Accessing the Nanoparticle Corona in Pulmonary Surfactant

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Abstract

Nanoparticles (NP) that come in contact with a biological fluid are opsonized by biomolecules such as proteins, which build a "corona".
This time-dependent layer of adherent biomolecules typifies the actual biological identity of the NP. Considering the many different NP with varying surface modifications which are produced worldwide, differences in resulting corona seem plausible and were identified in the coronas on NP in plasma [2, 3]. An attractive pharmaceutical target for various nanoparticles is the lung, as the air-blood barrier is a less than 2 µm thin layer with an enormous alveolar surface area larger than 100m^2. The vast amount of potentially polluted air, which passes through the lung, makes an effective maintenance system essential. In the alveolar region cells are only covered by a thin pulmonary surfactant (PS) layer and clearance is mainly carried out by alveolar macrophages. PS, secreted by type II alveolar cells, allows gas diffusion and its surface tension lowering effect is thus essential for stability of the alveoli during a breathing cycle. The surfactant layer consists of approximately 90% lipids (mainly phospholipids, especially DPPC) and 10% proteins with about half of them being surfactant specific proteins (SP). Before NP are either taken up by the alveolar cells or ingested by macrophages, they are coated by the PS building a lipid-protein-"corona".
So far, it remains to be elucidated whether the fate of inhaled NP depends on the coating obtained from the surfactant layer, though there is evidence for the influence of the SP on macrophage uptake [1]. Although understanding the surfactant-NP interaction is fundamental for the fate of NP in the lung, there is, so far, no reproducible method for the analysis of the NP-corona.

The unique composition, structure, and properties of the lipid-rich PS require different and more advanced analytical methods for the assessment of the NP-corona in the deep lung.
Hence, we used a native pulmonary surfactant preparation, isolated from porcine lungs, for the development of a method to access the lipid-protein-corona. Centrifugation, magnetic separation and density centrifugation were compared with three magnetic model particles (Phosphatidylcholine-, PEG-coated, and plain PLGA). Magnetic separation of NP was found to be superior to the other common techniques.
SDS-PAGE showed the impact of hydrophobicity on the PS corona and was verified by advanced label-free proteomics.

References

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Graphical Abstract