Short, long term fate and biodegradation of IONPs in vivo.

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Once a nanoparticle (NP) is administered *in vivo*, it interacts with components of a physiological environment what results in a formation of so called biomolecule corona.[1] Surrounding the NP corona is mostly composed of proteins (hence the protein corona (PC) definition) and it can dramatically change the nanomaterial size, aggregation state and interfacial properties.[2] As a result NP acquires a new biological identity that would dominate the behaviour of NPs *in vivo*.[3,4] Therefore, investigation of the PC is a benchmark in understanding and controlling NPs performance *in vivo*. Moreover, long term studies encompassing the whole NP lifecycle are necessary to clarify the fears concerning NPs safety. Thoroughly, unravelling of the interactions of commonly known nanomaterials with living organisms could diminish the huge discrepancy between the produced numerous nanoscale size therapeutics and scarce clinical outcomes.

Here we report the effect of the superparamagnetic iron oxide NPs (IONPs) surface modification with two hydrophilic molecules, either glucose (glc) or poly(ethylene glycol) (PEG), on protein adsorption, NPs fate and their biotransformation over 4 months. Although NPs@Glc and NPs@PEG bound similar amount of proteins *in vitro*, the differences found in the composition of both PCs corresponded to the NPs biodistribution *in vivo*. Whereas NPs@Glc were mostly accumulated in the liver and spleen, NPs@PEG were detected in various organs, including thymus or reproductive system organs. Moreover, by employing magnetic measurements we have found, that the biodegradation kinetic and therefore clearance of both NPs types was unequal. 4 months after the administration, NPs@PEG suffered a complete disaggregation and/or reduction of size, and were totally removed from the spleen, but not from the liver. On the other side, NPs@Glc clearance kinetic was higher in the liver than in the spleen, albeit here the degradation of the NPs in both organs was only partial. Interestingly, degradation tested *in vitro* was faster for NPs@Glc than for NPs@PEG demonstrating that the attached molecule is implicated in the protection against degradation in NPs with the same core-shell structure. The variation in the degradation rate observed *in vivo* could be therefore related not only with the attached molecules, but also with the associated PC, which composition may directly affect the degradation rate by lysosomal enzymes or indirectly by driving NPs accumulation in different cells.

References

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