Customized peptide stabilized gold nanoclusters as cellular bioprobes

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Abstract

Gold nanoclusters (AuNCs) are atomically precise nanoparticles, composed of few to hundred atoms with size 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).[1] Those species exhibit molecular-like properties, with the emergence of tuneable photoluminescence signal highly dependent on the core structure and the nature of the ligand. Due to their ultra-small size, surface easily to functionalize and photoluminescence in the near-infrared region, Au NCs have been recently developed for biomedical applications such as tumour diagnostic and bioimaging.[2]

Even if a large library of state Au NCs with the example of Au NCs stabilized by the peptide glutathione (Au_nGSH_m with n =15, 22, 25, 38)[3] have shown cellular internalisation in various types of cells, their uptake efficiency remains quite weak. To go further and overcome this issue, it is relevant to develop new atomically precise Au NCs able to be rapidly internalised into the cells. In literature, arginine containing peptides are often used as cell-penetration peptides. Indeed, at physiological pH (7.4) the positive guanidinium moiety interact 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 chose to synthesize highly photoluminescent Au NCs stabilized by arginine modified-glutathione peptides (GSH-Arg) in order to enhance membrane penetration and accumulation of Au NCs in cells. After the characterization of Au NC optical and physio-chemical properties, cell experiments were designed using human embryonic kidney cell lines (HEK β3) with Au NCs protected by GSH or by GSH-Arg at different particle concentration and at short incubation time (1 hour in DMEM+10%FCS). Preliminary results obtained by fluorescent microscopy and by flow cytometry indicated a faster and higher uptake of Au NCs-GSH-Arg than Au NCs-GSH with no apparent signs of cytotoxicity. At this stage, we believe those new Au NCs could be an interesting optical bioprobe used as fluorescent tag for drug therapy and for fundamental study of cell biology.

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