# ANIMAL HU-SCID MODEL OF VAGINAL TRANSMISSION OF HIV-1 FOR THE PRECLINICAL EVALUATION OF MICROBICIDES

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In this project we intend to evaluate at the preclinical level a series of microbicides which include gp-120 binding lectins as well as peptidomimetics of LFA-1 and mini-antibodies in single chain fragment variable (scFv) format. For this purpose an animal model consisting of Hu-SCID mice reconstituted with human lymphocytes and infected *via* vaginal transmission of HIV-1 will be used. In the present comunication data on the reliability on the Hu-SCID model in testing the plant lectins *Galanthus nivalis* agglutinin (GNA) and *Hippeastrum hybrid* agglutinin (HHA) will be presented and discussed.

## Inhibition of vaginal transmission of HIV-1 in hu-SCID mice by plant lectins the *Galanthus nivalis* and *Hippeastrum hybrid* in a gel formulation

Plant lectins [i.e., *Galanthus nivalis* agglutinin (GNA) and *Hippeastrum hybrid* (HHA) agglutinin (HHA)] were recently demonstrated to represent potential candidate anti-HIV microbicides; they lack mitogenic activity, do not lead to human blood cell agglutination, and show marked stability at relatively low pH and high temperatures for prolonged time periods. Preincubation of cell-free HIV particles or persistently HIV-infected cells with these plant lectins resulted in a further potentiation of their antiviral efficiency by at least 10- to 20-fold. The plant lectins clearly interact with the entry of HIV into its target cell.

A preclinical evaluation of the potential effectiveness of GNA and HHA also as a topical microbicide to prevent vaginal HIV-1 transmission in a humanized severe combined immunodeficient (Hu-SCID) mouse model has been recently investigated. Reconstituted mice received an intravaginal application of a GNA and HHA – containing gel 20 min prior to a non-invasive vaginal challenge with cell-associated HIV. The possible cytotoxic effect of GNA and HHA – containing-gel on lymphocytes was assessed and their *in vivo* migration was followed using fluorescently labelled human lymphocytes. Systemic infection was monitored by p24 antigen detection in culture supernatant from cocultured intraperitoneal cells using antigen capture enzyme-linked immunosorbent assay test and by the presence of integrated proviral HIV-1 DNA in DNA extracted from spleen cells. *In vivo* migration of labelled lymphocytes was examined by analysis of cells isolated from regional lymph nodes.

Preliminary results suggest that systemic infection was successfully inhibited by the presence of GNA and HHA containing gel at vaginal level. However, since the presence of contradictory results observed in the presence of the highest GNA and HHA concentrations (very likely due to the toxicity of the compounds) this observation has to be confirmed and more critically evaluated in additional studies.

## Publications of the project

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