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Oral presentation

OA021-02. Replicating measles-SHIV vaccine induces long term preservation of central memory CD4 cells in the gut of vaccinated macaques challenged with SHIV

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Background

Live attenuated vaccines are mostly appropriate for global mass immunization, controlling very efficiently global pandemics like polio or measles. Although a live attenuated HIV vaccine is not currently considered for safety reasons, a strategy based on the expression of HIV-1 particles through a live replicating viral vector might mimic the advantageous characteristics of live attenuated SIV.

Methods

With this aim, we generated a recombinant measles vaccine expressing simultaneously HIV-1 Gag and Env and evaluated its immunogenicity in mice and macaques. Measles vaccine is a live attenuated negative-stranded RNA virus proven to be one of the safest and most effective human vaccines. The efficacy of recombinant measles-HIV virus was evaluated in macaques after intrarectal SHIV challenge.

Results

In mice, the recombinant vaccine stimulated MV and HIV antibody with neutralizing activity, as well as cellular immunity composed of CD4 and CD8 T cells. In the macaque/SHIV model, the vaccine induced a 2–4 log reduction in acute viral load. More than 3 years after challenge, the macaques were sacrificed and T-cell populations were determined in different organs. We found that CD4 central memory T cells of the gut were preserved in vaccinated animals as compared to controls vaccinated with empty measles. We also demonstrated that recombinant measles-HIV infects human professional APC, such as dendritic and B cells, and induces efficient presentation of HIV-1 epitopes to autologous T-cells and subsequent activation of cytokine secretion by human HIV-1 Gag-specific T-cell clones *in vitro*.

Conclusion

The immunogenicity of measles-HIV virus results from its capacity to replicate *in vivo* after administration and to infect productively dendritic cells. This strategy, which is currently in the process of phase I human trial evaluation, provides a vaccine that might protect children and adolescents simultaneously from measles and HIV and be affordable to populations through the Expanded Program on Immunization.