

An Oral Tolerogenic Vaccine Protects Macaques from SIV Infection without Eliciting SIV-Specific Antibodies nor CTLs

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In the issue of Cell Reports of 27 December 2012 (Vol 2: 1736-1746) a French-Chinese tripartite collaboration between the Université Paris-Descartes (Dr. Jean-Marie Andrieu), the Institut de Recherche pour le Développement Montpellier (Dr. Wei Lu) and the University of Guangzhou in China (Dr. Song Chen) produced research results that are probably the most astonishing and revolutionary vaccine data published in 2012 [1].

Using the SIV model in Chinese macaques, the group headed by Jean-Marie Andrieu in Paris and Wei Lu in Montpellier were able to suppress the initial activation of SIV- positive CD4+ T-lymphocytes *in vivo* which is the crucial step that allows SIV to initiate replication and to establish infection. They used an oral vaccine made of inactivated SIVmac239 associated with a common commensal bacterium of the digestive tract known as *Lactobacillus plantarum* which is known to induce immunological tolerance to foreign antigens.

In contrast to what happens with all anti-viral vaccines, this oral tolerogenic vaccine elicited neither anti-SIV antibodies nor cytotoxic T-lymphocytes but induced instead a previously unrecognized class of SIV- specific, non-cytolytic CD8+ T-regulatory cells which prevented SIV+ CD4+ T-cell activation and suppressed SIV replication. By blocking SIV reverse transcription in CD4+ T-cells, the initial burst of virus replication was prevented and the vaccinated macaques were

protected from infection. Of the 16 vaccinated macaques that were challenged intra-rectally 3 to 14 months later with the homologous SIV strain as well as with the heterologous strain SIV-B670, 15 were solidly protected from SIV challenge. Since CD4+ T-cell activation drives both the initial SIV and HIV-1 replication in macaques and humans respectively, it is plausible that such a tolerogenic vaccine may also be effective against HIV-1 in humans and this will be certainly be investigated in the near future, either as a preventive or therapeutic vaccine.

This remarkable and totally unexpected breakthrough was obtained by an investigator-driven research that was not funded by the usual governmental and large scale organizations that support most of the ongoing HIV vaccine research world-wide. It was sponsored by a private benefactor who funded the project to the tune of 13 million Euros. This illustrates once again that success in basic vaccine research is unpredictable and that “risky” projects based on unorthodox thinking may deserve as much funding as the “safe” projects that are often preferred because they abide by current fashionable paradigms.

Reference

1. Lu W, Chen S, Lai C, Guo W, Fu L, et al. (2012) Induction of CD8+ regulatory T cells protect macaques against SIV challenge. Cell Rep 2: 1736-1746.

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