AIRWAY REOPENING PRODUCES DAMAGING MECHANICAL STRESSES THAT REDUCE LUNG EPITHELIAL BARRIER FUNCTION.

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While mechanical ventilation plays a vital, life-sustaining role during periods of respiratory distress, it also inflicts a host of irregular mechanical stresses on the delicate tissues of the airways and alveoli. The resulting ventilator-induced lung injury (VILI), characterized by pulmonary edema and epithelial damage, can escalate rapidly to life-threatening conditions such as acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). This study examines the effects of airway reopening on the pulmonary epithelium of fluid-occluded terminal airspaces. We focus our analysis on the consequent changes in paracellular permeability of the cell layer (using BODIPY-ouabain as a tracer molecule) and the altered expression of the proteins ZO-1 and claudin 4. These proteins of the epithelial tight junction (TJ) play an essential role in establishing and maintaining the primary barrier of the pulmonary epithelium to the paracellular passage of fluid into the airspaces of the lung. Our results indicate that a critical level of mechanical stress associated with low reopening velocities induces an epithelial recovery response which acts to fortify the TJ network of the airways to decrease paracellular permeability. This behavior may be highly significant in preserving barrier function and reducing pulmonary edema and VILI during mechanical ventilation.

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