Atomically precise gold nanoclusters stabilised by multivalent peptide with enhanced cell penetrating properties

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Gold nanoclusters (Au NCs) are atomically precise nanoparticles, composed of few to hundred atoms with sizes between 0.2 and 2 nm. Most of the Au NCs are commonly prepared by wet chemistry using stabilizing agents such as thiol molecules or biomolecules (peptides, proteins). These species exhibit molecular-like properties, with the emergence of tunable photoluminescence signal highly dependent on the core structure and the nature of the ligand. Due to their ultra-small size, surface easy to functionalize and fluorescence in the near-infrared region, Au NCs have been recently developed for biomedical applications such as tumor diagnostic and imaging.

Even if a large library of biocompatible Au NCs, mainly Au NCs stabilized by the peptide glutathione (AuₙSGₘ with n =15, 22, 25, 38),³ have shown cellular internalization in various types of cells, their uptake efficiency still remains quite weak. To overcome this issue, it is relevant to develop new atomically precise Au NCs able to be rapidly internalized into the cells. In the literature, arginine peptides are often used as cell-penetrating peptides. Indeed, at physiological pH (7.4) the positive guanidinium moiety interacts with the negatively charged proteoglycans and phosphate groups on the cell membrane. This strong interaction is also reinforced by hydrogen bonds and Van der Waals forces.⁴

We therefore developed a set of Au NCs stabilized by arginine modified-glutathione peptides with one, two or three arginines and evaluated the impact of these modifications on cell membrane interaction and cellular uptake. Optical and physio-chemical properties of these Au NCs were fully characterized and we confirmed their ultra-small size, good colloidal stability and their intense fluorescence in the red-near-infrared window. In vitro studies were performed using a human melanoma cell line (Colo 829). Results obtained by flow cytometry indicated that Au NCs stabilized by glutathione-arginine interacted more efficiently with cells than Au NCs stabilized by glutathione only. Kinetic of cell internalization was evaluated by confocal fluorescence microscopy and their absence of cellular toxicity was also monitored. Based on the results, we believe that these Au NCs are interesting optical probes that could also serve as drug delivery systems. Au NCs are thus promising theranostic compounds that should be further evaluated in vivo for cancer diagnostics and therapy.

References


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