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A Prototype HIV Lentivector DNA Vaccine that Controls Heterologous Challenge Virus in Macaques

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The pandemic of human immunodeficiency virus type 1 has caused infection in near 80 million individuals worldwide and the death of near half of these infected people while the other half is living with HIV-1 infection thanks to innovative antiviral therapies. Although these therapies were highly effective at controlling active virus replication, they failed to eradicate the reservoirs of latent virus that rebounds upon interruption of therapy. A large variety of classical and innovative strategies of vaccine development has been used and failed to generate a safe and efficacious vaccine that could efficiently control HIV in infected people or protect risk populations from HIV acquisition.

The main reasons of these failures are could be explained by the biologic properties of the virus and the complex host/virus interactions that the virus establishes during infection. Indeed, following the initial picture of viremia early post infection, the virus causes slow low chronic infection associated with a variety of strategies that help the virus to escape the host defences and to progressively eradicate or dysfunction the key cells of the host's immune system. Existence of a swarm of genetically and antigenically distinct variant in contaminated fluids during virus transmission adds further complications. Innovative strategies and vaccine prototypes are strongly needed to face these constraints and control this type of pathogens. We used the innovative DNA vaccine strategy to engineer lentivector-based DNA vaccine prototypes against HIV-1. We successfully tested these prototypes for their immunogenicity and protection against pathogenic viruses in animal models. Our latest prototype provided the demonstration in our recent experiment that a single DNA immunization was sufficient enough to induce long lasting immunity in all immunized macaques. Vaccine induced T cell immunity contained a variety of CD4+ and CD8+ T cells with both memory and effector phenotypes of cells including cells with high capacity of differentiation/proliferation and self-renewal. Humoral responses contained binding antibodies both to Gag and Env but were not associated with any neutralizing activity. As expected all 6 control and 6 vaccine macaques were all infected with the heterologous SIVmac251 challenge virus, since the design of this T-cell based vaccine was not for eliciting neutralizing antibodies capable of preventing acquisition of infection. Importantly however, the viremia was significantly lower in vaccinated group of macaques than that in controls after virus acquisition and then all 6 vaccinated animals progressively cleared their virus infection to barely detectable levels. Virus control was fully independent from neutralizing antibodies since all sera during 80 weeks before challenge and those collected up to 48 weeks post-challenge lacked any neutralizing activity against the challenge or the homologous virus to the vaccine. However, this low initial viremia in vaccines correlated with augmented IgA/IgG ratios in the rectal mucosa of all vaccinated animals compared with those of the controls. The clearance of viremia was found to be associated with increased central memory CD4+ and CD8+ T cells endowed with high capacity of proliferation upon homeostatic and antigenic stimulations.

Taken altogether, the data of this pilot study clearly demonstrate that a single immunization with our lentivector DNA vaccine has initiated long lasting immune responses that lack neutralizing antibodies but still significantly reduced the initial viremia by controlling virus acquisition and progressively cleared the challenge virus infection to barely detectable viremia.

Biography:

Yahia chebloune has completed his Ph.D at the age of 30 years from claude bernard lyon-1 university and postdoctoral studies from university of kansas school of medicine. He is research director at the CNRS and joseph fourier university of grenoble, leading the group of pathogenesis and lentivirus vaccination. He has published more than 80 papers in reputed journals and serving as an editorial board member of repute. His recent work is focusing on development of HIV-1 vaccine using the naturally attenuated animal lentivirus, caev as model and to study the mechanisms involved in latency/persistence of HIV/SIV in relation with pathogenesis