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International Conference on
Immunology and Immunotechnology

November 1-3, 2017 Barcelona, Spain

Allosteric Induction of the CD4-Bound Conformation of HIV-1 gp120

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Background: HIV-1 infection of target cells is mediated *via* the binding of the viral envelope protein, gp120, to the cell surface receptor CD4. This interaction leads to conformational rearrangements in gp120 forming or revealing CD4 induced (CD4i) epitopes which are critical for the subsequent recognition of the co-receptor required for viral entry. The CD4-bound state of gp120 has been considered as a potential immunogen for HIV-1 vaccine development.

In this research we propose an alternative means to induce gp120 into the CD4i conformation.

Results: Combinatorial phage display peptide libraries were screened against HIV-1 gp120 and short (14aa) peptides were selected that bind the viral envelope and allosterically induce the CD4i conformation. The lead peptide was subsequently systematically optimized for higher affinity as well as more efficient inductive activity. The peptide: gp120 complex was scrutinized with a panel of neutralizing anti-gp120 monoclonal antibodies and CD4 itself, illustrating that peptide binding does not interfere with or obscure the CD4 binding site.

Conclusions: Two surfaces of gp120 are considered targets for the development of cross neutralizing antibodies against HIV-1; the CD4 binding site and CD4i epitopes. By implementing novel peptides that allosterically induce the CD4i epitopes we have generated a viral envelope that presents both of these surfaces simultaneously.

Biography:

Anna Roitburd-Berman completed her B.Sc. in Biology at the George S. Wise Faculty of Life Sciences, Tel Aviv University in 2005 and proceeded with her studies in the Direct Ph.D. Program at the Department of Cell Research and Immunology, Tel Aviv University. Over the past 10 years she has been studying the interaction between the HIV-1 envelope glycoprotein, gp120, and its cellular receptor, CD4, in an attempt to harness this interaction and the resulting conformational change in gp120 for the construction of a novel immunogen for HIV-1.

Chen Piller completed her B.Sc. in Biology at the Department of Life Sciences, Ben-Gurion University of the Negevin 2012 and proceeded to complete her M.Sc. studies at the Department of Zoology, Tel Aviv University, in 2015. Since starting her Ph.D. in 2016, at the Department of Cell Research and Immunology, Tel Aviv University, she is focusing in generation of novel Epitope-based vaccine candidates, developed to specifically focus the immune response towards neutralizing viral epitopes.