OMICS Group Conferences
Accelerating Scientific Discovery
3rd World Congress on Virology
November 20-22, 2013 DoubleTree by Hilton Baltimore-BWI Airport, USA

# An oral SIV vaccine inducing non-cytotoxic MHC-Ib/E-restricted regulatory CD8+T-cells suppresses the activation of SIV positive CD4+T-cells and protects macaques from SIV challenges

**Jean-Marie Andrieu,**

*University of Paris-Descartes, France*

## Abstract

Since CD4+ T cell activation drives the initial burst of HIV/SIV replication *in vivo* (1,2) we explored in macaques whether an oral vaccine comprised of *Lactobacillus plantarum* (LP), a commensal bacterium that favors immune tolerance (3), and inactivated (i) SIVmac239 would induce CD4+T-cell unresponsiveness toward SIV antigens and thereby prevent the establishment of SIV infection.

SIV mac239 was produced in CEM174 cells and inactivated with aldrithiol-2 and heating. LP was cultured to reach a concentration of $10^{10}$ cfu/ml. Sixteen macaques of Chinese origin were intragastrically administered over 5 days, 35 doses of 30 ml of 4x $10^7$ copies/ml of iSIV plus 3x $10^9$ cfu/ml of living LP in maltodextrin (20%) solution. Eight animals received LP alone, and 8 animals received iSIV alone according to the same protocol. Specific antibody and CTL responses were tested by standard methods. The activation status (Ki 67+) of Gag positive CD4+T-cells was tested in the presence or absence of autologous or allogeneic CD8+T- cells of vaccinated and control macaques. To deplete macaques of CD8+T-cells *in vivo*, they were given an i.v. injection of a chimeric CD8 monoclonal antibody on days 0, 4, and 7.

The vaccine induced a class of non cytotoxic MHC-Ib/E-restricted CD8+ regulatory T cells (Tregs) which have not been described previously. These CD8+Tregs suppressed the activation of SIV positive CD4+T-cell and the *ex vivo* SIV replication in 15 of 16 animals without inducing SIV specific antibodies or CTLs. Of 16 macaques that were intrarectally challenged with SIVmac239 or an heterologous strain (SIVB670), 15 were sterilely protected while the 16 controls were infected. In four macaques that were rechallenged intravenously, plasma SIV levels peaked slightly and then dropped to undetectable levels, although the animals subsequently harbored intracellular SIV DNA. Infusion of CD8 antibodies confirmed the role of this new class of CD8+ Tregs in suppressing SIV in vivo. Given that SIV and HIV require activated CD4+T-cells in which to replicate, this preventive SIV vaccine should likely be transferable in Humans. Moreover, the induction of this class of CD8+T- regulatory cells could potentially be used therapeutically to suppress HIV replication in already infected patients. Finally, the tolerogenic vaccine approach described here could be exploited in the management of a wide range of immune disorders and is likely to have profound implications across the whole of immunology.

## Biography

Jean- Marie Andrieu, MD, is currently an Emeritus Professor at the University of Paris-Descartes, Paris, France and Wei Lu, MD, PhD is currently Research Director at the "Institut de Recherche pour le Developpement" (IRD) in Montpellier. They are working together since 1999 at the Laboratory of Molecular Oncology and Virology, University of Paris-Descartes. They published 50 papers and 3 books on HIV/SIV pathogenesis, treatment and vaccine development.