Gold nanoparticles capped with mannose glycans block HIV-1 gp120 binding to antibody 2G12 as studied by means of NMR and SPR techniques.

P.M. Enriquez-Navas[1], *P. Di Gianvincenzo*[1], *M. Marradi*[1], *O. Martínez-Avila*[1], *J. Angulo*[2], *S. Penadés*[1]

[1]*CIC-biomaGUNE/CIBER-BBN, Paseo Miramón 182, Parque Tecnológico, E-20009 San Sebastián, Spain.*
[2]*Instituto de Investigaciones Químicas (IIQ-CSIC) C/Américo Vespucio 49, E-41092 Sevilla, Spain.*
spenades@cicbiomagune.es

The human immunodeficiency virus (HIV) uses its envelope glycoprotein gp120 in the initial steps of infection. The immune system raises antibodies against it as a defensive mechanism. Human antibody 2G12 neutralizes a broad range of human immunodeficiency virus type 1 (HIV-1) isolates by binding an unusually dense cluster of carbohydrate moieties (*high-mannose* glycans) on the "silent" face of the virus envelope glycoprotein gp120.[1] Crystallographic studies revealed that 2G12 is highly specific for terminal Manα1→2Man of the glycans present in the gp120 [1,2]. 2G12 is one of the few monoclonal antibodies (mAb) able to neutralize a broad range of HIV-1 primary isolates. Understanding the atomic contacts that the antibody 2G12 makes to neutralize the virus is essential for the correct design of vaccines against HIV.

To understand better the molecular mechanism of HIV interactions, we have prepared gold glyconanoparticles that present oligomannosides (*manno*-GNPs) in a multivalent way in order to mimic the *high-mannose* clusters on gp120. [3] Previously, we have characterized the interactions between 2G12 and synthetic oligomannosides, which are structural motifs of the natural *high-mannose* of gp120. Using a new STD NMR protocol and theoretical calculations we have determined the minimum structural requirement for maximum affinity to 2G12 to be a trimannoside (Manα1→2Manα1→2Man). Based on these results, multivalent oligomannoside functionalized gold nanoclusters (glyconanoparticles) have been synthesized pursuing to improve the affinity of these monovalent ligands as multivalent ligands.

In the present work, we study by NMR the affinities of these glyconanoparticles towards 2G12 in solution. Their interactions with the antibody are compared to that of the monovalent ligands by competition STD NMR experiments. The binding of the GNPs to the 2G12 and the potency of *manno*-GNPs to inhibit the binding of gp120 to 2G12 were also studied by using Surface Plasmon Resonance (SPR) technology. NMR and SPR techniques identify the best multivalent *manno*-GNP inhibitor. The enhancement of the affinity observed for the *manno*-GNPs related to the monomeric oligomannosides due to the so-called *cluster effect* will be discussed.

References:

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