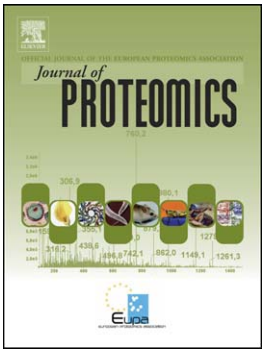

An environmental route of exposure affects the formation of nanoparticle coronas in blood plasma

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An environmental route of exposure affects the formation of nanoparticle coronas in blood plasma

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Nanoparticles (NPs) in contact with biological fluids become covered by a tightly bound layer of proteins, the "protein corona", giving a new biological identity to NPs as the cell machinery can engage with the coated surface differently than with the bare one. We here consider the scenario that exposure to nanoparticles occurs through an environmental route, exemplified by using hydrophobins, fungal proteins that are highly adhesive and secreted into the environment in large quantities by fungi. The highly secreted hydrophobin, HFBII of *Trichoderma reesei* is used as a model. In this work we have used a strategy to coat and characterize nanoparticles of different size and surface modification. Hydrophobin coated nanoparticles of varying size and surface modification are shown to strongly increase stability and dispersion of the NPs in human plasma compared to pristine particles. It is also shown that the presence of hydrophobin on the NPs results in a decrease of layer thickness and a change in composition of the protein corona, and that the hydrophobin remained strongly associated to the NPs in competition with plasma proteins. As a conclusion we therefore suggest that the route of exposure of nanoparticles strongly affect their surface properties and possible physiological behaviour**.**

Keywords

Nanoparticle hydrophobin corona DCS

Significance

This work shows how a self-assembling protein, class II hydrophobin HFBII, with interesting biocompatible coating properties, strongly adsorbs on polystyrene nanoparticles. HFBII is also shown to reduce aggregation of the NPs in human plasma which can increase bioavailability of NPs with potential use in biomedical applications. The results here are also of significance for understanding possible interactions of NPS with living organisms. Hydrophobins are secreted in large quantities into the environment by fungi and this work shows how the biological environment of NPs determines the surface and colloidal properties of the particles by forming a protein corona, and that the history of the particle environment, here simulated with hydrophobin exposure, affects both plasma protein corona formation and dispersion behaviour. This work thus simulates how alternative exposure routes affect nanoparticle properties, important in understanding the biological fate of NPs.

Introduction:

Nanoparticles (NPs) have found an increased use in the medical and industrial field with the result that environmental exposure of NPs is largely increasing [1,2]. The fate and transport of NPs through the environment is affected by different biomolecules adsorbing onto the NP surface which may alter the NP identity and following toxicity and interactions with organisms[3,4]. NPs in contact with biological fluid such as human plasma or serum have been shown to be covered by a tightly bound layer of proteins, the "protein corona"[1-10]. Human plasma contains about 4000 different proteins, whose abundance varies in the range of more than ten orders of magnitude[11], and only few tens of these proteins, that are rarely the most abundant ones, are predominantly associated with forming a strongly bound protein corona on nanoparticles, the "hard corona (HC)"[12-17]. While an external layer of proteins with less affinity (the "soft corona"[1]) will be in exchange with the environment [18] the proteins forming the hard corona are so strongly bound that they are in slow exchange[7]. In this work we use the concept of *in situ* corona (IS) to describe a corona that is analysed in the context of the environment were exposure occurs, in this case blood plasma. The HC in contrast is analysed by separating and washing the NPs from the unbound and loosely bound proteins which can be found in the media that they were exposed to. The importance of the corona proteins relies on the fact that the cellular machineries engage with the protein corona directly rather than with the pristine surface of