Patrice Debre et al., J Vaccines Vaccin 2014, 5:5
http://dx.doi.org/10.4172/2157-7560.S1.020

OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference on
Vaccines & Vaccination
September 24-26, 2014 Valencia Convention Centre, Spain

Characterization of a potent and broad neutralizing antibody that specifically recognizes a point-substitution in the 3S motif of the HIV-1 gp41 protein

Patrice Debre[1], **Caroline Petitdemange**[1], **Karim Dorgham**[1], **Abla Achour**[1], **Vincent Carvez**[2], **Joel Crouzet**[3], **Gabriella Scarlatti**[4] and **Vincent Vieillard**[1]
[1]INSERM, France
[2]AP-HP Hôpital Pitie-Salpêtrière, France
[3]InnaVirVax, France
[4]San Raffaele Scientific Institute, Italy

Objective: The hallmark of most successful vaccine is the ability to induce cross-reactive neutralizing antibodies (NAbs). Over the ensuing years, we have shown that a highly specific and conserved motif of the gp41, called 3S, induces expression of NKp44L, the cellular ligand for an activating NK receptor on $CD4^+$ T cells render them more sensitive to autologous NK lysis. The aim of this study was to show that a specific substitution inside this 3S motif permits the development of NAbs while preserving the capacity to block CD4 depletion.

Methodology: To further characterize the 3S peptide, an alanine-scanning inside the 3S motif was performed. We tested such effect on (a) the capacities to infect cells and (b) the ability of the corresponding peptides to induce production of Ab that elicits viral neutralization and/or inhibits NKp44L expression on CD4 T cells and NK cell function. Generation of monoclonal NAbs, and characterization of their Vh et Vκ domains.

Results: In this study, an alanine-scanning allowed us to identify a specific position in the 3S motif that totally inhibits HIV entry and expose it to a broad spectrum of neutralizing antibodies. Importantly, for the first time, we show that that a specific amino-acid substitution within a highly linear motif of the gp41 elicits strong neutralization capacity with impressive magnitude, breadth and ability to durability over cross clade viruses. Furthermore, our data also show that this acquisition of neutralization capacities preserves the unique ability of anti-3S Ab to inhibit NKp44L expression on $CD4^+$ T cells and their sensitivity to NK lysis. The generation of monoclonal NAbs has also permitted their molecular identification.

Conclusion: Our finding suggest that a specific substitution into the 3S motif may lead to the generation of bNAbs directed against the highly conserved motif of the gp41 and will provide foundation for novel vaccine strategies based on specific substitutions in highly conserved motif of the HIV Env protein.

Biography

Patrice Debre, MD, PhD is Professor of Immunology at University Pierre et Marie Curie and Pitie-Salpêtrière Hospital. He directed a federative institute on infection and immunity, an INSERM laboratory and a department of immunology. He has been an ambassador for the fight against HIV and communicable diseases and is a French representative at the Global Fund, UNITAID, EDCTP, UNAIDS, RBM. Well known specialist of HIV, he is author of more than 350 articles in Immunology, Immunopathology and Immunogenic. He is a corresponding member of the French Academy of Medicine.

patrice.debre@psl.aphp.fr