

## **Design and characterization of polymer-coated nanoparticles for bio-medical applications**

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Over the last two decades, the use of nanomaterials for medical applications has gained significant popularity from basic to applied research. More specifically, nanoparticles with tunable properties (*e.g.* plasmonic and magnetic behavior) possess the fascinating ability to convert radiation energy into heat, a feature of highly applicative interest in nanomedicine. In this context, nanoparticle surface functionalization with specific bio-compatible polymers containing precise chemical moieties (*e.g.* catechols, thiols and amines) enables a fine tuning of both, heat generation and their ultimate fate *in-vitro*. The core emphasis of this thesis relies on synthesizing such nanoparticles as well as characterizing their magneto-thermal signature and their behavior and interactions in biological milieu.

The synthesis of a well-defined catechol-poly(vinyl alcohol) coating polymer promotes long-term water stability and assists the formation of water-dispersible magnetic nano-clusters. The core size as well as the spacing between nanoparticles inside the cluster affects the magnetic properties and impact the energy conversion into heat. These findings led to the elaboration of a mathematical model suggesting that the linear response theory and the Stoner-Wohlfarth model could be unified. Moreover, a systematic investigation into the role of amine type (*i.e.* primary, secondary, or tertiary) on both proteins adsorption and subsequent cellular association revealed that four most significant differing proteins accounted for the amine bulkiness (*i.e.* serum albumin, alpha-2-HS-glycoprotein, hemoglobin subunit alpha and beta) play a major role in the nanoparticle-cell interaction. More specifically, primary amines on the particle surface were strongly correlated to the presence of alpha-2-HS-glycoprotein (Fetuin A) and promote cellular association. The current surface charge paradigm regarding nanoparticle-cell interactions has been reconsidered to a more confined surface parameter (*i.e.* the amine bulkiness). Finally the stability of the catechol group toward iron oxide surface was found to be altered in lysosomes. It was shown that the coating polymer containing primary amines, detached from the nanoparticle surface and ended-up in the cell nucleus while the iron oxide core remained in lysosomes. These findings suggest the formation of a polyplex occurring during the cell differentiation. Amino catecholic poly(vinyl alcohol) iron oxide nanoparticles have potential as DNA targeting technologies. Moreover, the iron oxide core suspected to dissolve in lysosomes might be recycled similarly to ferritin which in turn, would avoid nanoparticles accumulation. This thesis gives an insight in the rational design of functional nanomaterials and paves the way for the development of drug delivery systems

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