GOLD MANNO-NANOPARTICLES AS POTENTIAL MICROBICIDES AGAINST HIV INFECTION

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One of the mechanisms of vaginal infection by HIV is mediated by interactions between the virus envelope glycoprotein gp120 and DC-SIGN receptor of dendritic cells [1, 2]. The high mannose oligosaccharide $Man_9GlcNAc_2$ and the hybrid type oligosaccharide $GlcNAc_2Man_3$ seem to be involved in these interactions.

In order to inhibit the interaction between gp120 and DC-SIGN we have prepared gold nanoclusters capped with the mannose structural motives present in the gp120. These so-called Glyconanoparticles (GNPs) have been prepared by means of Glyconanotechnology, a technology developed in our laboratory to obtain multifunctional carbohydrate functionalised nanoclusters [3, 4]. GNPs are water soluble biofunctional gold nanoclusters, with globular shape, chemically well defined composition and an exceptional small core size which can be prepared in a simple way.

We have prepared and characterized a set of new water soluble mannose GNPs. The first step consists in synthesizing the neoglycoconjugates. Each of them are constituted of a mono- or oligomannoside head functionalized with different linkers. The linker were endowed of either a thiol group for attaching the neoglycoconjugate to the gold surface through a Au-S covalent bond. The neoglycoconjugates (mono-, di-, trisaccharides) are based on high mannose oligosaccharides and hybrid type structures present in the gp120 of the HIV virus. The resulting ligands have been incorporated with different densities (5 to 100%) at the surface of the gold nanocluster. Finally, mannose GNPs of different sizes (1 to 6 nm) have been synthesized to study if the GNP size can influence carbohydrate-protein interaction.

Fourteen gold *manno*-GNPs were first tested by surface plasmon resonance (SPR) as potential inhibitors of DC-SIGN binding to gp120 and in cell-based models to evaluate their effect inhibiting binding and dissemination of HIV-1 from cells bearing DC-SIGN to T cell populations. GNPs bearing Manα1-2Man showed 100% inhibition of DC-SIGN binding to gp120 at 50 nM concentrations by SPR and can directly inhibit HIV-1 binding to DC-SIGN$^+$ cells and subsequent *trans*-infection of T-cells. For complementary studies by SPR and flow cytometry, fluorescein-labelled and biotin-containing GNPs bearing Manα1-2Man are being prepared.

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