**SHEV**

**Project ID:** 280829  
**Funded under:** FP7-IDEAS-ERC

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**Stabilizing the exposure of neutralization epitopes on HIV-1 envelope glycoprotein trimer vaccines**

**From** 2012-01-01 **to** 2016-12-31, closed project

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**Project details**

<table>
<thead>
<tr>
<th><strong>Total cost:</strong></th>
<th><strong>Topic(s):</strong></th>
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<tbody>
<tr>
<td>EUR 1 499 943</td>
<td>ERC-SG-LS6 - ERC Starting Grant - Immunity and infection</td>
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<thead>
<tr>
<th><strong>EU contribution:</strong></th>
<th><strong>Call for proposal:</strong></th>
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<tbody>
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<td>EUR 1 499 943</td>
<td>ERC-2011-StG_20101109</td>
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<tr>
<th><strong>Coordinated in:</strong></th>
<th><strong>Funding scheme:</strong></th>
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<tbody>
<tr>
<td>Netherlands</td>
<td>ERC-SG - ERC Starting Grant</td>
</tr>
</tbody>
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**Objective**

The impact of HIV/AIDS on world healthcare is tremendous, particularly in the Third World. To curtail the HIV epidemic a cheap and effective vaccine is urgently needed, but despite massive research efforts no vaccine is available yet. Although most vaccines work by inducing neutralizing antibodies, HIV has evolved many ways to limit the induction and binding of neutralizing antibodies. The challenge is to engineer Env subunit vaccines that do induce neutralizing antibodies efficiently. One aspect that has been highly underappreciated is conformational heterogeneity of Env. Conformational flexibility is exerted at three different levels. First, flexible variable loops and N-glycans protruding from the conserved protein core cause “local flexibility” at the protein surface. Second, movement between the conserved inner and outer domain of gp120 causes “tertiary flexibility”. Third, movement of the three gp120 protomers in the trimeric complex, resembling a flower that opens and closes, causes “quaternary flexibility”. These three levels of flexibility provide very unstable targets for recognition by low affinity B cell receptors on naïve B cells, diminishing the chance of efficient B cell activation and the secretion of neutralizing antibodies. Using a number of novel structure-based vaccine design strategies that include the introduction of stabilizing disulfide bonds, we intend to remove the undesirable flexibility on Env trimers to provide a homogeneous and stable target to B cells. This should result in stabilized Env immunogens that are better in inducing neutralizing antibodies compared to the current state-of-the art Env vaccines. This is a highly interdisciplinary project on the crossroads of immunology and protein chemistry and should result in protein immunogens that elicit improved neutralizing antibody responses against HIV and should provide answers to fundamental questions on how B cells “see” protein immunogens.

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**Related information**

**Report Summaries**

Final Report Summary - SHEV (Stabilizing the exposure of neutralization epitopes on HIV-1 envelope glycoprotein trimer vaccines)

**News**

Exploiting HIV’s weaknesses to develop effective vaccines
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**Activity type:** Higher or Secondary Education Establishments

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**To know more**

http://erc.europa.eu/

**Subjects**

Biotechnology - Life Sciences - Medicine and Health

**Last updated on** 2017-07-12  
**Retrieved on** 2018-09-27

**Permalink:** https://cordis.europa.eu/project/rcn/102000_en.html