Controlling hydrophobicity and self-assembly of gold nanoclusters for cellular delivery

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Gold nanoclusters (Au NCs) are metal particle composed of ten to hundred atoms (~1-3 nm) that exhibit molecular-like properties in this ultra-small size regime. Their physico-chemical properties are highly driven by the nature of the protective ligands stabilizing the metal core in solution. Thanks to their photoluminescence in the visible and in the near-infrared region and to the ability to finely control their surface chemistry, Au NCs have found a growing interest in the field of nanomedicine. Au NCs could be seen then as potential theranostic agents combining delivery capacity and bioimaging features.

In this context, we design two different types of Au NC systems for cellular delivery: i) one based on Au NCs with a precise control of his hydrophobicity to enhance the cell internalization, and ii) a second one made of a 100 nm spherical self-assembled Au NCs to deliver biomolecules in cells.

Hydrophobicity of monodisperse Au NCs could be tuned during the synthesis using custom-made thioctic sulfobetaine molecule with an increased of alipathic chain length. Microscopic and physico-chemical characteristics confirm the ultra-small size of the metal core and the influence of hydrophobicity to reduce protein absorption on the particle surface. Optical characterization show an enhancement photoluminescence intensity with the hydrophobicity which could either associated to better protection of the “gold(I)-thiolate binding” to water molecules or to an increase in the rigidity of the network enabling a more efficient metal-ligand energy transfer. Studies performed on artificial phospholipid membranes integrated in microfluidic device and on various cell lines stress the importance to finely tune the hydrophobicity balance of Au NCs in order to improve the penetration on cell surface without inducing cytotoxicity.

Self-assembly of Au NCs were produced in a fast and simple approach using cationic polymers as cross-linkers. Monodisperse spherical self-assembled Au NC with pH dependent swelling properties was then used as a model system to investigate aggregation induced fluorescence enhancement mechanism as a function of the distance between Au NCs. Our observations suggest that Au NC cross-linking has a strong effect on the ligand-to-metal charge transfer and both radiative and nonradiative recombination rates of charge carriers could be responsible of the QY enhancement. With the use multimodal imaging techniques it was also demonstrated the ability to load these self-assembled Au NCs with biomolecules (peptide, antibody) with a more efficient cell uptake than the free biomolecules.

These studies demonstrate then the versatility of metal nanoclusters to design smart nanosystem and open new opportunities for therapy and diagnosis.

References