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MEMBRANE NETWORKS AND PROTEIN NANOSTRUCTURES AT THE RESPIRATORY AIR-LIQUID INTERFACE OF MAMMALIAN LUNGS

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Pulmonary surfactant, a lipid-protein complex assembled and secreted by the alveolar epithelium, is essential to sustain respiratory mechanics in air-breathing animals. This system forms lipid-based films at the air-liquid interface, which reduce drastically surface tension in a dynamic way along the continuous compression-expansion respiratory cycles. Stably low surface tension is strictly required to minimize the work of breathing and to prevent atelectasis, i.e. collapse of alveoli at the end of expiration. Lack of an operative surfactant is associated with severe respiratory pathologies such as respiratory distress in premature babies or acute respiratory distress in adults with lung injury and inflammation, which treatment often includes supplementation with an exogenous surfactant.

Surfactant lipids and proteins are assembled as membrane-based structures, which, once secreted, form a dense network of interconnected bilayers transferring very efficiently surface active lipids into the interface. Hydrophobic proteins SP-B and SP-C, take part of defined specialized nanostructures that facilitate membrane-membrane contacts and rapid diffusion of lipids across the thin water layer lining the epithelium. At the interface, surfactant proteins rearrange membranes to form a compact multilayer film providing strong mechanical resistance. In the recent years, we have studied the detailed structure of interfacial surfactant films with respect to lateral organization of lipid and protein species and the compression-driven formation of three-dimensional arrangements and their role to stabilize the interface under conditions mimicking respiratory dynamics.

The development of simplified surfactant models combining synthetic lipids and proteins purified from animal lungs or produced by molecular biology techniques is a major objective to design new improved therapeutical preparations.