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Title: Watching the lung work: An in vitro 3-D microfluidic device to challenge pulmonary drug delivery strategies with high end microscopy

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Body: During tissue development, lung cells are exposed to mechanical forces and communicate via biochemical signals directing their shape and function. The unique alveolar-capillary interface relates to cellular transport and cell differentiation and has particular impact on the understanding of pulmonary edema und cystic fibrosis. Our model allows exploring the delicate cellular compositions of lung tissue which is highly intricate and requires advanced technology. For that, we cultured freshly isolated AT II and immortal AT I cells from rat on the apical side in close contact to the air-liquid interface and HEMC-1 were seeded on the basolateral side. Our preliminary experiments were performed on cell culture inserts, thus we verified the functionality by measuring cell viability, morphogenesis, transepithelial resistance (TER) and tight junction protein expression under different conditions. The coculture formed a confluent monolayer and TER was significantly increased after two days interface contact. Applying different culture conditions had no effect on tight junction's expression and cell viability; though adding of dexamethason lead to a concentration dependent TER increase. Next, we will implement our coculture in a transparent microfluidic chamber that mimics the dynamic microenvironment of an intact lung and enables long-term cell culturing at the air-liquid-interface. Our 'artificial lung' model will facilitate the visualization of cellular processes in a live cell imaging manner. This approach will improve the current pathophysiological understanding of alveolar transport in general, and further accelerate pulmonary drug delivery research.