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A tolerogenic vaccine against AIDS in Chinese macaques.

Jean-Marie Andrieu and **Wei Lu**
Institut de Recherche sur les Vaccins et l'Immunothérapie des Cancers et du SIDA
Centre Universitaire des Saints Pères, Université de Paris-Descartes, 45 rue des Saints Peres, Paris 75006, France

Over the last decade, our laboratory has developed a tolerogenic mucosal vaccine against AIDS in the Chinese macaque model. Here, we report the successive steps of this discovery study..

The vaccine consisted in killed/inactivated SIVmac239 (iSIV) particles adjuvanted by the Bacillus of Calmettee and Guerin (BCG) or by Lactobacillus Plantarum (LP) or Lactobacillus Rhamnosus (LR).

Without adjuvant, the vaccine administered by intra-gastric route induced usual SIV-specific humoral and cellular immune responses but no post-challenge protection. In contrast, out of 24 macaques immunized with the vaccine adjuvanted by the BCG, LP or LR and further challenged intra-rectally with high doses of SIVmac239 or SIVB670, 23 were sterilely protected for up to five years while usual SIV-specific immune responses were suppressed in all of them. On the other hand, all macaques of Indian origin immunized by the same adjuvanted vaccine were not protected.

We then discovered that vaccinated Chinese macaques developed a previously unrecognized class of non- cytolytic MHC- Ib/E-restricted CD8+T-cells (or CD8+T-Regs) that

had the ability to suppress the activation of SIV RNA-infected CD4+T-cells and inhibited thereby the (activation-dependant) reverse-transcription of the virus and prevented the establishment of SIV infection.

Finally, we sought and found a similar population of HLA-E-restricted CD8+T-Regs in Human elite controllers (a small group of HIV-infected patients whose viral replication is naturally inhibited). Ex-vivo, their CD8+T- Regs were shown to suppress viral replication according to the same mechanism as that discovered in vaccinated Chinese macaques. Importantly, we found that all these elite controllers had an homo or heterozygote HLA-Bw4-80I genotype.

Taking into account the longevity and the high percentage of vaccine-protected Chinese macaques together with the concomitant identification of a robust ex-vivo correlate of protection and the discovery of similar CD8+T-Regs in Human elite controllers, preventive and therapeutic HIV vaccines should be envisaged in Humans.

Biography

Jean-Marie Andrieu is a Professor of Medicine (Hematology) since 1982. He is the Director of the Institute of Research on Vaccines and Immunotherapy of Cancer and AIDS (IRVICS) at Paris-Descartes University. For 30 years, he is interested in the modulation of the immune system in HIV infection.

jean-marie.andrieu@parisdescartes.fr
louis.luwei@ird.fr