GM-CSF Co-Expressing DNA/MVA HIV/AIDS Vaccine

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WHO, April 17, 2012
GeoVax DNA/MVA Vaccine Expresses Immature Virus-Like-Particles (VLPS)

- Designed to Elicit both Antibody and T cells

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VLPs Display Native Env, Goal to Elicit Ab to Native Env
Comparison of Env Structure to Env Expressed in Rv144 Trial

GeoVax Vaccine
- DNA Prime
- MVA Boost

Rv144 Trial, 31% Protection
- ALVAC Prime
- Bivalent Gp120 Boost

Viral or Cell Membrane
GM-CSF as a Vaccine Adjuvant

- Best to express in cells (more effective than recombinant protein)

- Level of expression important
  - 30-300 ng/10^6 cells most success
  - Too much GM-CSF – expand myeloid suppressor cells, inhibit adaptive response

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**Preclinical Trial Regimen**

Vaccination
SIVmac239 immunogens

Repeat Rectal Challenge (MID$_{30}$)
SIVsmE660

Heterologous Challenge:
91% related in Gag, 83% in Env

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GM-CSF Enhanced Ab Responses

- Enhanced Env-specific IgG for:
  - Neutralizing activity
  - ADCC
  - Avidity

- Enhanced SIV-specific IgA for:
  - Specific activity in rectal secretions

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GM-CSF, Enhanced Protection

No. of challenges to infection correlated with avidity for challenge Env, $r=0.9$, $p=0.001$

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Sufficient Protected animals to Test 2\textsuperscript{nd} and 3\textsuperscript{rd} Series of Challenges

\begin{itemize}
\item \textbf{Vaccination} Ch.1 -12
  - SIV239
  - SIVE660
\item \textbf{Boost} Ch.13-24 Ch. 25-36
  - SIVE660
  - SIV251
\end{itemize}

\begin{itemize}
\item Dg Dg M M
  - 0
  - 0.5
  - 0.9
\item M
  - 2.1
  - 2.6
  - 3.1
\end{itemize}

\textbf{SIV 251, Very Difficult to Neutralize}

WHO, April 17, 2012
# Summary of Challenge Results

<table>
<thead>
<tr>
<th>Virus</th>
<th>Challenge numbers</th>
<th>Time initiated</th>
<th>Per exposure efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIVE660</td>
<td>1-12</td>
<td>1 year</td>
<td>90%</td>
</tr>
<tr>
<td>SIVE660</td>
<td>13-24</td>
<td>2.6 years</td>
<td>*94%</td>
</tr>
<tr>
<td>SIV251</td>
<td>25-36</td>
<td>3.1 years</td>
<td>*72%</td>
</tr>
</tbody>
</table>

*Based on animals that were not previously infected

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Preclinical Protection against SIV251: Vaccinations with SIV Prototypes for Rv144 and GeoVax Vaccines*

*Data from independent trials

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Summary

• DNA/MVA Vaccine co-expressing VLPs and GM-CSF elicits highly promising protection in the preclinical model

• Protection correlates with avidity of Env-specific Ab for Native Env

• Concept being tested in humans by the HIV Vaccine Trials Network in HVTN 094
Immunogens for HVTN 094

GEO-D03

MVA62B

MVA Deletion II
MVA Deletion III

DgDgMMM schedule, 8 week intervals for inoculations

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Lessons Learned

1. Co-expressed GM-CSF can augment both systemic and mucosal Ab

2. VLP are good immunogens for raising protective Ab

3. “Non-neutralizing” antibodies elicited by native Env can prevent HIV acquisition

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