HIV Vaccines: Time for a New Vision

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EpiVax
GAIA Vaccine Foundation
Brown University and now . . .
Institute for Immunology and Informatics,
University of Rhode Island

University of Georgia April 8 2008
AIDS killed 2.5 million people in 2007.
During 2007, 5 million people became infected with HIV which inevitably leads to AIDS if untreated.
There will more than 120 Million people dying of AIDS in 2010.
Africa, Asia, disproportionately affected . . .

The majority of people with HIV, some 95% of the global total, live in the developing world.
In 2007, an estimated 700,000 children aged 14 or younger became infected with HIV.

Over 90% were babies born to HIV-positive women, who acquired the virus at birth or through their mother's breast milk.

More than 600,000 of these babies and children live in Africa.

The number of babies dying from AIDS in the US dropped to near zero.
By the end of 2007, the epidemic left behind 20 million AIDS orphans, who had lost one or both parents to AIDS before the age of 15.
Treatment is Cost Saving

Brazil demonstrates effect of investing in HIV care:

Cost of antiretroviral drug purchases, avoided expenditures and final costs to the Ministry of Health Brazil, 1997 - 2001*

Source: Ministry of Health Brazil, 2001

* Estimated data
The need outstrips available funds

Projected available resources and resource needs in low- and middle-income countries: 2003-2005
Is asking for treatment for all –

... “Too much”?

4 Billion for treating HIV/AIDS worldwide and

? > 500 Billion for Iraq?

Total: US $4.4 billion

Projected annual expenditure requirements for HIV/AIDS care and support by 2007, by region

For most of the world, a vaccine is the only hope...

• no clinics
• no doctors
• no medications
• no condoms
• what is her chance of surviving HIV?
A vaccine could save millions of lives

New adult HIV infections in low- and middle-income countries

Total new infections averted by an AIDS vaccine between 2015-2030

Vaccine introduction

Base

Low scenario

Medium scenario

High scenario

30% efficacy, 20% coverage

5.5 million

50% efficacy, 30% coverage

17 million

70% efficacy, 40% coverage

28 million

IAVI impact forecasting; Policy Brief #10, November 2006
Should we be surprised it is taking so long? Vaccine Dev’t in Perspective

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Discovery of Cause</th>
<th>Vaccine Developed</th>
<th>Years Elapsed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertussis</td>
<td>1906</td>
<td>1926</td>
<td>20</td>
</tr>
<tr>
<td>Polio</td>
<td>1908</td>
<td>1955</td>
<td>47</td>
</tr>
<tr>
<td>Measles</td>
<td>1953</td>
<td>1983</td>
<td>30</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>1973</td>
<td>1995</td>
<td>22</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1965</td>
<td>1981</td>
<td>16</td>
</tr>
<tr>
<td>HIV</td>
<td>1983</td>
<td>None as yet</td>
<td>25 and still counting!</td>
</tr>
</tbody>
</table>
Outline

- Basic aspects of HIV relevant to vaccine design
  - Vaccines
  - A new vision
The HIV Virus

HIV is a *retrovirus*: it carries RNA that converts to DNA in the infected host cell
LIFE CYCLE OF HIV-1

HIV – CD4+ T-Cell

RNA
Reverse transcriptase
DNA
Protease
Nucleus
CD4+ T-Cell
Entry - Binding to CD4 and Chemokine Receptor

Two Step Entry - Note Variable Loops on gp160 and hidden site of gp41
CD₄ T-cell as HIV Factory

100 Billion new viral particles per day

CD₄ T cell decline – immune paralysis
Retrovirus process permits evolution

Reverse Transcriptase converts this RNA to DNA... but only after making numerous mistakes

The host cell transcribes and translates the altered HIV DNA, churning out thousands of identical mutant HIV virions

In an HIV-infected patient, this process occurs simultaneously in millions of cells, each generating a different mutant...

There also exists evidence that divergent HIV strains can recombine in a single host, inducing a less frequent but more drastic mutation
HIV Evolution

2 Processes Behind HIV Evolution

- genetic drift
- selection for more fit virus variants

The Stats

- $10^9$-$10^{10}$ virions generated daily
- Mutations = $10^{-5}$ per BP per generation (conservative estimate)
- HIV Genome ~ $10^4$ BP
- $>10^8$ mutant viruses produced every day
Viral Evolution enables escape from T cell recognition

HIV Viral epitopes are seen by T cells in context of MHC (HLA)
Examples of immune escape

- These are some published examples of epitope escape
- Note that epitopes can be represented by strings of letters

<table>
<thead>
<tr>
<th>HLA</th>
<th>HIV gene</th>
<th>Sequence</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>B8</td>
<td>gag p17</td>
<td>GGKKKYKL</td>
<td>Distorts α-1 helix</td>
</tr>
<tr>
<td></td>
<td></td>
<td>--R------</td>
<td></td>
</tr>
<tr>
<td>B8</td>
<td>gag p24</td>
<td>DIYKRWII</td>
<td>Not seen by some CTL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E------</td>
<td></td>
</tr>
<tr>
<td>B8</td>
<td>gag p17</td>
<td>GGKKKYKL</td>
<td>Does not bind*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>--Q------</td>
<td></td>
</tr>
<tr>
<td>B8</td>
<td>nef</td>
<td>FLKEKGGGL</td>
<td>Does not bind*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>--E------</td>
<td></td>
</tr>
<tr>
<td>B8</td>
<td>pol/RT</td>
<td>GPKVKQWPL</td>
<td>Antagonises</td>
</tr>
<tr>
<td></td>
<td></td>
<td>--R------</td>
<td></td>
</tr>
<tr>
<td>B27</td>
<td>gag p24</td>
<td>KRWIILGLNK</td>
<td>Does not bind*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>--K------</td>
<td></td>
</tr>
<tr>
<td>B44</td>
<td>env</td>
<td>AENLWVTYVY</td>
<td>Rapid off-rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>--K------</td>
<td></td>
</tr>
<tr>
<td>A11</td>
<td>nef</td>
<td>AVDLHFLK</td>
<td>Does not bind</td>
</tr>
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<td></td>
<td></td>
<td>--R------</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>nef</td>
<td>QVPLRPMTYK</td>
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<td></td>
<td>...........</td>
<td></td>
</tr>
</tbody>
</table>
Phylogenetic Analysis of Sequences From one Patient
Evolution of HIV worldwide

Adapted from J. Mullins

~30% divergent growing by 1%/yr

~50% vs. HIV-1 (M)

~55% vs. HIV-1 (M)

HIV-2 / SIV
Comparing the variability of HIV, influenza, and HCV
Trees drawn on the same scale

Influenza HA gene
HA1 domain

“Sydney-like “
Canadian Influenza A

N = 96 1996 global
H3N2 viruses

N = 193, DR Congo
Group M, 1997

CRF01

Summary - immunopathogenesis

Key points of the lifecycle from the immune (vaccine) perspective:

- Near impossible task of preventing HIV entry
- HIV variability (T and B cell epitopes)
- HIV latency (integration)
- Destruction of immune defense tissues
  - *Activation of T cells increases risk of infection*
Goals of an HIV Vaccine

- Prevent infection
- Prevent disease
- Prevent secondary transmission
The Simple Approach to HIV

- recombinant protein (gp120)
- Vaxgen
- (and Chiron)
"The development of an HIV vaccine may diverge from the classic paradigm for viral vaccines....There is optimism that even a less-than-perfect vaccine could benefit both individual recipients and the at-risk community."
Some individuals control HIV VL

The level of HIV in the blood stream predicts subsequent survival

RNA particles/ml plasma

Interquartile ranges

Rapid Progression
59,987

Slow Progression
28,240
11,843

One year

Reduction of “Set Point”
Walker, AIDS Vaccine 2001
Potential end-points of HIV-vaccine efficacy trials

**CONTROL** (or ineffective vaccine)
- no protection

**PRIMARY END-POINT**
- protection against HIV (sterilizing immunity)
  - no infection

**SECONDARY END-POINTS**
- protection against disease (modification of the course of HIV infection in vaccine recipients)
  - initial infection "controlled"
  - establishment of chronic infection with low viral load
Recall HIV Stages

Acute
  “flu”

Chronic
  asymptomatic ....

AIDS
  symptomatic

CD8 T cells

CD4 T cells

viral load
CD4 correlated with Viral load (HIV-RNA level in plasma) predicts course of HIV disease

<table>
<thead>
<tr>
<th>Viral RNA copies/cc</th>
<th>Progression to AIDS within the next 5 yrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5,000 copies/cc</td>
<td>8%</td>
</tr>
<tr>
<td>5,000 - 13,000</td>
<td>26%</td>
</tr>
<tr>
<td>13,000 - 36,000</td>
<td>49%</td>
</tr>
<tr>
<td>&gt;36,000 copies/cc</td>
<td>62%</td>
</tr>
</tbody>
</table>

Vaccines that Suppress HIV? Promise and Problems

Larry Corey IAC 2002
Relationship to Viral Load and Heterosexual Transmission
(Rakai Discordant Couple Trial, n=415)


RNA Viral Load in HIV+ Source Partner
Mathematical Model of Impact of a Vaccine That Reduced Viral Load Over Time
(Ira Longini, Emory University)
Outline

- Basic aspects of HIV relevant to vaccine design
- Vaccines
  - A new vision
HIV vaccine approaches

- recombinant protein (gp120)
- synthetic peptides (V3)
- naked DNA
- live-recombinant vectors (viral, bacterial)
- whole-inactivated virus
- live-attenuated virus
Phase IIb Studies of Merck HIV Vaccine Candidate

Ad5 Vector Expressing 3 Internal HIV Genes – gag, pol, nef (Clade B)

- Merck V520-023/HVTN 502 (n=3,000) - opened 12/2004
- HVTN 503 (n=3,000) opened 1/2007
Immunizations Are Discontinued in Two HIV Vaccine Trials

- Merck product: Ad5 vector expressing *gag, pol, nef* (clade B)
- STEP (Merck V520-023/HVTN 502): vaccine did not protect against infection or result in lower viral load
- PHAMBILI (HVTN 503) immunizations also paused
### Merck Ad5 Vaccine Failure Nov 2007

<table>
<thead>
<tr>
<th>Titer</th>
<th>ALL</th>
<th>Low</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine</td>
<td>49</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>Placebo</td>
<td>33</td>
<td>24</td>
<td>9</td>
</tr>
</tbody>
</table>

49 HIV infections in the vaccine group and 33 among those who received placebo (Oct 17, 2007).

But in individuals with the highest levels of Ad5 antibody, 21 infections in vaccinees compared to 9 in placebo.
Summary

- Study design and execution allowed timely assessment of both primary endpoints
- There was no evidence that vaccination prevented infection or lowered viral setpoint
- There were more infections in vaccinees than placebo recipients
  - This trend was more pronounced in participants with high baseline Ad5 titers
- Lack of efficacy did not appear to be explained by sub-optimal immune responses in vaccinees
Breadth of CTL responses induced by MRKAd5 Trivalent Vaccine from Phase I trial using 9-mer peptide pools

1 Other epitopes (helper T) are likely not detected in this screen
2 Gag: 62 peptide minipools; Pol: 105 minipools; Nef: 27 minipools; each minipool consists of eight 9-aa peptides (with 8-aa overlaps)
No vaccine efficacy observed in reducing viral load set point.

Was this a failure of CD8+ T cells to recognize incoming virus or HIV-1 escape from vaccine-induced responses early in infection?
Vaccination may not induce T cell recognition of HIV Viral epitopes presented by challenge strain of virus.
Summary of VL Setpoint: MITT population (males)

Much to Do: STEP Study (Examples)

- Thoroughly evaluate what immune responses did not work
  - balance of CD4+ and CD8+ T-cell responses
  - multifunctionality of responses
  - magnitude of responses against each insert sequence

- Assess impact of route of exposure on vaccine failure

- Sequence acute viruses for database

- Continue to follow HIV+ persons to evaluate course of disease
If set point is lowered in volunteers vaccinated with T-cell vaccine:

- Determine if set point correlates with clinical outcome
- Establish immune correlates of protection
- Determine if secondary virus transmission is impacted
- Optimize T-cell immunity for breadth and character of response
Much to Do: T Cell-Based Vaccines (cont.)

In the interim:

- Advance alternative rAd serotypes that are insensitive to pre-existing rAd5 immunity

- Optimize the immunogenicity of alternative designs (e.g. DNA, Pox and others)

- Examine relative efficacy of systemic vs. mucosal immunization in non-human primate models; improve mucosal immunization approaches and assays
## Selected Differences Between VRC and Merck AIDS Vaccines

<table>
<thead>
<tr>
<th>Feature</th>
<th>VRC</th>
<th>Merck</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td>DNA prime/rAd boost</td>
<td>rAd prime/rAd boost/ rAd boost</td>
</tr>
<tr>
<td>Immunogens</td>
<td>Env A, Env B, Env C Gag, Pol, Nef, Gag-Pol</td>
<td>Gag, Pol, Nef</td>
</tr>
<tr>
<td>Study Population</td>
<td>Mostly heterosexual + MSM</td>
<td>Mostly MSM + IDU/heterosexual</td>
</tr>
<tr>
<td>Immune Responses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4</td>
<td>Diversity of response</td>
<td>Low CD4 response</td>
</tr>
<tr>
<td>CD8</td>
<td>High magnitude of response</td>
<td>Measurable response</td>
</tr>
<tr>
<td>IgG</td>
<td>High titer with boost</td>
<td>Minimal titer with boost</td>
</tr>
<tr>
<td>SIV Protection Model</td>
<td>Survival</td>
<td>None</td>
</tr>
</tbody>
</table>
## Ongoing HVTN Trials: Phase II

<table>
<thead>
<tr>
<th>Protocol Number</th>
<th>Status as of December 2007</th>
<th>Prime</th>
<th>Boost</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Class</td>
<td>Producer</td>
</tr>
<tr>
<td>HVTN 502/Merck 023 (Step) (n=3000)</td>
<td>Closed to accrual</td>
<td>Nonreplicating adenoviral vectors (clade B Gag-Pol-Nef)</td>
<td>Merck</td>
</tr>
<tr>
<td>HVTN 204 (n=480)</td>
<td>Closed to accrual</td>
<td>DNA plasmids (clade B Gag, Pol, Nef; clade A,B,C Env)</td>
<td>NIH VRC</td>
</tr>
<tr>
<td>HVTN 503 (n=801)</td>
<td>Closed to accrual</td>
<td>Nonreplicating adenoviral vectors (clade B Gag-Pol-Nef)</td>
<td>Merck</td>
</tr>
</tbody>
</table>
AIDS Vaccines in Clinical Trials - 2007

**DNA vectors**

- Clade C, ADARC
- Clade B-minigenes
- Clade B-nuclear anchor, FIT Biotech
- Clade B, MVA*
- Multiclade-A,B,C, Ad5*
- Multiclade Micro particle, gp140*
- Multiclade, gp120*
- Multiclade-ABC, MVA*
- Clade C, Johns Hopkins
- Clade B’, Changchun Baike
- Clade B/C, NYVAC*

**Viral Vectors - Adenovirus**

<table>
<thead>
<tr>
<th>Clade</th>
<th>Developer(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad-5 (Clade B)</td>
<td>Merck</td>
</tr>
<tr>
<td>Ad-5 (Clades A,B,C), [DNA]</td>
<td>NIH-VRC</td>
</tr>
<tr>
<td>Ad-6 (Clade B)</td>
<td>Merck</td>
</tr>
</tbody>
</table>

**Viral Vectors - Pox**

- Canarypox (Clade B/E), gp120* Aventis
- MVA (Clade C) IAVI-Therion
- MVA* (Clade C) IAVI-ADARC
- MVA (Clade B), [fowlpox] Therion
- MVA (Clade B), [DNA] GeoVax
- MVA (Clade A/E), [DNA] WRAIR
- MVA (Clade B/C) Changchun Baike
- Fowlpox (Clade B) [MVA] Therion
- NYVAC (Clade C) [DNA] EuroVac
- Vaccinia (Cocktail) St. Jude’s

**Viral Vectors - Other**

- VEE (Clade C) AlphaVax [formerly IAVI]
- AAV-2 (Clade C) IAVI-TGEN
Which of these vaccines addresses HIV Variability?: HIV is A Global Problem

40 million persons living with HIV/AIDS

Building an HIV vaccine for the world
Outline

- Basic aspects of HIV relevant to vaccine design
- Vaccines
- A new vision
What kind of HIV Vaccine?

- Effective everywhere in the world
- Against any strain of HIV
- Broad T cell response
- Reduce the chance of transmission
- Low risk (no live vector)
- Low Cost if not entirely free
- Could be made in developing world
- Scaleable

And with collaboration of “developing world” scientists
The GAIA HIV Vaccine

GAIA

Global Alliance to Immunize against AIDS
An AIDS Vaccine without Borders

Globally relevant, globally accessible
An Epitope-Based “World Clade” Vaccine

Epitopes - Minimal Essential Unit of Information

- Use immunoinformatics to identify “Achilles’ heel of HIV
- Confirm in context of ‘healthy’ HIV-infected patients
- Reduce non-essential components - Limit Toxicity
- Highly conserved across time and clades of HIV
- Tailored to be presented in HLA of all types of genetic backgrounds

And . . .

- Make the vaccine free of developing world countries
  Globally relevant and globally accessible
For HIV - variability is a HUGE problem

Adapted from J. Mullins
Distribution of HIV-1 Clades

current vaccines

current epidemic

source: Los Alamos National Laboratory
"GAIA" HIV Vaccine

Multiple epitopes that are conserved across clades
### GAIA Vaccine - From Gene to Vaccine

<table>
<thead>
<tr>
<th>In Silico</th>
<th>EpiMatrix / ClustiMer / OptiMatrix [class I and class II alleles] Conservatrix / BlastiMer</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Vitro</td>
<td>HLA binding assay ELISpot - ELISA - Multiplex ELISpot - T regulatory T cell profiling</td>
</tr>
<tr>
<td>In Vector</td>
<td>DNA vaccines VaccineCAD Vaccine delivery / formulation optimization / detolerizing delivery agents</td>
</tr>
<tr>
<td>In Vivo</td>
<td>HLA DR3, DR4 transgenic mice HLA class I transgenic mice Vaccination, Dose, Route, Adjuvant</td>
</tr>
</tbody>
</table>
Our approach: search for the HIV virus “Achilles’ heel” using immunoinformatics
Conservatrix: Find conserved epitopes in variable pathogens (think HIV, HCV etc.)

HIV protein sequences

Conserved epitope
T help essential; Conserved T help an obstacle

“The goal of an HIV vaccine for one clade to protect against other clades may be more limited by the ability to provide CD4 T cell help than the ability to elicit CD8 effector functions.”

Immunogenic Consensus Epitopes

Conserved epitopes

CTRPNNTRK

Conserved epitope

Epi-Assembler

Immunogenic consensus
Using our tools, we have found HIV epitopes that are highly conserved over time and across HIV subtypes.
Current GAIA Epitope Summary

> 400 epitopes mapped
> 300 tested (ELIspot)
> 200 confirmed (>67%)

HLA A2, A3, A24, B7, B44 and Class II (clustered)

Both Supertype and Promiscuous Epitopes
Improving Vaccine Design by aligning epitopes: Vaccine-CAD

Design the arrangement of the epitopes to minimize the immunogenicity of junctional peptides and focus the immune response to the desired epitopes

De Groot AS, Marcon L, Bishop EA, Rivera D, Kutzler M, Weiner DB, Martin W. HIV vaccine development by computer assisted design: the GAIA vaccine. Vaccine. 2005
Intended Protein Product: Many epitopes strung together in a “String-of-Beads”

Reverse Translation: Determines the DNA sequence necessary to code for the intended protein. This DNA is assembled for insertion into an expression vector.

DNA insert

DNA Vector

Protein product (folded)
Epitope-based vaccines Protect HLA DR Mice from 5X LD$_{50}$ LVS Challenge
GAIA Vaccine Collaboration

Laboratoire de la Biologie Moléculaire Appliquée

Dr. Ousmane Koita (FAST) U. Bamako
Hope Center Clinic (Centre D’Espoir)

Front line HIV care and Prevention – GAIA Vaccine Foundation

... 2008
When will we have an HIV Vaccine?
### Phases of HIV vaccine trials

<table>
<thead>
<tr>
<th>Phase</th>
<th>Sample</th>
<th>I/E criteria</th>
<th>Endpoints</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>20-50</td>
<td>Healthy, HIV-uninfected at lower risk for HIV-infection; dose, regimen</td>
<td>Safety, preliminary Immunogenicity</td>
<td>18-24 m</td>
</tr>
<tr>
<td>II</td>
<td>200-500</td>
<td>(Healthy), HIV-uninfected at lower to higher risk, dose; regimen</td>
<td>Safety, Immunogenicity</td>
<td>18-24 m</td>
</tr>
<tr>
<td>III</td>
<td>5000-10,000</td>
<td>HIV-uninfected, at risk (CSW, discordant couples, general population)</td>
<td>Expanded safety Efficacy Correlates of protection</td>
<td>3-5 years</td>
</tr>
</tbody>
</table>

10 years
Potential Availability Of Efficacy Data From Current & Planned Trials*

*Assuming no early termination

Attendance, J Flores
### AIDS Vaccines in Preclinical Pipeline - 2007

<table>
<thead>
<tr>
<th>In trials 2007-2009</th>
<th>NIAID/CHAVI</th>
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<tbody>
<tr>
<td>Ad 35 prototype</td>
<td>NIH-VRC</td>
</tr>
<tr>
<td>Ad 35</td>
<td>IAVI-Crucell</td>
</tr>
<tr>
<td>Chimeric Adeno</td>
<td>Harvard-Crucell</td>
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<tr>
<td>VSV</td>
<td>Wyeth</td>
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<td>Measles</td>
<td>GSK</td>
</tr>
<tr>
<td>MVA</td>
<td>SAAVI; WRAIR</td>
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<tr>
<td></td>
<td>Chimeric Adeno Vectors</td>
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<td></td>
<td>BCG</td>
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<td>VSV</td>
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<td></td>
<td>Adeno: Chimeric and Ad-11</td>
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<td></td>
<td>Pox: NYVAC, MVA</td>
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<tr>
<td></td>
<td>Low sero-prevalent AAV</td>
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<td>Reovirus</td>
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<td>Newcastle Disease</td>
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<td>HIV/VEE Chimeras</td>
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<td></td>
<td>HIV/VSV Chimeras</td>
</tr>
<tr>
<td></td>
<td>BCG</td>
</tr>
</tbody>
</table>

IAVI Vector Program
Sendai
CMV
Simian Adeno (GSK)
GAIA Vaccine Status: Now “Pre Phase I”

- 286 highly conserved HIV CTL/Th epitopes mapped
- 186 epitopes in the last three years
- 149 confirmed
- 10 constructs synthesized
- 6 tested (4 A2 AAY+/--; 2 Class II = original/reorderd)
- 3 work! Positive responses in HLA transgenic mice
- More constructs in progress
- Phase I trial preparation in Mali, W. Africa
More resources are being invested …more needed

Annual average by country relative to national wealth (2003-2005)

Investment in AIDS vaccine R&D
Total over 2005 = US$759 mn

<table>
<thead>
<tr>
<th>% of GDP (x10^-3)</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0 – 5.0</td>
<td>United States</td>
</tr>
<tr>
<td>3.0 – 4.0</td>
<td></td>
</tr>
<tr>
<td>2.0 – 3.0</td>
<td>Ireland</td>
</tr>
<tr>
<td>1.0 – 2.0</td>
<td>Canada, South Africa, Netherlands</td>
</tr>
<tr>
<td>0.5 – 1.0</td>
<td>Denmark, Norway, Sweden, United Kingdom</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>Australia, Brazil, China, Finland, France, Germany, India, Italy, Japan, Russia, Thailand</td>
</tr>
</tbody>
</table>

Based on a 2006 study by the HIV Vaccines and Microbicides Resource Tracking Working Group; full report available at: www.hivresourcetracking.org. The study reviewed national, not sub-national or provincial, public sector data. Cuba is not captured as no GDP data is available. Estimates of 2005 investment include NIH CHAVI funds but not Gates Grand Challenges/Gates Foundation.
War Budget

Spending on War 2008
= $1.4 TRILLION (US = $711 B)
Global spending on AIDS Vaccines
= $759 M
= 0.1 % of amount spent on war.

Source: Center for Arms Control and Non-Proliferation, February 20, 2008.
A safe, effective and globally accessible AIDS vaccine is possible. One day it could save the lives of tens of millions of people.

But AIDS has not benefited from the same level of public or political support that propelled the war on polio.

The March of Dimes crusade started in 1930. By 1955—25 years later—we had a vaccine.

25 years later—we cannot say the same about AIDS.

Jon Cohen, science writer who has followed the field for more than 20 years says that AIDS vaccine researchers are always strapped for funds, and their funds are mainly allocated by their publication record. Instead of thinking—how do I make a vaccine faster—they are thinking—'What can I publish next?'

In fact, research spending on AIDS vaccines today totals only approximately US $700 million dollars a year, about the cost of five Hollywood movies.

Where is our March of Dimes for an AIDS Vaccine?
Is this asking for “Too much”?

One vaccine, start to finish: 20 Million

Ours: already part way there

Yet >500 Billion for Iraq?

http://www.nationalpriorities.org/costofwar_home
Hope is a vaccine

GAIA

http://www.gaiavaccine.org
Alliance Globale pour la Lutte contre le SIDA

Espoir/Hope – SIDA n’est pas la Mort/AIDS is not Death

Identité/Dépistage – Get Tested

Transmission/Prévention – Stop Transmission

Famille/Fidélité/Femme – Family/Few Partners/MTCTP

Communauté/Together we can stop HIV

Hope is a Vaccine / Tenez à l’Espoir – http://www.GAIAVaccine.org