Luminescent gold nanoclusters for extracellular vesicles, cellular labelling and biosensing

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Gold nanoclusters (AuNCs) appear as a recent class of non-toxic fluorophores. Their brightness, ultrasmall size (< 2 nm), large window of fluorescence lifetime (1ns – 1µs) and good biocompatibility make them an attractive alternative as fluorescent probes for biological labeling and bioimaging. We developed a chemical platform providing various charged AuNC with potential sensitivity to the environment for biosensing and bioimaging applications.

The extracellular vesicles (EVs) are well-known membrane-limited particles that are secreted by healthy and cancerous cells. EVs are identified in human follicular fluid as a mode of communication in the ovarian follicle [1]. In addition, EVs involved in cell-cell communication are considered as biomarkers for early cancer diagnosis. The analysis of their content and their labeling with easily detectable nanoparticles could enable the development of a powerful tool for the early diagnosis of specific diseases.

Therefore, we investigated the interaction between ultrasmall luminescent gold nanoclusters and lipidic or biological extracellular vesicles (EVs). As opposed to larger gold nanoparticles, the smaller size of AuNCs not only prevents the deformation of biological membranes but also allows labeling with higher spatial resolution [2].

By adjusting the surface ligands, these nanoprobes are easily internalized into cells and in vivo organisms such as Arabidopsis plant or cancerous cell lines. We demonstrated their in vivo targeting ability because of specific recognition groups [3] and biosensing by fluorescence because of their sensitivity to microenvironment.

The ultra-small size of AuNCs make them attractive to encapsulate them into liposomes without damaging the compartment integrity and then to be delivered into the extracellular vesicles. We demonstrated first the encapsulation of the AuNC into liposomes for drug delivery. Exosome-like-sized vesicles (LUVs) containing Au NCs were obtained with an encapsulation yield of 40%, as estimated from ICP-MS [4]. Finally, the composition of the liposome membrane was optimized to induce their fusion with EVs evidenced by flux cytometry and croyTEM (Submitted paper). The fused EVs encapsulating the AuNC were successfully separated by size exclusion chromatography. Such nanostructures offer promising candidates for fluorescent in vivo biosensing and biolabeling.

References

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Biography:

Valérie Marchi received her engineer diploma in Physical Chemistry from the Ecole Supérieure de Physique et Chimie Industrielles (ESPCI, Paris, France) in 1994. She acquired an expertise in Supramolecular Chemistry and Organized Soft Matter during her Ph.D (supervised byProf J.-M. Lehn,Collège de France, Paris). After postdoctoral researchin the laboratory of Biophysik (Prof. E.Sackmann, TUM Munich, Germany)and in Fukuoka (Prof T. Kunitake, Japan),she joinedthe laboratory of Prof J.-M.Lehn as research associateat the CNRSin1998. She moved to theUniversity Rennes in 2004 to developher research groupin the field of nanoparticlesand Organized Soft Matterfor: i) targeting and modulation of the self-assembling of proteins,ii) gold nanorods or quantum rods structured assemblies, iii) photoelectrochemical activation of biocatalysts. She focuses currently on the optical properties of nanostructured materials for biosensing and bio-imaging including original bioactivated gold nanoclusters.