GLYCO-GOLD NANOPARTICLES DECORATED WITH IMINOSUGARS AS MULTIVALENT ENHANCERS OF GCASE ENZYME

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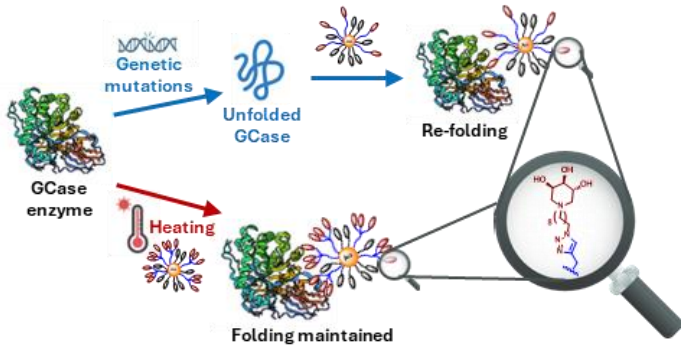
The lysosomal enzyme β-glucocerebrosidase (GCase) hydrolyses the glucosyl moiety of glucosylceramide and glucosylsphingosine. GCase defective activity is involved in the metabolic disorder Gaucher Disease and, more recently, emerged to be correlated also with Parkinson's disease [1]. Therefore, functional GCase enhancers may act as new therapeutics for such pathologies, both lacking disease-modifying drugs.
In this context we report the first multivalent iminosugars (namely, *N*-heterocyclic sugar analogues) built onto a glyco-gold nanoparticle core (glyco-AuNPs) capable of stabilizing or enhancing the activity of GCase. An *N*-nonyltrihydroxypiperidine was selected as the bioactive iminosugar unit and further functionalized, via copper catalysed alkyne-azide cycloaddition, with a thiol-ending linker that allowed the conjugation to the gold core. The bioactive ligands were obtained with either a linear monomeric or a dendritic trimeric arrangement of the iminosugar. The concentration of the bioactive iminosugar on the gold surface was modulated with different amounts of a glucoside bearing a short thiol-ending spacer as inner ligand. The new mixed-ligand coated glyco-AuNPs were fully characterized with different techniques (UV-vis, TEM, ^{1}H-NMR). The biological evaluation suggested a different behaviour in stabilizing wild-type recombinant GCase or mutant GCase from Gaucher Disease patients' cells depending on the iminosugar presentation (e.g. linear vs branched ligand) [2].



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2. F. Buco, F. Clemente, A. Morrone, C. Vanni, S. E. Moya, F. Cardona, A. Goti, M. Marradi, C. Matassini, *Bioconjugate Chem.* **2025**, *36*, 92-103.