

## Designing inorganic nanoparticles for biotechnological applications

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In the last decades, inorganic nanoparticles have been steadily gaining more attention from scientists from a wide variety of fields such as material science, engineering, physics or chemistry. The very different properties compared to that of the respective bulk, and thus intriguing characteristics of materials in the nanometre scale, have driven nanoscience to be the centre of many basic and applied research topics. Moreover, a wide variety of recently developed methodologies for their surface functionalization provide these materials with very specific properties such as drug delivery and circulating cancer biomarkers detection. In this talk we describe the synthesis and functionalization of magnetic and gold nanoparticles as therapeutic and diagnosis tools against cancer:

-Pseudo-spherical gold nanoparticles derivatized with with fluorescent dyes, cell penetrating peptides and small interfering RNA (siRNA) complementary to the proto-oncogene myc have been tested using a hierarchical approach including three biological systems of increasing complexity: *in vitro* cultured human cells, *in vivo* invertebrate (freshwater polyp, *Hydra*) and *in vivo* vertebrate (mouse) model. Selection of the most active functionalities was assisted step by step through functional testing adopting this hierarchical strategy.<sup>1</sup> Merging these chemical and biological approaches lead to a siRNA/RGD gold nanoparticle capable of targeting tumor cells in lung cancer xenograft mouse model, resulting in successful and significant c-myc oncogene downregulation followed by tumor growth inhibition and prolonged survival of the animals.<sup>2</sup>

-Gold nanoprisms (NPRs) have been functionalized with PEG, glucose, cell penetrating peptides, antibodies and/or fluorescent dyes, aiming to enhance NPRs stability, cellular uptake and imaging capabilities, respectively.<sup>3</sup> Cellular uptake and impact was assayed by a multiparametric investigation on the impact of surface modified NPRs on mice and human primary and transform cell lines. Under NIR illumination, these nanoprobe can cause apoptosis. Moreover, these nanoparticles have also been used for optoacoustic imaging,<sup>4</sup> as well as for tumoral marker detection using a novel type of thermal ELISA nanobiosensor using a thermosensitive support.<sup>5</sup>

-Magnetic nanoparticles functionalized with DNA molecules and further hybridizing with different length fluorophore-modified DNA have allowed the accurate determination of temperature spatial mapping induced by the application of an alternating magnetic field.<sup>6</sup> Due to the design of these DNAs, different denaturalization temperatures (melting temperature,  $T_m$ ) could be achieved. The quantification of the denaturalized DNA, and by interpolation onto a Boltzmann fitting model, it has been possible to calculate the local temperature increments at different distances, corresponding to the length of each modified DNA, from the surface of the nanoparticles. The local increments achieved were up to 15°C, and the rigidity conferred by the double strand DNA allowed to evaluate the temperature at distances up to 5.6 nm from the nanoparticle surface.

### References

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