

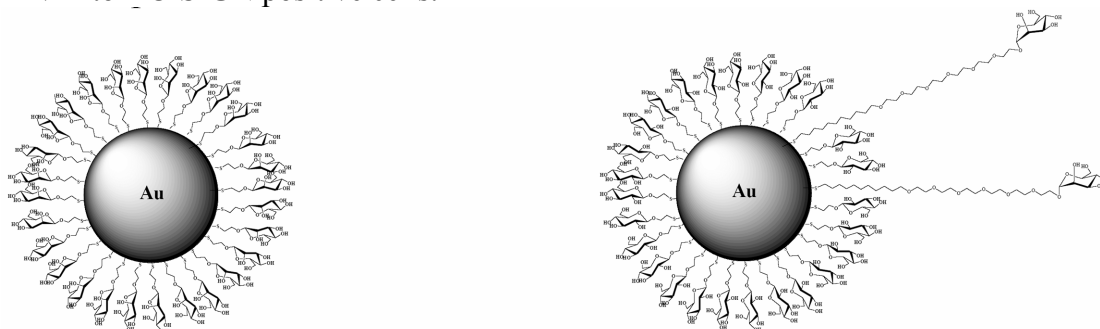
## GOLD MANNO-NANOPARTICLES AS TOOLS TO UNDERSTAND INTERACTIONS BETWEEN gp120 AND DC-SIGN RECEPTOR

Olga M. Martínez-Ávila, Caroline J. Clavel\*, Soledad Penadés

*Grupo de Carbohidratos. Instituto de Investigaciones Químicas, CSIC, C/Américo Vespucio 49, 41092 Sevilla, SPAIN*  
*caroline@iiq.csic.es; penades@iiq.csic.es*

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. The latter specifically recognizes oligomannosides through protein-carbohydrate interaction. Previous work has shown that GlcNAc<sub>2</sub>Man<sub>3</sub> pentasaccharide is able to inhibit the interaction between the gp120 and the DC-SIGN receptor<sup>1</sup>. Nevertheless since this inhibition is of low affinity the design of better inhibitors is of significant value. One possible strategy to enhance affinity between ligand and receptor is to introduce multivalency. For this reason we decided to use glyconanoparticles (GNPs), which are sugar-functionalised gold nanoclusters with a 3D polyvalent carbohydrate display presentation and globular shape<sup>2</sup>. Preparation and characterization of GNPs by analytical techniques (TEM, AFM, NMR, microanalysis...) <sup>3</sup> have recently been developed in our laboratory. These GNPs are highly soluble under physiological conditions, stable against enzymatic degradation and non-toxic. Lactose nanoparticles have been shown to inhibit the metastasis of melanoma cell in mice<sup>4</sup>.

We have now prepared new water-soluble gold glyconanoparticles by coupling thiol-functionalised mannose glycoconjugates to the gold cluster, in order to intervene in the HIV/cell adhesion process. The neoglycoconjugates were synthesized attaching the mono-, di- or tri- mannosides to a linker. Different types of linkers, in terms of length and nature (aliphatic or aliphatic/ethylene glycol-mixed chains) have been used. The resulting ligands have been incorporated with varying densities between 5 and 100% at the surface of the gold nanocluster as shown below. The glyconanoparticles have all been characterized by NMR, microanalysis and TEM. Preliminary results indicate that mannose nanoparticles are able to inhibit the binding between the whole HIV-1 to DC-SIGN positive cells.



*Gold mannonanoparticles with different linkers and different densities.*

<sup>1</sup> H. Feiberg et al. *Science*, **2001**, 294, 2163-2166.

<sup>2</sup> J.M. de la Fuente et al. *Angew. Chem. Int. Ed. Engl.*, **2001**, 40, 2258-2261

<sup>3</sup> S. Penadés et al. *Chem.Eur. J.*, **2003**, 9, 1909-1921.

<sup>4</sup> J. Rojo et al. *ChemBioChem.*, **2004**, 5, 291-297.