ESF – Short Visit Grant – Applicant: Daniele Dell'Orco

Scientific Report

Project: Biophysical strategies to study the interaction of peptide-covered nanoparticles with cellular targets: preliminary *in vitro* and computer simulation results

Background and motivation

Proteins, lipids, and carbohydrates found in any biologic fluid interact with nanoparticles, thus creating a complex corona around the particle surface. The composition and characteristics of this corona is determined by the particle surface and the chemical nature of the surroundings. The corona is dynamic in its nature and the proteins undergo continuous association/dissociation processes at characteristic rates, until equilibrium is reached [1]. Experimental evidence showed that very abundant biomolecules bind at first, but they are subsequently replaced by less abundant biomolecules with higher affinity [1-3]. Such behavior has been recently rationalized and quantified by mathematical modeling [4]. The detailed study of the nanoparticle-protein corona has opened new challenges and question as on the next investigations to be performed, especially toward the characterization of nanotoxicity of such systems.

In a former meeting that took place in Lund, the applicant and his co-workers discussed some possible experimental and computational strategy to investigate the effect of the corona on the delivery of specific nanoparticles modified according to some selective target-receptor interaction to occur. The present visit focused on the possibility to perform the analysis of the first data obtained in the context of the results of simulations.

Project outcome

The influence of peptide (or other specific ligand)-covered nanoparticles on selected biochemical pathways, which are normally triggered by the interaction of peptides with cellular targets is a novel and promising field in nanotoxicity and nanobiomedicine. In order to achieve successful delivery of engineered nanoparticles into a biological compartment it is fundamental to quantitatively understand how the interaction between peptides/ligands and targets is influenced by the nanoparticle and its dynamic nature.

During the visit the results from preliminary computer simulations of the same interactions have been presented to the team in Lund and discussed in the light of the recent experimental findings obtained there. A comparison between the data collected and the simulation outcome was made, finding general consistency, thus pointing out the difficulty of achieving successful delivery rate in the presence of the corona that competes, in terms of nanoparticles surface, with selected targets. In detail, an estimate of the delivery success rate of the peptide toward its receptor as a function of some measurable parameter, such as the receptor size, the association rate constant (related to the diffusion of the nanoparticle-bound peptide) and the affinity for the receptor was assessed from numerical simulation. This computational investigation was found to provide a range of conditions that are experimentally testable and would help to optimize the delivery of the nanoparticle-bound peptides in the presence of corona-forming proteins. The team plans to present the outcome of simulations and experiments in a scientific article.

References

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4. Dell'Orco D, Lundqvist M, Oslakovic C, Cedervall T, Linse S. (2010) PLoS One 3;5(6):e10949