<td>Nature 2002 Jan 17;415(6869):331-5</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Challenge, Immunogenicity To compare vaccine vector delivery systems: 3 formulations of a plasmid DNA vector (MVA) and a replication incompetent adenovirus type 5 vector expressing SIV gag protein.</td>
</tr>
<tr>
<td><strong>Species/Subspecies</strong></td>
<td>Macaca mulatta (Rhesus macaque)</td>
</tr>
</tbody>
</table>
### Trial Summaries

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>pV1R-SIVmac239-gag</td>
<td>DNA</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>MVA-SIVgag</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Ad5-SIVgag</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

### Challenge
- SHIV89.6P  

### Main Findings
- A replication-incompetent Ad5 vector, used either alone or as a booster inoculation after priming with a DNA vector elicited the most effective response.
- After challenge with a pathogenic SHIV, the animals immunized with Ad5 vector exhibited the most pronounced attenuation of the virus infection.
- The replication-defective adenovirus is a promising vaccine vector for development of an HIV-1 vaccine.

### NHP.306.2

#### Replication-incompetent adenoviral vaccine elicits effective anti-immunodeficiency-virus immunity


### Objectives
- Challenge, Immunogenicity  
  To test attenuated strains of Salmonella expressing fragments of the SIV Gag protein fused to the type III-secreted SopE protein for the ability to prime virus-specific CTL responses in rhesus macaques.

### Species/Subspecies
- Macaca mulatta (Rhesus macaque)

### Vaccine Name
- pV1R-SIVmac239-gag  
- MVA-SIVgag  
- Ad5-SIVgag

### Challenge
- SHIV89.6P

### Main Findings
- Strong Gag-specific CTL responses were consistently detected, and tetramer staining revealed the expansion of Gag181-189-specific CD8+ T-cell responses in peripheral blood also in lymphocytes isolated from the colon.
- A significant percentage of the Gag181-189-specific T-cell population in each animal also expressed the intestinal homing receptor α4β7.
- Salmonella-primed/MVA-boosted animals did not exhibit improved control of virus replication following a rectal challenge with SIVmac239.

### NHP.308

#### Mucosal priming of simian immunodeficiency virus-specific cytotoxic T-lymphocyte responses in rhesus macaques by the Salmonella type III secretion antigen delivery system

- **Authors**: Evans DT, Chen LM, Gillis J, Lin KC, Harty B, Mazzara GP, Donis RO, Mansfield KG, Lifson JD, Desrosiers RC, Galan JE, Johnson RP

### Objectives
- Challenge, Immunogenicity, Pathogenicity  
  To study the effect of interferon-γ and interleukin-4 on viral load, immunogenicity, and protective properties of Nef-lacking mutants of SIV-expressing SIV-IL4 or SIV-IFN.

### Species/Subspecies
- Macaca mulatta (Rhesus macaque)

### Vaccine Name
- rSalmonella typhimurium-SIVgag  
- rSalmonella typhi-SIVgag  
- MVA-SIVmac239gag

### Challenge
- SIVmac239  
- SHIV89.6P

### Main Findings
- Strong Gag-specific CTL responses were consistently detected, and tetramer staining revealed the expansion of Gag181-189-specific CD8+ T-cell responses in peripheral blood also in lymphocytes isolated from the colon.
- A significant percentage of the Gag181-189-specific T-cell population in each animal also expressed the intestinal homing receptor α4β7.
- Salmonella-primed/MVA-boosted animals did not exhibit improved control of virus replication following a rectal challenge with SIVmac239.

### NHP.309

#### Replication, immunogenicity, and protective properties of live-attenuated simian immunodeficiency viruses expressing interleukin-4 or interferon-gamma

- **Authors**: Stahl-Hennig C, Gundlach BR, Dittmer U, ten Haaf P, Heeney J, Zou W, Emile D, Sopper S, Uberla K
- **Journal**: Virology 2003 Jan 20;305(2):473-85

### Objectives
- Challenge, Immunogenicity, Pathogenicity  
  To study the effect of interferon-γ and interleukin-4 on viral load, immunogenicity, and protective properties of Nef-lacking mutants of SIV-expressing SIV-IL4 or SIV-IFN.

### Species/Subspecies
- Macaca mulatta (Rhesus macaque)
**Vaccine Name**
SIV-IL4  
**Type:** Live Attenuated Virus  
**Route:** Intravenous

**Vaccine Name**
SIV-IFN  
**Type:** Live Attenuated Virus  
**Route:** Intravenous

**Challenge**
SIVmac239/nef-open  
**Route:** Intravenous

**Main Findings**
- During the acute phase of infection, the cell-associated viral load, but not the plasma viral RNA load, was approximately 10-fold lower in SIV-IFN-infected macaques than in SIV-IL4-infected animals.
- The viral load declined to hardly detectable levels 4 months postinfection in all animals.
- The titers and affinity of SIV antibodies were higher in SIV-IL4-infected macaques than in SIV-IFN-infected animals.
- Subsequent challenge with SHIV revealed protection in the absence of neutralizing antibodies.

**NHP.310**  
**Increased virus replication and virulence after serial passage of human immunodeficiency virus type 2 in baboons**

**Authors**

**Journal**

**Objectives**
Pathogenicity  
To enhance the pathogenicity of HIV-2 in order to shorten the amount of time to the development of disease in baboons.

**Species/Subspecies**
Papio cynocephalus (Baboon)

**Challenge**
**Route:** Intravenous

**Main Findings**
- After these serial passages, virus levels in plasma, peripheral blood mononuclear cells (PBMC) and lymphatic tissues in the acutely infected baboons were increased.
- Within 1 year of the HIV-2 infection, all of the inoculated baboons showed specific signs of AIDS-related disease progression within the lymphatic tissues, such as vascular proliferation and lymphoid depletion.
- HIV-2(UC2) isolate recovered after several serial passages in baboons will be useful in future studies of AIDS pathogenesis and vaccine development by using this animal model.

**NHP.312**  
**Increased mucosal transmission but not enhanced pathogenicity of the CCR5-tropic, simian AIDS-inducing simian/human immunodeficiency virus SHIV(SF162P3) maps to envelope gp120**

**Authors**

**Journal**

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Challenge**
SHIVSF162-PC  
**Route:** Intravenous, Vaginal or perivaginal

**Main Findings**
- SHIVSF162-PC was as infectious as SHIVSF162, and intermediate in pathogenicity between SHIVSF162 and SHIVSF162-P3.
- Fusogenic capacity and inhibition by T-20 fusion inhibitor were also assayed.
- Compared to wild-type SHIV(SF162) gp120, P3 gp120 conferred in vitro neutralization resistance and increased entry efficiency of the virus, but was compromised in its fusion-inducing capacity.
- In vivo, SHIV(SF162PC) infected 2/2 and 2/3 rhesus macaques by the intravenous and intravaginal routes, respectively.
- Although peak viremia reached $10^6$ to $10^7$ RNA copies per ml of plasma in some infected animals and was associated with depletion of gut-associated CD4(+) lymphocytes, none of the animals maintained a viral set point that would be predictive of progression to disease.

**NHP.313.1**  
**Global Dysfunction of CD4 T-Lymphocyte Cytokine Expression in Simian-Human Immunodeficiency Virus/SIV-Infected Monkeys Is Prevented by Vaccination**

**Authors**
McKay PF, Barouch DH, Schnitz JE, Veazey RS, Gorgone DA, Lifton MA, Williams KC, Letvin NL

**Journal**

**Objectives**
Challenge, Immunogenicity  
To assess the functional capacity of CD4+ T lymphocytes in rhesus monkeys both prospectively during the course of a simian immunodeficiency virus (SIV) infection and in a cohort of SIV/SIV-infected animals with nonprogressive disease.
Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Loss of the capacity of peripheral blood CD4+ T lymphocytes to express cytokines was first detected in SIV-infected monkeys during the peak of viral replication during primary infection and persisted thereafter.
- Infected monkeys with progressive disease had peripheral blood CD4+ T lymphocytes that expressed significantly less cytokine than infected monkeys that had undetectable viral loads and intact CD4+ T-lymphocyte counts.
- CD4+ T lymphocytes from vaccinated monkeys that effectively controlled the replication of a highly pathogenic immunodeficiency virus isolate following a challenge had a preserved functional capacity.

NHP.313.2  Global Dysfunction of CD4 T-Lymphocyte Cytokine Expression in Simian-Human Immunodeficiency Virus/SIV-Infected Monkeys Is Prevented by Vaccination

Authors: McKay PF, Barouch DH, Schmitz JE, Veazey RS, Gorgone DA, Liiton MA, Williams KC, Letvin NL

Objectives: Pathogenicity To compare the CD+ T cell profile in progressor and nonprogressor rhesus monkeys infected with SIV/SHIV.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Small difference between the cytokine expression profiles of the peripheral blood CD4+ T lymphocytes from normal monkeys and those from SIV/SHIV-infected clinical nonprogressor monkeys.

NHP.318  Multi-envelope HIV vaccine safety and immunogenicity in small animals and chimpanzees

Authors: Lockey TD, Slobod KS, Caver TE, D’Costa S, Owens RJ, McClure HM, Compans RW, Hurwitz JL

Objectives: Immune response To compare the multi envelope vaccine vs. those containing a single component, inoculated by cutaenous or subcutaenous route.

Species/Subspecies: Pan Troglodytes (Chimpanzee)

Main Findings:
- Cutaenous lesions were not required to elicit HIV-1 envelope or vaccinia virus-humoral immune response.
- Antibody responses could be substantially enhanced with envelope booster immunization.
- Immune response to envelope protein persisted to >1 year.
- Multi-envelope vaccines are more immunogenic than those containing a single envelope component.

NHP.319  Evidence for immune-mediated reduction of viral replication in Macaca nemestrina mucosally immunized with inactivated SHIV(89.6)


Species/Subspecies: Macaca mulatta (Rhesus macaque)

Main Findings:
- Anti-SHIV T-cell responses were significant only in primed and boosted animals (group 2). Primed and boosted animals also showed significantly decreased viral loads compared to boosted only.

NHP.320  Identification of the V1 region as a linear neutralizing epitope of the simian immunodeficiency virus SIVmac envelope glycoprotein

## Trial Summaries

### Objectives
Immunogenicity.

### Species/Subspecies
Macaca mulatta (Rhesus macaque)

### Vaccine Name

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIV-Mac-32H</td>
<td>Live Virus</td>
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<tr>
<td>SIV-Mac-MPBMC</td>
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<td>oligomeric gp130</td>
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<td>pCMV-gag-mod</td>
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<td>Intramuscular</td>
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<td>HIV-IIIB-p55gag-VLP</td>
<td>Virus-like Particle</td>
<td>Intramuscular</td>
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<tr>
<td>p55Gag</td>
<td>Purified Viral Products</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>pSHIV-NM-3rn ZF1*</td>
<td>DNA</td>
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<tr>
<td>SHIV-NM-3rN</td>
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<td>SIVmac239Δ3</td>
<td>Live Attenuated Virus</td>
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</tr>
<tr>
<td>SIVmac239Δ3+</td>
<td>Live Attenuated Virus</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>pSIVNef-TPA</td>
<td>DNA</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

### Main Findings

- Rhesus macaques infected with clone Mac32H or immunized with Mac gp130 developed neutralizing antibodies directed at an epitope in the V1 region of Env

### NHP.321 (12719603)
**Induction of broad and potent anti-human immunodeficiency virus immune responses in rhesus macaques by priming with a DNA vaccine and boosting with protein-adsorbed polylactide coglycolide microparticles**

#### Authors

#### Journal

#### Objectives
Immunogenicity.

### Species/Subspecies
Macaca mulatta (Rhesus macaque)

### Vaccine Name

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
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</thead>
<tbody>
<tr>
<td>pCMV-gag-mod</td>
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<td>Intramuscular</td>
</tr>
<tr>
<td>HIV-IIIB-p55gag-VLP</td>
<td>Virus-like Particle</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>p55Gag</td>
<td>Purified Viral Products</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

- Priming with Gag DNA and boosting with Gag protein adsorbed to polylactide coglycolide microparticles produced a stronger and broader immune response than either vaccine alone

### NHP.322 (1286756)
**DNA vaccination of macaques by a full-genome simian/human immunodeficiency virus type I plasmid chimera that produces non-infectious virus particles**

#### Authors

#### Journal
J Gen Virol 2003 Aug;84(Pt 8):2237-2244

#### Objectives
Challenge, Immunogenicity To evaluate the immunogenicity and protection from challenge of a full-genome SHIV plasmid in rhesus monkeys.

### Species/Subspecies
Macaca mulatta (Rhesus macaque)

### Vaccine Name

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
</tr>
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<tbody>
<tr>
<td>pSHIV-NM-3rn ZF1*</td>
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<td>Intramuscular</td>
</tr>
<tr>
<td>SHIV-NM-3rN</td>
<td></td>
<td>Intravenous</td>
</tr>
</tbody>
</table>

- High CTL activity in vaccinees.
- In all macaques vaccinated, peak plasma virus loads after homologous challenge with SHIV were 2 to 3 orders of magnitude lower than those of the naive controls, and virus loads fell below the level of detection at 6 weeks post-challenge suggesting that the vaccination regimen in this study was partially effective.

### NHP.323 (12919751)
**Convergent evolution of SIV env after independent inoculation of rhesus macaques with infectious proviral DNA**

#### Authors
Buckley KA, Li PL, Kimhani AH, Hofmann-Lehmann R, Liska V, Anderson DC, McClure HM, Ruprecht RM

#### Journal
Virology 2003 Aug 1;312(2):470-80

#### Objectives
Pathogenicity.

### Species/Subspecies
Macaca mulatta (Rhesus macaque)

### Vaccine Name

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
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</thead>
<tbody>
<tr>
<td>SIVmac239Δ3</td>
<td>Live Attenuated Virus</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>SIVmac239Δ3+</td>
<td>Live Attenuated Virus</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>pSIVNef-TPA</td>
<td>DNA</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>
### Main Findings

- Rhesus macaques inoculated with SIV-MAC239, MAC239-delta3 or Mac239-delta3+ pathogenic revertant of delta3, each developed similar mutations, indicative of convergent evolution, in env

### NHP.324.1

**Boosting of SIV-specific immune responses in rhesus macaques by repeated administration of Ad5hr-SIVenv/rev and Ad5hr-SIVgag recombinants**

**Authors**

**Journal**
Vaccine 2003 Sep 8;21(25-26):4022-35

**Objectives**
Challenge To evaluate ELISPOT reactivity to Gag, Env and Rev proteins after each of 2 inoculations with Adenovirus-Env-Rev and Adenovirus-Gag vectors.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- Ad5hr-SIVenv  
  **Type:** Recombinant Vector (virus/bacteria)  
  **Routes:** Oral, Intranasal
- Ad5hr-SIVmac239gag  
  **Type:** Recombinant Vector (virus/bacteria)  
  **Routes:** Oral, Intranasal

**Challenge**
SIVmac251  
**Route:** Intrarectal

**Main Findings**
- Vaccination with 2 Ad4hr vectors containing SIV-smH4 Env-Rev and SIV-Mac239 Gag was followed by ELISPOT cellular immune response detection, and antibody titre of humoral responses.
- The second immunization significantly boosted both responses.
- Second paper described intrarectal challenge with SIV-Mac251 at week 42.
- All animals developed persistent infection, but viral burden at peak viremia was reduced (14 fold; P < 0.0001) in vaccinated animals as compared to controls.
- Viremia at set point was not significantly reduced in vaccinated animals compared to controls.

### NHP.325

**Different patterns of immune responses but similar control of a simian-human immunodeficiency virus 89.6P mucosal challenge by modified vaccinia virus Ankara (MVA) and DNA/MVA vaccines**

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- SIV-HIV89.6 DNA vaccine  
  **Type:** DNA  
  **Route:** Intradermal
- rMVA 89.6  
  **Type:** Recombinant Vector (virus/bacteria)  
  **Routes:** Intradermal, Intramuscular
- SHIV89.6P  
  **Route:** Intrarectal

**Main Findings**
- Although individual animals in DNA/MVA and MVA/MVA groups had varying levels of antibody and CD8 T-cell response, all controlled challenge virus, as measured by viral load and decline in CD4 T-cells, equally well post challenge.
**NHP.327.1** Early protection against pathogenic virus infection at a mucosal challenge site after vaccination with attenuated simian immunodeficiency virus
(14970317)
Authors Tenner-Racz K, Hennig CS, Uberla K, Stoiber H, Ignatius R, Heeney J, Steinman RM, Racz P
Journal Proc Natl Acad Sci U S A 2004 Feb 17;
Objectives Challenge, Immunogenicity
Exp 1: To investigate long-term protection induced by live attenuated delta deleted SIV.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVDeltaNU Type: Live Attenuated Virus Routes: Intravenous, Other
Challenge SIVmac251 Route: Other
Main Findings
• Experiment 1 and experiment 2: A traumatic application of attenuated SIVmac239Deltanef vaccine to the tonsils of rhesus macaques provided protection against challenge 26 weeks later with infectious SIVmac251 applied through this route.
• 10/10 vaccinates did not show significantly raised RNA levels in the plasma or increase in infected cells in lymphoid tissue after challenge (exp. 2).
• Vaccine virus was found in the tonsils of all vaccinates, but challenge virus was only detected at this portal of entry in 4/10 monkeys.
• During tonsillar SIVDeltanef vaccination, infection is blocked early at the entry portal.

**NHP.328** (12885879) Potent, persistent induction and modulation of cellular immune responses in rhesus macaques primed with Ad5hr-simian immunodeficiency virus (SIV) env/rev, gag, and/or nef vaccines and boosted with SIV gp120
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Ad5hr-SIVenv Type: Recombinant Vector (virus/bacteria) Routes: Intratracheal, Oral, Intranasal
Vaccine Name Recombinant HIV-1 gag core (p24,p15) antigen Type: Recombinant Subunit Protein Route: Intratracheal
Vaccine Name Ad5hr-SIVmac239gag Type: Recombinant Vector (virus/bacteria) Routes: Intratracheal, Oral, Intranasal
Vaccine Name Ad5hr-SIVnefδ1-13 Type: Recombinant Vector (virus/bacteria) Routes: Intratracheal, Oral, Intranasal
Vaccine Name SIVmac251-gp120 Type: Purified Viral Products Route: Intramuscular

**NHP.330** (12804847) Specificity and effect on apoptosis of Tat antibodies from vaccinated and SHIV-infected rhesus macaques and HIV-infected individuals
Objectives
Immunogenicity, Immunotherapy To study the recognition of several Tat mutants as well as various synthetic Tat fragments by anti-Tat monoclonal antibodies and by IgG antibodies in SHIV-infected macaques (also human long-term survivals infected with HIV).

Species/Subspecies
Macaca mulatta (Rhesus macaque)

Vaccine Name
Tat8-53 Type: Synthetic Protein/Peptide Routes: Intramuscular, Intranasal

Vaccine Name
Tat1-20 Type: Synthetic Protein/Peptide Routes: Intramuscular, Intranasal

Vaccine Name
Tat 19-53 Type: Synthetic Protein/Peptide Routes: Intramuscular, Intranasal

Vaccine Name
Tat 19-53m Type: Synthetic Protein/Peptide Routes: Intramuscular, Intranasal

Vaccine Name
Tat 1-61 Type: Synthetic Protein/Peptide Routes: Intramuscular, Intranasal

Vaccine Name
Tat 44-61 Type: Synthetic Protein/Peptide Routes: Intramuscular, Intranasal

Main Findings
• Tat peptides inoculated into Rhesus macaques produced antibody responses capable of inhibiting functions of extracellular Tat protein.

NHP.332 (9223407) Protection of SIVmac-infected macaque monkeys against superinfection by a simian immunodeficiency virus expressing envelope glycoproteins of HIV type 1
Authors
Journal

Objectives
Challenge, Immunogenicity To determine whether host immune responses to envelope glycoprotein are an essential component of the immunity to primate lentiviruses.

Main Findings
• Superinfection of SIVmac-infected macaque monkeys with a large dose of SHIVsbg resulted in isolation of the chimeric SHIVsbg by coculture of PBMCs from 4/5 SIV-infected monkeys, but 3 animals were protected from extracellular SHIV viremia and did not seroconvert to HIV-1 glycoproteins.
• In the 2 SIV-infected monkeys that did develop SHIV viremia, cell-associated viral load was reduced at least 100-fold.

NHP.334 (12970419) Cellular immunity elicited by human immunodeficiency virus type 1/ simian immunodeficiency virus DNA vaccination does not augment the sterile protection afforded by passive infusion of neutralizing antibodies
Authors
Journal

NHP.335 (12850342) Mucosal administration of three recombinant Mycobacterium bovis BCG-SIVmac251 strains to cynomolgus macaques induces rectal IgAs and boosts systemic cellular immune responses that are primed by intradermal vaccination
Authors
Ruprecht RM, Ferrantelli F, Kitabwalla M, Xu W, McClure HM
Journal
Vaccine 2003 Jul 28;21(24):3370-3

NHP.336 (12719580) Molecular features of the broadly neutralizing immunoglobulin G1 b12 required for recognition of human immunodeficiency virus type 1 gp120
Authors
Journal
J Virol 2003 May;77(10):5863-76

NHP.339 (12359458) Chimeric human papilloma virus-simian/human immunodeficiency virus virus-like-particle vaccines: immunogenicity and protective efficacy in macaques
Authors
Journal
Virology 2002 Sep 15;301(1):176-87

Objectives
Challenge, Immunogenicity To evaluate HPV-HIV VLPs for immunogenicity and protective immunity using a mucosal SHIV challenge model in macaques and to evaluate a DNA vaccine prime and HPV-HIV VLP boost approach to induce T cell mediated immunity in macaques.

Species/Subspecies
Macaca nemestrina (pigtailed macaque)
Vaccine Name: Pooled SIVgag/HIVtat.rev DNA vaccine  
Type: DNA  
Routes: Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

Vaccine Name: HPV/SHIV-VLP  
Type: Virus-like Particle  
Routes: Intrarectal, Intramuscular

Challenge: SHIV.229(mn)  
Route: Intrarectal

Main Findings:
- HPV L1 antibodies were induced in all immunized macaques.
- Weak antibody or T cell responses to the chimeric SHIV antigens were detected only in animals receiving the DNA prime/HPV-SHIV VLP boost vaccine regimen.
- Significant but partial protection from a virulent mucosal SHIV challenge was detected only in the prime/boosted macaques and not in animals receiving the HPV-SHIV VLP vaccines alone, with 3/5 prime/boosted animals retaining some CD4 T cells following challenge.

NHP.340 (14498982)  
**Multigene DNA prime-boost vaccines for SHIV89.6P**


**Objectives**
- Challenge, Passive Immunization

**Species/Subspecies**
- Macaca nemestrina (pigtailed macaque)

NHP.341 (14627745)  
**Transfer of neutralizing IgG to macaques 6 h but not 24 h after SHIV infection confers sterilizing protection: Implications for HIV-1 vaccine development**

**Authors:** Nishimura Y, Igarashi T, Haigwood NL, Sadjadpour R, Donau OK, Buckler C, Plishka RJ, Buckler-White A, Martin MA

**Journal:** Proc Natl Acad Sci U S A 2003 Dec 9;100(25):15131-6

**Objectives**
- Challenge, Passive Immunization

**Main Findings**
- HIV-2 expression library immunization induced HIV-2-specific memory responses but low levels of CD8+ cell anti-viral responses and neutralizing antibodies.
- Immunization with HIV-2 expression library did not significantly alter the viral load in vaccinated animals compared to control group.
- The approach does not provide protection in baboons against intravenous challenge with HIV-2.

NHP.344 (12519210)  
**Immune responses in baboons vaccinated with HIV-2 genetic expression libraries**

**Authors:** Locher CP, Sykes KF, Blackbourn DJ, Johnston SA

**Journal:** J Med Primatol 2002 Dec;31(6):323-9

**Objectives**
- Challenge, Immunogenicity
- To evaluate the effectiveness of an HIV-2 vaccine made from a genomic expression library in baboons.

**Main Findings**
- HIV-2 expression library immunization induced HIV-2-specific memory responses but low levels of CD8+ cell anti-viral responses and neutralizing antibodies.
- Immunization with HIV-2 expression library did not significantly alter the viral load in vaccinated animals compared to control group.
- The approach does not provide protection in baboons against intravenous challenge with HIV-2.

NHP.345 (14741150)  
**Avipox-based simian immunodeficiency virus (SIV) vaccines elicit a high frequency of SIV-specific CD4+ and CD8+ T-cell responses in vaccinia-experienced SIVmac251-infected macaques**

**Authors:** Nacsa J, Radaelli A, Edghill-Smith Y, Venzon D, Tsai WP, Morghen Cde G, Panicali D, Tartaglia J, Franchini G

**Journal:** Vaccine 2004 Jan 26;22(5-6):598-607

**Objectives**
- Immunogenicity, Immunotherapy, Chemotherapy
- To test the ability of ALVAC- or fowlpox-based SIV vaccines to boost SIV-specific CD4+ and CD8+ T-cell responses in 10 vaccinia-experienced macaques infected with SIVmac251.

**Species/Subspecies**
- Macaca mulatta (Rhesus macaque)

**Vaccine Name**
- SIVmac251  
  **Type:** Live Virus  
  **Route:** Intrarectal

**Vaccine Name**
- FP-SIV-gp (FP74)  
  **Type:** Recombinant Vector (virus/bacteria)  
  **Route:** Intramuscular

**Vaccine Name**
- ALVAC-SIV-gp  
  **Type:** Recombinant Vector (virus/bacteria)  
  **Route:** Intramuscular

**Main Findings**
- The 2 vaccine modalities effectively boosted both CD4+ and CD8+ SIV-specific T-cell response despite prior exposure to the vaccinia-derivative NYVAC vector, suggesting that sequential boosting with either avipox-based vector vaccine candidate is a realistic approach in immune therapy of HIV-1-infected individuals.
NHP.346  (14645590)  Multispecific vaccine-induced mucosal cytotoxic T lymphocytes reduce acute-phase viral replication but fail in long-term control of simian immunodeficiency virus SIVmac239


Objectives Challenge, Immunogenicity To ascertain the effect of vaccine-induced multispecific mucosal CTL.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings
• The vaccination induced virus-specific CTL and CD4+ helper T lymphocytes with CTL frequencies as high as 20,000/million peripheral blood mononuclear cells.
• The final rMV A vaccination, delivered intravenously, engendered long-lived mucosal CTL.
• Massive early anamnestic cellular immune responses controlled acute-phase viral replication; however, the 3 vaccinees were unable to control virus replication in the chronic phase.
• Multispecific mucosal CTL, in the absence of neutralizing antibodies, can achieve a modicum of control over early viral replication but unable to control chronic-phase viral replication after a high-dose mucosal challenge with a pathogenic simian immunodeficiency virus.

NHP.348.1  Immunogenicity in pig-tailed macaques of poliovirus replicons expressing HIV-1 and SIV antigens and protection against SHIV-89.6P disease (14585346)

Authors Fultz PN, Stallworth J, Porter D, Novak M, Anderson MJ, Morrow CD


Objectives Immunogenicity To determine whether poliovirus replicons expressing various HIV-1 Env and SIVmac239 Gag antigens would be immunogenic in macaques.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name Polio (Sabin 1) - HIV-1.gag/env (1) Type: Recombinant Vector (virus/bacteria) Routes: Intrarectal, Intranasal

Vaccine Name Polio (Sabin 1) - HIV-1.gag/env (2) Type: Recombinant Vector (virus/bacteria) Routes: Intrarectal, Intranasal

Vaccine Name Polio (Sabin 2) - HIV-1.gag/env (3) Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

Vaccine Name Polio (Sabin 2) - HIV-1.gag/env (4) Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

Vaccine Name rgp140-env (HIV-1.89.6) Type: Recombinant Subunit Protein Route: Intramuscular

NHP.348.2  Immunogenicity in pig-tailed macaques of poliovirus replicons expressing HIV-1 and SIV antigens and protection against SHIV-89.6P disease (14585346)

Authors Fultz PN, Stallworth J, Porter D, Novak M, Anderson MJ, Morrow CD


Objectives Challenge, Immunogenicity.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name rgp140-env (HIV-1.89.6) Type: Recombinant Subunit Protein Route: Intramuscular

Vaccine Name Polio-LAI/IIIB-Env Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

Vaccine Name Polio-SIVmac239gag Type: Recombinant Vector (virus/bacteria) Route: Intramuscular

Challenge SHIV89.6P Route: Intravenous

NHP.349  (14585221)  Gp120-alum boosting of a Gag-Pol-Env DNA/MVA AIDS vaccine: poorer control of a pathogenic viral challenge


Species/Subspecies Macaca mulatta (Rhesus macaque)
### Trial Summaries

<table>
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<th>Vaccine Name</th>
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<td>Soluble 89.6 gp120 protein</td>
<td>Recombinant Subunit Protein</td>
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<tr>
<td>SIV-HIV89.6 DNA vaccine</td>
<td>DNA</td>
<td>Intradermal</td>
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<tr>
<td>rMAV 89.6</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intradermal, Intramuscular</td>
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**Challenge**

<table>
<thead>
<tr>
<th>SHIV89.6P</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrarectal</td>
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</table>

**NHP.350 (14583643)**

**Evaluation of simian immunodeficiency virus-specific immune responses induced by a defective proviral DNA vaccine in macaques**

**Authors**

Takeda A, Nakamura H, Matano T

**Journal**


**Objectives**

Immunogenicity To examine if macaques vaccinated with FMSIV DNA and an mCAT1-expression plasmid DNA (pCMVmCAT1) had SIV-specific T-cell levels significantly higher than control macaques vaccinated with replication-negative FMSIV DNA vaccine.

**Species/Subspecies**

Macaca mulatta (Rhesus macaque)

**Vaccine Name**

- FMSIV
  - Type: DNA
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

**Main Findings**

- SIV-specific CD4+ T cells and SIV-specific CD8+ T cells were efficiently induced in macaques vaccinated with FMSIV plus mCAT1 DNAs and levels of SIV-specific CD4+ T cells and SIV-specific CD8+ T cells in the group II macaques were significantly higher than those in the control group.
- Macaques immunized with FMSIV plus pCMVmCAT1 had significantly higher levels of plasma anti-p27 antibodies than those in the control both at week 3 and week 8 after the initial vaccination.

**NHP.351 (14557642)**

**Multigene DNA priming-boosting vaccines protect macaques from acute CD4+-T-cell depletion after simian-human immunodeficiency virus SHIV89.6P mucosal challenge**

**Authors**


**Journal**


**Species/Subspecies**

Macaca nemestrina (pigtailed macaque)

**Vaccine Name**

- pCMVmCAT1
  - Type: DNA
  - Routes: Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

**Main Findings**

- Macaques immunized with FMSIV plus pCMVmCAT1 had significantly higher levels of plasma anti-p27 antibodies than those in the control both at week 3 and week 8 after the initial vaccination.

**NHP.352 (14512560)**

**Microarray profiling of antibody responses against simian-human immunodeficiency virus: postchallenge convergence of reactivities independent of host histocompatibility type and vaccine regimen**

**Authors**

Neuman de Vegvar HE, Amara RR, Steinman L, Utz PJ, Robinson HL, Robinson WH

**Journal**


**Species/Subspecies**

Macaca fascicularis (cynomolgus macaque)

**Vaccine Name**

rBCG-SIV

**Challenge**

- SIVmac251
  - Route: Intrarectal

**Main Findings**

- Intradermal immunization of cynomolgus macaques with a multi-component rBCG vaccine induces CTL responses targeted against 3 SIVmac251 antigens.
- PBLs from rBCG-SIV3-immunized monkeys produce interferon-gamma in response to SIV antigens and production increases after the mucosal booster.
- Anti-Gag IgAs are detected in rectal lavages of rBCG-SIV3-immunized monkeys only after the mucosal booster.
- rBCG-SIV3 does not protect against a highly pathogenic SIVmac251 challenge despite induction of anamnestic immune responses.

**NHP.354 (15096801)**

**Immunogenicity of HIV-1 Env and Gag in baboons using a DNA prime/boost regimen**

1306 HIV Immunology and HIV/SIV Vaccine Databases 2003
Authors: Leung L, Srivastava IK, Kan E, Legg H, Sun Y, Greer C, Montefiori DC, zur Megede J, Barnett SW


Objectives: To evaluate the immunogenicity of sequence-modified HIV env and gag in baboons using DNA prime and protein boost strategy.

Species/Subspecies: Papio cynocephalus (Baboon)

Vaccine Name:
- pCMV-gag-mod
  Type: DNA
  Route: Intramuscular

- pCMVKm2-gp140mut
  Type: DNA
  Route: Intramuscular

- CMVKm2-gp140TM
  Type: DNA
  Route: Intramuscular

- o-gp140-US4
  Type: Synthetic Protein/Peptide
  Route: Intramuscular

- p55gagSF2
  Type: DNA
  Route: Intramuscular

- p55gagSF2
  Type: Synthetic Protein/Peptide
  Route: Intramuscular

- p55gagSF2
  Type: Synthetic Protein/Peptide
  Route: Intramuscular

Main Findings:
- Modest antibody responses and low or no lymphoproliferative responses were observed following multiple DNA immunizations.
- Strong antibodies and substantial antigen-specific lymphoproliferative responses were seen following booster immunizations with oligomeric Env protein (o-gp140US4) in MF59.
- Neutralizing antibody responses were scored against T cell line adapted HIV-1 strains after the protein boosters, but neutralizing responses were low or absent against homologous and heterologous primary isolate strains.

Main Findings:
- In combination with an appropriate adjuvant (lipid-based adjuvant or mineral carrier complex), immunization with recombinant gp160 led to the appearance of gp160-primed T cells.
- The memory T-cell response toward the immunogen gp160 was substantial and long-lasting.

Main Findings:
- In challenge, Immunogenicity To investigate a prime-boost strategy in macaques using priming with replicating adenovirus recombinants encoding SIV env/rev, gag, and/or nef genes, followed by boosting with SIV gp120 or an SIV polypeptide.

Species/Subspecies: Macaca mulatta (Rhesus macaque)

Vaccine Name: SIVIG-2
Type: Passive Antibody
Route: Intramuscular
Trial Summaries

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Type:</th>
<th>Routes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad5hr-SIVmac239gag</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intratracheal, Oral, Intranasal</td>
</tr>
<tr>
<td>Ad5hr-SIV nef δ1-13</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intratracheal, Oral, Intranasal</td>
</tr>
<tr>
<td>Ad5hr-SIV smH4 env/rev</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intratracheal, Oral, Intranasal</td>
</tr>
<tr>
<td>Mono-gp120H (89.6)</td>
<td>Recombinant Subunit Protein</td>
<td>Intratracheal, Oral, Intranasal</td>
</tr>
<tr>
<td>HIV env&lt;sub&gt;Mr&lt;/sub&gt;/rev(pCEv)</td>
<td>DNA</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>SIVmac251-gp120</td>
<td>Purified Viral Products</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

Main Findings

• Priming with replicating adenovirus recombinants encoding SIV env/rev, gag, and/or nef genes, followed by boosting with SIV gp120 or an SIV polypeptide mimicking the CD4 binding region of the envelope, protects rhesus macaques from intrarectal infection with the highly pathogenic SIV(mac251).
• Within immunization groups exhibiting significant protection, a subset (39%) of macaques have exhibited either no viremia, cleared viremia, or controlled viremia at the threshold of detection, now more than 40 weeks postchallenge.
• Protection in macaques did not correlate with the Mamu A*01 allele.

NHP.365 (14645581) Intravenous inoculation of replication-deficient recombinant vaccinia virus DIs expressing simian immunodeficiency virus gag controls highly pathogenic simian-human immunodeficiency virus in monkeys

Authors Izumi Y, Ami Y, Matsuo K, Someya K, Sata T, Yamamoto N, Honda M
Objectives Challenge, Immunogenicity To assess the immunogenicity and protection induced by immunization with rDIsSIVgag.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name Vaccinia-rDIsSIVgag Type: Recombinant Vector (virus/bacteria) Route: Intravenous
Challenge SHIV-C2/1 Route: Intravenous
Main Findings

• Intravenous inoculation of 10<sup>6</sup> PFU of rDIsSIVGag in cynomologus macaques induced significant levels of gamma interferon (IFN-gamma) spot-forming cells (SFC) specific for SIV Gag.
• Antigen-specific lymphocyte proliferative responses were also induced and were temporally associated with the peak of IFN-gamma SFC activity in each macaque.
• CD4(+) T lymphocytes were maintained in the peripheral blood and lymphoid tissues of the immunized macaques after challenge with pathogenic SHIV.

NHP.366 (15004179) Control of Simian/Human Immunodeficiency Virus Viremia and Disease Progression after IL-2-Augmented DNA-Modified Vaccinia Virus Ankara Nasal Vaccination in Nonhuman Primates

Authors Bertley FM, Kozlowski PA, Wang SW, Chappelle J, Patel J, Sonuyi O, Mazzara G, Montefiori D, Carville A, Mansfield KG, Aldovini A
Objectives Challenge, Immunogenicity
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pVacc4 DNA Type: DNA Route: Intranasal
Vaccine Name rMVA.SIVmac239gagpolHIVenv Type: Recombinant Vector (virus/bacteria) Route: Intranasal
Challenge SHIV89.6P Route: Intranasal
Main Findings

• The vaccine and challenge induced humoral responses, by the detection of both binding and neutralizing SHIV-specific IgG in plasma, and SHIV-specific IgA in rectal secretions.
• After rectal challenge of vaccinated and naive animals with SHIV89.6P, all animals became infected. However a subset of animals was protected from CD4+ T cell loss and AIDS development.
• SHIV DNA/MVA vaccine administered nasally can stimulate rectal antiviral IgA but was not effective at inducing antiviral systemic IgG.
IL-2/Ig or IL-12 DNA and the rMVA added to the vaccination did not result in significant differences in these humoral immune responses.

**NHP.367 (15003872)**

**Priming B cell-mediated anti-HIV envelope responses by vaccination allows for the long-term control of infection in macaques exposed to a R5-tropic SHIV**

**Authors**

**Journal**
Virology 2004 Mar 1;320(1):167-80

**Main Findings**
- Antibodies elicited by the SF162gp140 immunogen recognize elements of the V1, V2, and V3 loops, the CD4-binding site, and the C1 and C2 regions on the homologous SF162 gp120.
- Deletion of the V2 has a two-fold effect: 1) it alters the immunogenicity of the V3 and V1 loops, and 2) it renders the C5 region immunogenic.
- Sterilizing immunity was not achieved.
- All vaccinated animals effectively controlled and remained free of disease over 3 years of observation.

**NHP.368 (14980480)**

**Functional simian immunodeficiency virus Gag-specific CD8+ intraepithelial lymphocytes in the mucosae of SIVmac251- or simian-human immunodeficiency virus KU2-infected macaques**

**Authors**
Stevceva L, Momiuszko M, Alvarez X, Lackner AA, Franchini G

**Journal**
Virology 2004 Feb 20;319(2):190-200

**NHP.369 (14610180)**

**Simian-human immunodeficiency virus escape from cytotoxic T-lymphocyte recognition at a structurally constrained epitope**

**Authors**
Peyerl FW, Barouch DH, Yeh WW, Bazick HS, Kunstman J, Kunstman KJ, Wolinsky SM, Letvin NL

**Journal**
J Virol 2003 Dec;77(23):12572-8

**NHP.370 (14550583)**

**Enhanced immunogenicity of SIV Gag DNA vaccines encoding chimeric proteins containing a C-terminal segment of Listeriolysin O**

**Authors**
Ye L, Bu Z, Skee MJ, Ziegler HK, Compans RW, Yang C

**Journal**
Virus Res 2003 Nov;97(1):7-16

**NHP.371 (15018712)**

**Evaluation of combination DNA/replication-competent Ad-SIV recombinant immunization regimens in rhesus macaques**

**Authors**
Malkevitch N, Rohde D, Pinczewski J, Aldrich K, Kalyanaraman VS, Letvin NL, Robert-Guroff M

**Journal**

**NHP.372 (14722663)**

**Simian immunodeficiency virus promoter exchange results in a highly attenuated strain that protects against uncloned challenge virus**

**Authors**

**Journal**

**NHP.373 (14593121)**

**High attenuation and immunogenicity of a simian immunodeficiency virus expressing a proteolysis-resistant inhibitor of NF-kappaB**

**Authors**

**Vaccines**
## NHP.374 (15016855) Qualitative T-helper responses to multiple viral antigens correlate with vaccine-induced immunity to simian/human immunodeficiency virus infection


**Objective** Challenge, Immunogenicity To determine whether immunization with multiple antigens can influence individual Th responses and increase protection relative to a single antigen.

<table>
<thead>
<tr>
<th>Species/Subspecies</th>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macaca mulatta (Rhesus macaque)</td>
<td>pc-synTat (HIV-IIIIB)</td>
<td>DNA</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>pc-syngp120 (SHIV-189.6p)</td>
<td>DNA</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>pc-synGag (SIVmac239)</td>
<td>DNA</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>HIV-189.6 Env gp140-ISCOM</td>
<td>Recombinant Subunit Protein</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>SIVmac239 Gag-Pol-ISCOM</td>
<td>Recombinant Subunit Protein</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>tat protein</td>
<td>Recombinant Subunit Protein</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>SHIV89.6P</td>
<td>Route</td>
<td>Intravenous</td>
</tr>
</tbody>
</table>

## NHP.375 (15047809) Highly effective control of an AIDS virus challenge in macaques by using vesicular stomatitis virus and modified vaccinia virus Ankara vaccine vectors in a single-boost protocol

**Authors** Ramsburg E, Rose NF, Marx PA, Mefford M, Nixon DF, Moretto WJ, Montefiori D, Earl P, Moss B, Rose JK

**Objective** Challenge, Immunogenicity To compare the effectiveness of single prime-boost protocol consisting of VSV vectors expressing SHIV Env, Gag, and Pol proteins to that of VSV vector prime followed with a single boost with MVA expressing the same SHIV proteins.

<table>
<thead>
<tr>
<th>Species/Subspecies</th>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macaca mulatta (Rhesus macaque)</td>
<td>pc-synTat (HIV-IIIIB)</td>
<td>Type</td>
<td>Intramuscular</td>
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<tr>
<td></td>
<td>pc-syngp120 (SHIV-189.6p)</td>
<td>Type</td>
<td>Intramuscular</td>
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<td></td>
<td>pc-synGag (SIVmac239)</td>
<td>Type</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>HIV-189.6 Env gp140-ISCOM</td>
<td>Type</td>
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<tr>
<td></td>
<td>SIVmac239 Gag-Pol-ISCOM</td>
<td>Type</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>tat protein</td>
<td>Type</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>SHIV89.6P</td>
<td>Route</td>
<td>Intravenous</td>
</tr>
</tbody>
</table>

## NHP.376 (15047820) Induction of autoantibodies to CCR5 in macaques and subsequent effects upon challenge with an R5-tropic simian/human immunodeficiency virus

**Authors** Chackerian B, Briglio L, Albert PS, Lowy DR, Schiller JT

**Objective** Challenge, Immunogenicity To generate autoantibodies against CCR5 in macaques and to assess their role in protection from challenge with R5-tropic SHIV.

**Main Findings**
- 5 rhesus macaques injected with VLP-SA-EC1 developed antibodies against CCR5. IV challenge with SHIV resulted in infection, but some ability to control viremia.

## NHP.377 (15140996) Passive immunotherapy in simian immunodeficiency virus-infected macaques accelerates the development of neutralizing antibodies


**Objective** Challenge, Passive immunotherapy.

<table>
<thead>
<tr>
<th>Species/Subspecies</th>
<th>Vaccine Name</th>
<th>Type</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macaca mulatta (Rhesus macaque)</td>
<td>SIVIG</td>
<td>Type</td>
<td>Intravenous</td>
</tr>
<tr>
<td></td>
<td>SIVsmE660</td>
<td>Route</td>
<td>Intravenous</td>
</tr>
</tbody>
</table>

**Main Findings**
- SIVIG treatment significantly delayed disease.
• Virus levels in PBMC and plasma predict disease outcome.
• Gag-specific CTLs were detected in macaques surviving beyond 1 year.
• Infused IgG delayed binding antibody and accelerated NAb production.

**NHP.378** (15149785)  
**Human immunodeficiency virus type 2 DNA vaccine provides partial protection from acute baboon infection**  
**Journal** Vaccine 2004 Jun 2;22(17-18):2261-72  
**Objectives** Challenge, Immunogenicity  
To determine if GM-CSF and B7-2 could boost immune responses to an HIV-2 DNA vaccine and help protect baboons against HIV-2 challenge by the intravaginal route.

**Species/Subspecies** Papio cynocephalus (Baboon)  
**Vaccine Name** HIV-2UC2.tat.nef.gag  
**Type:** DNA  
**Routes:** Intradermal, Intramuscular, Intranasal  
**Challenge** HIV-2 (UC2-9429)  
**Route:** Vaginal or perivaginal  

**Main Findings**  
• Baboons immunized with HIV-2 DNA vaccine with or without the genetic adjuvants had significant reductions in the viral loads in the peripheral blood mononuclear cells (PBMC) following challenge (P=0.028) while the reductions in their plasma viremia were suggestive of a protective effect (P=0.1).  
• Partial protection against HIV-2 vaginal challenge, as measured by reduced viral load, can be achieved using only a DNA vaccine formulation.

**NHP.379** (15193413)  
**Enhancement of DNA vaccine potency in rhesus macaques by electroporation**  
**Journal** Vaccine 2004 Jun 23;22(19):2489-93

**NHP.380** (12551968)  
**Changes in the immunogenic properties of soluble gp140 human immunodeficiency virus envelope constructs upon partial deletion of the second hypervariable region**  
**Authors** Srivastava IK, VanDorsten K, Vojtech L, Barnett SW, Stamatosatos L  
**Objectives** Immunogenicity  
To identify the envelope regions whose immunogenicity is altered following V2 loop deletion.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Main Findings**  
• Antibodies elicited by the SF162gp140 immunogen recognize elements of the V1, V2, and V3 loops, the CD4-binding site, and the C1 and C2 regions on the homologous SF162 gp120.  
• Deletion of the V2 has a two-fold effect: 1) it alters the immunogenicity of the V3 and V1 loops, and 2) it renders the C5 region immunogenic.

**NHP.381** (15220422)  
**Heterologous envelope immunogens contribute to AIDS vaccine protection in rhesus monkeys**  
**Authors** Letvin NL, Huang Y, Chakrabarti BK, Xu L, Seaman MS, Beaudry K, Korioth-Schmitz B, Yu F, Rohne D, Martin KL, Miura A, Kong WP, Yang ZY, Gelman RS, Golubeva OG, Montefiori DC, Mascola JR, Nabel GJ  
**Objectives** Challenge, Immunogenicity  
To evaluate a plasmid DNA prime-recombinant replication-defective adenovirus (ADV) boost immunization strategy for an HIV vaccine.

**Species/Subspecies** Macaca mulatta (Rhesus macaque)  
**Main Findings**  
• Vaccine regimens Gag-Pol-Nef immunogens that included the matched or mismatched Env immunogens conferred better protection against CD4+ T-lymphocyte loss than that seen with comparable regimens that did not include Env immunogens.  
• T-lymphocyte immunity to Env can broaden the protective cellular immune response to HIV despite significant sequence diversity of the strains of the Env immunogens and can contribute to immune protection in this AIDS vaccine model.
• The control group had significantly higher peak viral loads than the vaccinated monkeys. However, the 3 groups of experimentally vaccinated monkeys did not differ significantly in their peak viral loads (P = 0.28, Kruskal-Wallis test).

NHP.382 (15210746) Cytotoxic T Lymphocyte-based Control of Simian Immunodeficiency Virus Replication in a Preclinical AIDS Vaccine Trial
Objectives Challenge, Immunogenicity.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings
• 5/8 vaccinees controlled viral replication and had undetectable plasma viremia after 5 weeks of infection.
• 5/8 macaques rapidly selected for CTL escape mutations in Gag, indicating that vaccine-induced CTLs successfully contained replication of the challenge virus.
• Vaccine induction of highly effective CTLs can result in the containment of replication of a highly pathogenic immunodeficiency virus.

NHP.384 (15242543) Multiprotein HIV type 1 clade B DNA/MVA vaccine: construction, safety, and immunogenicity in Macaques
Objectives Immunogenicity To construct and test a Gag-Pol-Env DNA/MVA vaccine.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pGA2/JS2-HIV-1.gag.pol.env Type: DNA Route: Intramuscular
Vaccine Name MVA/HIV 48 Type: Recombinant Vector (virus/bacteria) Route: Intramuscular
Main Findings
• The vaccine constructs contain the gag region derived from HIV-1 HXB2 and do not include the zinc finger mutations found in pGA2/JS2; pol was from pGA2/JS2 including the RT mutations.
• Safety: by abrogating reverse transcription, inactivating RNase H activity and strand transfer activity, Env gene was expression-defective.
• Safety: No adverse effects of the inoculations on the vaccinated monkeys.
• Vaccine elicited cellular as well as humoral immunity.
• Vaccine elicited T cells were at, or below, the level of detection following the DNA primes, rapidly expanded after the rMVA booster and then contracted into memory.
• CD4 and CD8 epitopes are found throughout Gag and Env inserts of the vaccine.
• The immunizations elicited only low levels of raised antibody.

NHP.385 (9557706) Recombinant vaccine-induced protection against the highly pathogenic simian immunodeficiency virus SIV(mac251): dependence on route of challenge exposure
Objectives Challenge.
Main Findings
• Vaccination with NYVAC-SIV-gpe carrying SIV-Mac-251 gag pol and env protected against intrarectal, but not intravenous infection with SIV-Mac-251, as determined by culture of virus. Viral loads were lower in vaccinated-infected than in non-vaccinated controls.
NHP.386  (15113931)  **Induction of disease by a molecularly cloned highly pathogenic simian immunodeficiency virus/human immunodeficiency virus chimera is multigenic**  
*Authors* Sadjadpour R, Theodore TS, Igarashi T, Donau OK, Plishka RJ, Buckler-White A, Martin MA  
*Species/Subspecies* Macaca mulatta (Rhesus macaque)  
*Challenge* SHIV-DH12clone7, SHIV-DH12clone8  
*Route*: Intravenous  
*Main Findings*  
- SHIV\_DH12\_R-CLone7 induces rapid CD4 decline in rhesus macaques whereas the SHIV\_DH12R parental clone does not. Substitution of the clone 7 env into the nonpathogenic parental background did not confer pathogenicity. Amino acid changes in multiple genes were required for pathogenic effect.

NHP.387  (10570196)  **Emergence of a highly pathogenic simian/human immunodeficiency virus in a rhesus macaque treated with anti-CD8 mAb during a primary infection with a nonpathogenic virus**  
*Journal* Proc Natl Acad Sci U S A 1999 Nov 23;96(24):14049-54  
*Species/Subspecies* Macaca mulatta (Rhesus macaque)  
*Challenge* SHIV-MD14YE (DH12)  
*Route*: Intravenous  
*Main Findings*  
- Mutations in many genes resulted in increased pathogenicity of the SHIV-DH12R clone.

NHP.388  (11861859)  **Evolution of a human immunodeficiency virus type 1 variant with enhanced replication in pig-tailed macaque cells by DNA shuffling**  
*Authors* Pekrun K, Shibata R, Igarashi T, Reed M, Sheppard L, Patten PA, Stemmer WP, Martin MA, Soong NW  
*Objectives* Pathogenicity.  
*Main Findings*  
- A SHIV composed primarily of HIV-1 sequences with a SIV-Mac239 YE version of Nef was created and passaged to achieve a molecular clone that replicates in pig-tailed macaque PBMCs and can infect macaques. SIVMD17 accession number AF465242

NHP.389  (9237701)  **Infection and pathogenicity of chimeric simian-human immunodeficiency viruses in macaques: determinants of high virus loads and CD4 cell killing**  
*Authors* Shibata R, Maldarelli F, Siemon C, Matano T, Parta M, Miller G, Fredrickson T, Martin MA  
*Species/Subspecies* Macaca fascicularis (cynomolgus macaque), Macaca nemestrina (pigtailed macaque)  
*Challenge* SHIV-MD14YE (DH12), SHIV\_MD1  
*Route*: Intravenous  
*Main Findings*  
- SHIV\_MD1 carrying HIV-1 subtype B sequences from clones pNL43 (vpr) and DH12 (tat-nef) in a SIV\_Mac239 background, produced slower CD4+ T-cell decline in pig-tailed macaques than SHIV\_MD14YE in which the HIV-1 nef in SHIV\_MD1 was replaced by SIV\_Mac239 nef with R17Y plus Q18E mutations  
- The nef with R17Y plus Q18E mutations had previously been shown to be determinants of pathogenicity in the SIV\_SMM9 to SIV\_PBJ14 series of viruses.

NHP.390  (8648760)  **Requirements for lymphocyte activation by unusual strains of simian immunodeficiency virus**  
*Authors* Du Z, Ilyinskii PO, Sasseville VG, Newstein M, Lackner AA, Desrosiers RC  
*Species/Subspecies* Macaca mulatta (Rhesus macaque)  
*Main Findings*  
- A single amino acid change in Nef R17Y was shown to be sufficient to confer pathogenicity to non-activated macaque T-cells in SIV\_Mac239 and that conversely, Y17R reversion in SIV\_PBJ14 eliminated the lymphocyte activation phenotype of that highly pathogenic clone.
### NHP.391 (10888632)
**Short- and long-term clinical outcomes in rhesus monkeys inoculated with a highly pathogenic chimeric simian/human immunodeficiency virus**

**Authors:** Endo Y, Igarashi T, Nishimura Y, Buckler C, Buckler-White A, Plishka R, Dimitrov DS, Martin MA  
**Species/Subspecies:** Macaca mulatta (Rhesus macaque)  
**Challenge:** SHIV.DH12R-PS1  
**Route:** Intrarectal, Intravenous, Vaginal or perivaginal  
**Main Findings:**  
- SHIV DH12R, derived from SHIV MD14YE by passage in rhesus macaque, induces CD4+ T-cell loss in rhesus macaques in a dose-dependent manner. The DH12R inoculum was uncloned, and higher doses apparently allow more antibody neutralization escape variants to survive.

### NHP.392 (7769705)
**Isolation and characterization of a syncytium-inducing, macrophage/T-cell line-tropic human immunodeficiency virus type 1 isolate that readily infects chimpanzee cells in vitro and in vivo**

**Species/Subspecies:** Pan Troglodytes (Chimpanzee)  
**Challenge:** HIV-1.DH12  
**Route:** Intravenous  
**Main Findings:**  
- Of 23 different HIV-1 isolates tested, only one (DH12) was able to initiate infections in all chimpanzee PBMC cultures tested. The DH12 isolate was inoculated into three chimpanzees and was able to establish a robust infection with symptoms including lymphadenopathy and rashes.  
- All DH12 clones sequenced had defective vpu genes, although the GenBank entry for the complete genome AF069140 was submitted with the ATA defective start codon corrected to ATG.

### NHP.393 (7769705)
**Isolation and characterization of a syncytium-inducing, macrophage/T-cell line-tropic human immunodeficiency virus type 1 isolate that readily infects chimpanzee cells in vitro and in vivo**

**Main Findings:**  
- Neutralizing antibodies from a chimpanzee infected with HIV-1 isolate DH12 can protect macaques from a SHIV containing the DH12 envelope gene. The recipient serum titre needed to protect 99% of macaques from 75 TCID50 IV inoculation was calculated to be 1:38.

### NHP.394 (11836389)
**Determination of a statistically valid neutralization titer in plasma that confers protection against simian-human immunodeficiency virus challenge following passive transfer of high-titered neutralizing antibodies**

**Authors:** Nishimura Y, Igarashi T, Haigwood N, Sadjapour R, Plishka RJ, Buckler-White A, Shibata R, Martin MA  
**Species/Subspecies:** Macaca nemestrina (pigtailed macaque)  
**Vaccine Name:** Chimp-anti-HIV-IgG  
**Type:** Passive Antibody  
**Route:** Intravenous  
**Main Findings:**  
- Neutralizing antibodies from a chimpanzee infected with HIV-1 isolate DH12 can protect macaques from a SHIV containing the DH12 envelope gene. The recipient serum titre needed to protect 99% of macaques from 75 TCID50 IV inoculation was calculated to be 1:38.

### NHP.395 (15356916)
**CCR5 targeted SIV vaccination strategy preventing or inhibiting SIV infection**

**Authors:** Bogers WM, Bergmeier LA, Oostermeijer H, ten Haaft P, Wang Y, Kelly CG, Singh M, Heeney JL, Lehner T  
**Journal:** Vaccine 2004 Aug 13;22(23-24):2974-84  
**Objectives:**  
- Challenge, Immunogenicity To attempt to prevent SIV infection by (a) upregulating the three CC chemokines, (b) eliciting antibodies to CCR5 and (c) downmodulating the cell-surface expression of CCR5.

**Species/Subspecies:** Macaca mulatta (Rhesus macaque)  
**Vaccine Name:** HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27  
**Type:** Recombinant Subunit Protein  
**Route:** Intramuscular
Trial Summaries

**Challenge**
SIVmac8980  
**Route:** Intramuscular

**Main Findings**
- Immunization with protein (HSP70) covalently linked to the CCR5 peptides, SIV gp120 and p27 protected rhesus monkeys from infection after challenge with SIVmac8980

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**NHP.396** (15452269)  
**Heterologous human immunodeficiency virus type 1 priming-boosting immunization strategies involving replication-defective adenovirus and poxvirus vaccine vectors**

**Authors**  

**Journal**  

**Objectives**  
Immunogenicity  
To assess the ability of poxvirus vectors to boost Ad5-primed responses as a means of enhancing the levels of vaccine-elicited responses.

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Main Findings**
- Heterologous Ad5 priming-poxvirus boosting regimen induced a significantly greater immune response in rhesus monkeys than immunization elicited by homologous prime-boost regimens with the individual vectors or by a heterologous poxvirus priming-Ad5 boosting regimen.

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**NHP.397** (15302953)  
**Macaques infected long-term with attenuated simian immunodeficiency virus (SIVmac) remain resistant to wild-type challenge, despite declining cytotoxic T lymphocyte responses to an immunodominant epitope**

**Authors**  

**Journal**  
J Gen Virol 2004 Sep;85(Pt 9):2591-602

**Objectives**  
Challenge, Immunogenicity  
To investigate mechanisms of protective immunity induced by live, attenuated SIV.

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Vaccine Name**  
SIV.GX2  
**Type:** Live Attenuated Virus

**Challenge**  
SIVmac220  
**Route:** Intravenous

**Main Findings**
- 3 macaques immunized with live attenuated SIVmacGX2 were resistant to challenge with an uncloned pool of wild-type SIVmac220, whereas four naive controls became infected.
- Both attenuated (vaccine) and wild-type (challenge) viruses induced a disseminated CD8+ T-cell response, which was of a higher magnitude in lymphoid tissues than in the periphery.

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**NHP.398** (9732063)  
**Rhesus macaques that become systemically infected with pathogenic SHIV 89.6-PD after intravenous, rectal, or vaginal inoculation and fail to make an antiviral antibody response rapidly develop AIDS**

**Authors**  
Lu Y, Pauza CD, Lu X, Montefiori DC, Miller CJ

**Journal**  
J Acquir Immune Defic Syndr Hum Retrovirol 1998 Sep 1;19(1):6-18

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Challenge**  
SHIV89.6PD  
**Route:** Intrarectal, Intravenous, Vaginal or perivaginal

**Main Findings**
- The pathogenicity of an uncloned stock of SHIV-89.6P was tested in 12 rhesus macaques. Two were injected IV, 6 were inoculated intravaginally, and 4 were inoculated intrarectally. Intravenous inoculation resulted in peak viremia in 7 days vs 14 days for mucosal inoculation.

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**NHP.399** (12163269)  
**A novel chimeric Rev, Tat, and Nef (Retanef) antigen as a component of an SIV/HIV vaccine**

**Authors**  
Hel Z, Johnson JM, Trynishowska E, Tsai WP, Harrod R, Fullen J, Tartaglia J, Franchini G

**Journal**  

**Species/Subspecies**  
Macaca mulatta (Rhesus macaque)

**Main Findings**

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Retanef is a synthetic open reading frame encoding epitopes from Rev, Tat and Nef proteins. Inserted into the NYVAC vaccinia virus vector, and injected into naïve macaques, it induced CTL responses. It also boosted responses 2 to 7-fold in previously infected macaques undergoing HAART.

### NHP.400 (15258286)

**Recombinant poxvirus boosting of DNA-primed rhesus monkeys augments peak but not memory T lymphocyte responses**

**Authors**

**Journal**

**Objectives**
Challenge, Immunogenicity To assess the relative immunogenicity including a CTL response of vaccine regimens that included a cytokine-augmented plasmid DNA prime and a boost with DNA or recombinant pox vectors.

**Species/Subspecies**
Macaca mulatta (Rhesus macaque)

**Vaccine Name**

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>DNA Type</th>
<th>Route</th>
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<tbody>
<tr>
<td>HIV-1 89.6P Env gp140 (KB9) DNA</td>
<td>DNA</td>
<td>Intramuscular</td>
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<tr>
<td>SIV mac239 Gag DNA</td>
<td>DNA</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Recombinant fowlpox (rFPV).SHIV89.6P env</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intradermal, Intramuscular</td>
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<tr>
<td>Recombinant fowlpox (rFPV) SIVmac239 gag</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intradermal, Intramuscular</td>
</tr>
<tr>
<td>Recombinant MVA-SHIV89.6P env</td>
<td>Recombinant Vector (virus/bacteria)</td>
<td>Intradermal, Intramuscular</td>
</tr>
<tr>
<td>Recombinant MVA-SIVmac239 gag</td>
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<tr>
<td>Recombinant vaccinia virus (rVac).SHIV89.6P Env</td>
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</table>

**Challenge**
SHIV89.6P  Route: Intravenous

**Main Findings**

- Recombinant vaccinia virus, recombinant modified vaccinia Ankara (MVA), and recombinant fowlpox were comparable in their immunogenicity.
- Whereas the magnitude of the peak vaccine-elicited T lymphocyte responses in the recombinant pox virus-boosted monkeys was substantially greater than that seen in the monkeys immunized with plasmid DNA alone, the magnitudes of recombinant pox boosted CTL responses decayed rapidly and were comparable to those of the DNA-alone-vaccinated monkeys by the time of viral challenge.
- The memory T cell responses for the three vaccines were comparable.
- Protection from clinical disease in all groups of experimentally vaccinated monkeys was similar.
- The steady-state memory, rather than the peak effector vaccine-elicited T lymphocyte responses, may be the critical immune correlate of protection for a CTL-based HIV vaccine.

### NHP.401 (15269383)

**Enhanced cellular immunity and systemic control of SHIV infection by combined parenteral and mucosal administration of a DNA prime MVA boost vaccine regimen**

**Authors**

**Journal**
J Gen Virol 2004 Aug;85(Pt 8):2407-19

**Objectives**
Challenge, Immunogenicity

**Species/Subspecies**
Macaca fascicularis (cynomolgus macaque)

**Main Findings**

- Recombinant fowlpox, recombinant modified vaccinia Ankara (MVA), and recombinant fowlpox were comparable in their immunogenicity.
- Whereas the magnitude of the peak vaccine-elicited T lymphocyte responses in the recombinant pox virus-boosted monkeys was substantially greater than that seen in the monkeys immunized with plasmid DNA alone, the magnitudes of recombinant pox boosted CTL responses decayed rapidly and were comparable to those of the DNA-alone-vaccinated monkeys by the time of viral challenge.
- The memory T cell responses for the three vaccines were comparable.
- Protection from clinical disease in all groups of experimentally vaccinated monkeys was similar.
- The steady-state memory, rather than the peak effector vaccine-elicited T lymphocyte responses, may be the critical immune correlate of protection for a CTL-based HIV vaccine.

### NHP.402 (15308348)

**Long-term protection against SHIV89.6P replication in HIV-1 Tat vaccinated cynomolgus monkeys**

**Authors**

**Journal**
J Gen Virol 2004 Sep 3;22(25-26):3258-69

**Main Findings**

- Recombinant fowlpox, recombinant modified vaccinia Ankara (MVA), and recombinant fowlpox were comparable in their immunogenicity.
- Whereas the magnitude of the peak vaccine-elicited T lymphocyte responses in the recombinant pox virus-boosted monkeys was substantially greater than that seen in the monkeys immunized with plasmid DNA alone, the magnitudes of recombinant pox boosted CTL responses decayed rapidly and were comparable to those of the DNA-alone-vaccinated monkeys by the time of viral challenge.
- The memory T cell responses for the three vaccines were comparable.
- Protection from clinical disease in all groups of experimentally vaccinated monkeys was similar.
- The steady-state memory, rather than the peak effector vaccine-elicited T lymphocyte responses, may be the critical immune correlate of protection for a CTL-based HIV vaccine.

### NHP.403 (15105535)

**Protective efficacy of a multicomponent vector vaccine in cynomolgus monkeys after intrarectal simian immunodeficiency virus challenge**

**Authors**

**Journal**
J Gen Virol 2004 May;85(Pt 5):1191-201
### VI-F

**Vaccine Trial References**

<table>
<thead>
<tr>
<th>Author(s)</th>
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<tr>
<td>Abel K, La Franco-Scheuch L, Rourke T, Ma ZM, De Silva V, Fallert B, Beckett L, Reinhart TA, Miller C.,</td>
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Vaccine Trial References


Evans DT, Chen LM, Gillis J, Lin KC, Harty B, Mazzara GP, Donis RO, Mansfield KG, Lifson JD, Control of viral replication and disease onset in cynomolgus monkeys by HIV-1


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Vaccines

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Schlienger K, Montefiori DC, Mancini M, Riviere Y, Tiollais P, Michel M., Vaccine-induced neutralizing antibodies directed in part to the simian immunodeficiency virus (SIV) V2 domain were unable to protect rhesus monkeys from SIV experimental challenge. J Virol 1994;68(10):6578-88. Trial: NHP.254


Ui M, Kuwata T, Igarashi T, Buki K, Miyazaki Y, Kozyrey IL, Enose Y, Shimada T, Uesaka H, Yamamoto H, Miura T, Hayami., Protection of macaques against a SHIV with a homologous HIV-1 Env and a pathogenic SHIV-89.6P with a heterologous Env by vaccination with multiple gene-deleted SHIVs. Virology 1999;265(2):252-63. Trial: NHP.28


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