# A disease-focussed approach in understanding pulmonary biomolecule corona

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Pulmonary delivery of therapeutics, e.g., biologics, antibiotics and chemotherapeutics is an attractive strategy to provide localised treatment for diseases such as lung cancer and chronic obstructive pulmonary disorder (COPD). However, upon inhalation, nanoparticles strongly interact with proteins and surfactant lipids found in the lungs to form a biomolecule corona. In the context of systemic administration, it is well established that the biomolecule corona mediates subsequent cellular interaction and biological response, although this is still underdefined for pulmonary delivery. We previously have shown the structure and composition of lipid-based nanoparticles to significantly alter the protein corona formed, resulting in varied cellular uptake profiles[1]. An albumin rich corona impaired the internalisation of liposomes across epithelial and macrophage cell line, while presence of apolipoprotein H (ApoH) on liquid crystalline lipid nanoparticles resulted in an enhanced cellular uptake. While these findings provided fundamental evidence for the formation and influence of a pulmonary biomolecule corona, they do not provide an accurate representation of the fate of nanoparticles in a diseased state. To understand this, bronchoalveolar lavage fluid (BALF) from COPD and lung cancer in vivo models were harvested and analysed for differences in protein and lipid composition compared to healthy BALF. Conventional liposomes were incubated with the different types of BALF and changes in formation of biomolecule corona were investigated using label-free proteomics approach. Further, structural changes to the liposomes upon contact with biomolecules were examined using the biological small angle X-ray scattering beamline (BioSAXS) at the Australian Synchrotron. Following this, liposomes in presence of biomolecules were examined for their cellular internalisation kinetics in A549 epithelial cells and RAW264.7 macrophages, providing a comprehensive understanding on the biological fate of pulmonary nanomedicine. This study highlights the importance of evaluating performance of nanoparticles in an environment closely mimicking the target disease, improving design of future pulmonary drug delivery systems, while facilitating clinical translation of promising approaches.

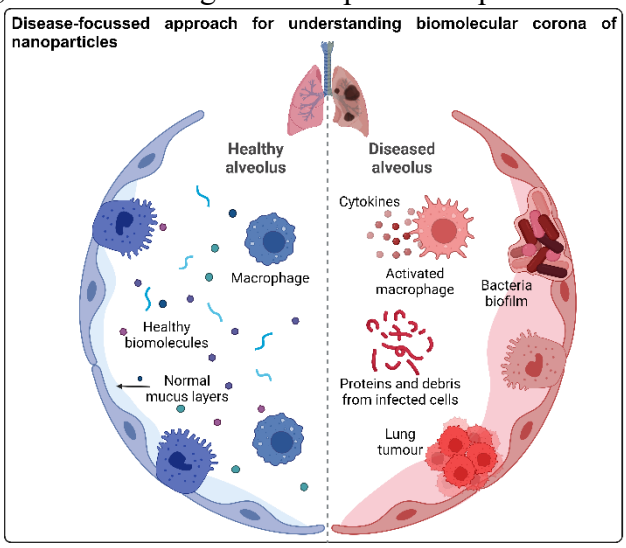


**Figure 1:** Schematic illustrating the differences in biomolecule composition of lungs in a healthy versus diseased state[2].

**References:**
[1] Subramaniam, S.; et al. *Journal of Colloid and Interface Science* **2023**, 641: 36-47.
[2] Subramaniam, S.; et al. *European Journal of Pharmaceutics and Biopharmaceutics* **2024**, under review.