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Proteins adsorption upon nanoparticles: from the physicochemical basis to the functional impacts

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The production and utilization of nanoparticles has been strongly increasing over the last decades, raising concerns regarding their biological effects and health hazards. Due to their nanometric size, nanoparticles have two major properties, (i) a high specific surface and (ii) the ability to cross biological barriers. Thus, they can interact with a large amount of biological compounds (especially proteins) and impact biological processes.
We study adsorption of proteins on silica nanoparticles (SiNP). We used yeast protein extracts in order to assess which kinds of proteins tend to adsorb on SiNP and which do not. Using proteomics (mass Spectrometry Shotgun analysis), we identified several hundreds of adsorbed and non-adsorbed proteins. The statistical comparative analysis of these two sets of proteins revealed the physicochemical determinants relevant for adsorption: the overrepresentation of arginine residues and of large disordered regions, as well as an impoverishment in secondary structures and hydrophobic aminoacids. These results are consistent with the notion that disorder and flexibility favor protein adsorption.
Using GO term analysis, we also evidenced that RNA binding proteins have a marked affinity for SiNP. We selected one of them, NPL3, a protein carrying poly(A) mRNA from nucleus to cytoplasm. We constructed two truncated mutants fused to GFP (see figure) and found that the C-ter region of NPL3 containing several repetitions of the Arg-Gly-Gly (RGG) motif is responsible for the high affinity of the protein for SiNP.
In vivo, the Arg residue of RGG motif is frequently dimethylated. We synthesized peptides (25-mer) containing RGG repetitions and some versions where Arg residues were dimethylated. The data indicate that Arg dimethylation significantly increases the affinity of the peptides for SiNP. We are currently planning to use calorimetry with these peptides in order to assess if the adsorption process, in these cases, is entropy or enthalpy driven.
Our data opens the way for predicting potential biological impacts of nanoparticles.