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Characterisation of the intracellular surfactant-pool in a mouse-model of pulmonary fibrosis

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Alveolar epithelial type II (AEII) cells are crucial for surfactant metabolism, keeping alveoli open, dry and clean. In recent years, increasing evidence has been found that dysfunctions of AEII cells play a central role in the development of pulmonary fibrosis. This has been attributed to an increased endoplasmatic reticulum stress and alterations in autophagy of AEII cells. Autophagy is a conserved mechanism known to degrade cellular components (e.g. organelles, misfolded proteins) by formation of autophagosomes. Amiodarone is a drug which can induce a fibrotic remodeling in the lung. In the present study, we characterized the intracellular surfactant pool (defined by the total amount of lamellar bodies (LB)) and autophagy within AEII cells in the amiodarone mouse model of pulmonary fibrosis. Using design-based stereology we observed a marked increase in the intracellular surfactant pool after amiodarone treatment within two weeks which was associated with hyperplasia and hypertrophy of AEII cells.

Immuno-gold labeling showed a preferable binding of LC3b at the limiting membrane as well as in the interior of the LB in both control and amiodarone treated mice. Autophagosomes as defined by pure morphological criteria were found preferably after amiodarone exposure. TEM tomography was used to characterize the 3-dimensional morphology of autophagosomes within AEII cells after amiodarone exposure. A contact between the LB and the autophagosome could be observed in the TEM tomogram, meaning that these structures share the source of lipid.