PREVENTION OF HIV-MUCOSAL BARRIER INTERACTION BY NEW SYNTHESISED CARBOSILANE POLYANIONIC DENDRIMERS

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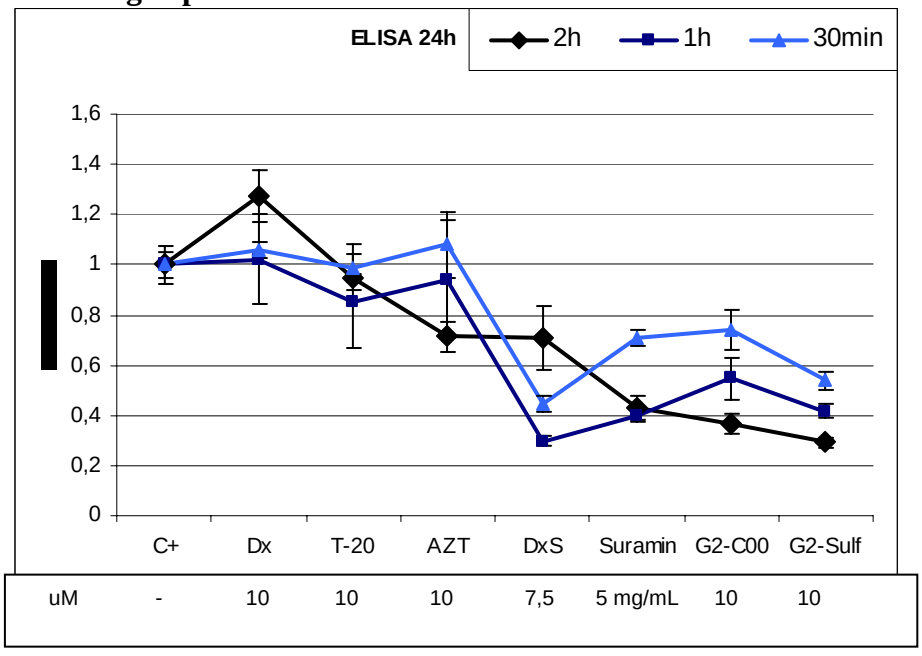
The female genital tract is the primary route for heterosexual transmission of HIV and the mechanism of virus-epithelial vaginal cells interaction is poorly understood. In this context the development of nanosystems for its use as microbicides could be a point of inflexion in the prevention of HIV infection. We are designing three new generations of carbosilane polyanionic dendrimers (CPDs) with broad-spectrum antiviral activities and minimal toxicities (data not shown, under patent). We have been tested these CPMs using the endometrial epithelium-derived cell line HEC-1A and two different HIV isolates NL4.3 (X4 isolate) and BaL (R5 isolate). We found that cells are capable of sequestering large numbers of HIV-1 particles but are refractory to cell-free viral infection. The preincubation of cells with Suramin and Dextran Sulfate decrease HIV-1 strain adherent to the plasma membrane. We found an increase of anti-adherent effect using G2-CPM, without toxicity at 10µM. Our results show until 90% of inhibition treating cells 2h pre-infection. Evaluation of chemokines attracting monocytes/macrophages and proinflammatory cytokines release that could enhance HIV-1 spread, are under analysis. Our preliminary data indicate that G2-CPM is a promising candidate for development as a vaginal microbicide and a therapeutic agent.

References:

1. McCarthy et al, Molecular pharmaceutics, 2005,vol. 2, no. 4, 312-318
2. Fletcher et al, Retrovirology, **2006**, 3:46

Figures:

%Inhibition of antigen p24. Pretreatement of CPMs



%Inhibition of antigen p24. and viability by Lactato DesHidrogenase assay