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Efficacy of a mixture of synthetic peptides overlapping the conserved CBD1 epitope in gp41 of HIV-1 to protect against SHIV162P3 rectal challenge in cynomolgus macaques

Ara Hovanessian
CNRS - Université Paris Descartes, France

The synthetic CBD1 peptide corresponding to the conserved caveolin-1 binding domain of HIV-1 glycoprotein gp41 (CBD1 epitope: CSLEQIWNNMTWMQWDK) elicits the production of antibodies in rabbits, mice, and macaques that inhibit infection of primary CD4+ T lymphocytes by various primary HIV-1 isolates. In a detailed study in mice we then showed that peptides overlapping the caveolin-1 binding motif (CBM: IWNNMTWMQW) containing the N-terminal conserved isoleucine residue, when fused to a T helper epitope, induce high titered HIV-neutralizing antibodies. Interestingly, immune sera raised against a given peptide do not cross-react with related CBM-derived peptides, thus suggesting the existence of distinct neutralizing determinants, which probably reflect the dynamic conformational features of the CBD1 epitope in gp41. CBD1- and CBM-based peptides therefore provide specific immunogens for an efficient vaccine preparation against HIV/AIDS infection.

In our current study in cynomolgus macaques, the immunogenicity and efficacy of the CBM-based peptide-cocktail vaccine-formulation (CBM-based chimeric peptides, the CBD1 peptide, T helper epitope-peptides, and [CpG and Montanide ISA 51]) is evaluated in cynomolgus macaques in two phases: firstly by monitoring humoral and cellular immune responses in the immunized animals, and secondly challenging them with a replication competent chimera simian/human immunodeficiency virus (SHIV). All immunized animals have responded by the production of high tittered specific antibodies. The immunized macaques with the corresponding control animals will now be challenged by the rectal route with a low dose viral (SHIV162P3) inoculum, once a week for 10 weeks. Animals will then be monitored for the humoral and cellular immune response, T cell subsets, plasma viral load, and any clinical or behavioural changes. The final results will be presented at the meeting in November 2011.

Biography

Ara Hovanessian (Director of Research 1, CNRS) has completed his Ph.D. at the age of 30 years from King's College, University of London with the thesis research work at the National Institute for Medical Research, Mill Hill. Then as a senior investigator, he spent 26 years at the 'Institut Pasteur' in close collaboration with Luc Montagnier. Since 2004, he is at CNRS-Université Paris Descartes where he conducts two major projects: 1) on the development of a synthetic vaccine for AIDS, and 2) on the development of synthetic peptides for cancer therapy. His research discoveries include: The interferon-induced 2'-5' oligoadenylate synthetase and protein kinase PKR, HIV-2 glycoproteins, Inhibitors of HIV entry, synthetic vaccines against HIV, surface-nucleolin as a target in cancer therapy. He has several patents, and published > 190 scientific articles (PubMed) 75% of which he is the first or the last author.