Generation of immunogens based on VLPs carrying HIV-1 envelopes from patients with broadly neutralizing responses within the first 6 months of infection

Eloisa Yuste
AIDS Immunopathogenesis Unit
Spanish AIDS Research Network (RIS)
Instituto de Salud Carlos III
Madrid
Panels of recombinant viruses used for screening

<table>
<thead>
<tr>
<th>Virus</th>
<th>Subtipo</th>
<th>Tropismo</th>
<th>Tier</th>
</tr>
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<tbody>
<tr>
<td>VI191</td>
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<tr>
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<td>B</td>
<td>X4</td>
<td>1A</td>
</tr>
<tr>
<td>AC10</td>
<td>B</td>
<td>R5</td>
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<tr>
<td>92BR025</td>
<td>C</td>
<td>R5</td>
<td>1B</td>
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<tr>
<td>92UG024</td>
<td>D</td>
<td>X4</td>
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<tr>
<td>CM224</td>
<td>AE</td>
<td>R5</td>
<td>2</td>
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**Detection of Broadly Neutralizing Activity within the First Months of HIV-1 Infection**


AIDS Research Unit, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; HIVACAT, Barcelona, Spain; AIDS Immunopathogenesis Unit, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain; Infectious Diseases Service, Hospital Clinic-IDIBAPS, University of Barcelona, Barcelona, Spain; Fraunhofer Institute for Biomedical Engineering, Aachen, Germany; Infection Biology Laboratory, Universitat Pompeu Fabra, and Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain; Vaccine Research Center, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA

**✓ 887 and 936 sera neutralize viruses across 4 subtypes**

<table>
<thead>
<tr>
<th>d.p.i.</th>
<th>VSV</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>AE</th>
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<tr>
<td>VI 191 Tier 2</td>
<td>887</td>
<td>96</td>
<td>40</td>
<td>320</td>
<td>200</td>
<td>220</td>
<td>&lt;20</td>
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</table>

**D.p.i. Days post infection**

**✓ Neutralization maps to a V2 glycan dependent epitope**

**887**

**936**

**2G 12**

**PG 9**

**JRC SF**

**JRCSF.N160K**

**JRCSF.N332A**
Full length Env-SOS-T constructs

887 SOS-T

936 SOS-T

887 and 936 SOS-T Env pseudotyped viruses are infectious
VIRUS LIKE PARTICLE (VLP) GENERATION: Env-SOS-T + dGag (Dr. C. Brander, Irsicaixa)

- 887 and 936-SOS-T Envs are VLP-associated and can form trimers.
- VLPs showed a spheric shape and 170nm in diameter.
- VLPs incorporate trimers.
- VLPs were homogeneous and incorporate trimers.

EM: PG16

NTA: 35022
### VLPs: antigenicity

<table>
<thead>
<tr>
<th>Antibody</th>
<th>V1-V2</th>
<th>CHO-V3</th>
<th>CD4bs</th>
<th>Fusion peptide</th>
<th>Interface</th>
<th>CD4i</th>
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<tbody>
<tr>
<td>PG16</td>
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<td>2G12</td>
<td>VRC01</td>
<td>PGT151</td>
<td>35022</td>
<td>17b</td>
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</tbody>
</table>

**887**

**936**

- **Green**: 887
- **Purple**: 936
- **Black**: mock

**Antibodies specific for native trimers** (PGT145, VRC01 and 35022) and the **CD4bs** bind VLP associated Envs

- **Fusion peptide**
- **gp120-gp41 interface**
- **No bNAb: CD4i**

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**References**: GESIDA 2018