Reactivation of Pulmonary Surfactant by Hyaluronan Implication of Depletion forces and Entanglement Effect

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Pulmonary surfactant is a complex mixture of lipids and proteins lining the alveolar air-water interface. By lowering the surface tension at the respiratory interface, pulmonary surfactant stabilizes the respiratory epithelium against physical forces tending to collapse. Dysfunction of surfactant in the lungs is associated with respiratory pathologies such as acute respiratory distress syndrome (ARDS) or meconium aspiration syndrome (MAS), where naturally occurring inhibitory agents reach the lung. We have observed significant differences in the interfacial performance of surfactant preparations in the presence or absence of inhibitory agents in a captive bubble surfactometer (CBS). Using this model, we have confirmed the higher resistance to inhibition of preparations combining pulmonary surfactant and polymers such as hyaluronan and the potential use of these additives to design new therapeutic surfactant preparations. In the present study we have analysed the effect of hyaluronan on the structure and surface activity of pulmonary surfactant to describe the possible mechanism for reactivation. We have observed significant effects in structural properties such as aggregation of surfactant membranes, or the size, distribution and packing of phase segregated lipid domains, when hyaluronan is present in the bulk phase. We have also observed refining on the composition of surfactant that consists on an enrichment of saturated phospholipids, the most surface active components. Surprisingly, we have detected no apparent direct interaction between surfactant complexes and hyaluronan even though we have observed a 100% of transfer of surfactant complexes into the interface only in the presence of this polymer. All of these irreversible changes on surfactant structure and function are observed only at a polymer concentration above 1 mg/ml, in which the polymer forms a meshwork, due to the entanglement effect. We propose that this polymer meshwork is the responsible for the entropy-mediated changes in surfactant structure may enhance surfactant function and thus resistance to inactivation.