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Effect of coating in opsonisation process and cellular uptake of iron oxide nanoparticles

L. Lartigue,[1] N. Luciani,[1] A. Dencausse,[2] C. Factor,[2] C. Wilhelm,[1] F. Gazeau[1]
[1] *Laboratoire Matières et Systèmes Complexes (MSC), UMR 7057 CNRS/Université Paris - Diderot, Paris, France.*
[2] *Entreprise Guerbet, 16-24 rue Jean Chaptal, 93600 Aulnay-sous-Bois, France.*
E-mail : lenaic.lartigue@univ-paris-diderot.fr

Abstract:

Nanoparticles (NPs) in living organism interact with biomolecules (proteins, natural organic materials, detergents, and enzymes), forming a “bio-nano interface”.**[1]** At this interface, a dynamic exchange with biomolecules created a “protein corona”, influencing both the surface state and the local organization of nanoparticles.**[2]** The covering of the nanoparticles surface with protein (a process called opsonization) is governed by the intrinsic characteristic of the nanomaterial (size, shape, charge, coatings…).

Therefore what the cells see when presenting the nanoparticles can be very different from the initial state of NPs. The way cells interact with, recognize and process the nanoparticles will depend on their interactions with plasma proteins (a process called opsonization), with crucial implications for the practice of nanomedicine. For superparamagnetic MRI constrast agent, both the MR relaxivities and pharmacokinetics will be sensitive to opsonization. Quantitative methods are therefore needed to probe the binding dynamics of proteins on nanoparticles and its effect on macrophage uptake. In this work, we developed a specific method to quantify the protein corona on magnetic nanoparticles and its effect on colloidal stability. In a second step, we investigated the impact of the protein corona on the nanoparticles internalization in macrophage.

The optical birefringence induced by an external magnetic field in a suspension of magnetic nanoparticles results from the alignment of their magnetic moments and the associated optical axes along the field.**[3]** The birefringence relaxation in zero field follows a stretched exponential law, $I(t)/I_0 = \exp(-t/\tau)^{\alpha}$, reflecting the hydrodynamic radius of the nanoparticles protein complexes. The kinetics of protein binding and complex size was quantified for iron oxide nanoparticles (8 nm) with different surface coatings, incubated in rat plasma (1%, 10%, 20%, 50% or 100% in volume) or albumin (0.1, 0.5 or 1 mM). Thus these complexes were incubated with macrophages derived from THP-1 cells and the cellular uptake was quantified by magnetophoresis.

We observe different behaviors depending on the initial surface coating of nanoparticles: NPs with a glucose derivative ligand interact very weakly with blood proteins conserving a remarkably good dispersion in plasma. By contrast, the strong interactions of citrate-coated NPs with proteins yield to two populations of NP-protein complexes, one with good dispersion and the other with an aggregated state. Remarkably, the nature of complexes affects their uptake by THP-1–derived macrophages.

We demonstrate quantitatively that the nanoparticle's coating plays a significant role in the opsonization process**.** Moreover, we show that the protein corona and the colloid stability are two important factors in the nanoparticles uptake by macrophages. In conclusion, this work opens new windows for understanding of the nanoparticles becoming in vivo after their subsequent opsonisation.

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