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## List of Abbreviations

| | |
|---|---|
| VILI | Ventilator-induced lung injury |
| MV | Mechanical Ventilation |
| IL-8 | Interleukin-8 |
| TNF-α | Tumor necrosis factor-α |
| PDMS | Poly(dimethylsiloxane) |
| EC | Endothelial cells |
| FEA | Finite element analysis |

**Abstract**

DEVELOPMENT OF ARTIFICIAL ALVEOLI TO STUDY VENTILATOR-INDUCED LUNG INJURY

by

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Ventilator-induced lung injury (VILI) is a significant health risk for patients placed on mechanical ventilators when the ventilator settings required to sustain life can instead exacerbate or initiate significant lung injury and inflammation. VILI occurs in 5-15% of mechanically ventilated patients with an associated mortality rate of 34-60% and is characterized by increased pulmonary edema, impairment of the surfactant system, and a massive inflammatory response. VILI manifests itself primarily on the level of the alveolus where the cells of the alveolar epithelium undergo abnormally high cyclic strains during ventilation which can result in structural disruption and cytokine release. The successful development of strategies to suppress the damaging effects of VILI depends on understanding the mechanisms of injury yet the specific causes remain unknown. *In vitro* methods to study VILI including whole lung models and cell stretching devices are either macroscopic or low throughput. To overcome these limitations of traditional systems and to provide an added degree of physiological relevance is to use microtechnology to recreate aspects of biological environments seen *in vivo* where

microfluidics and other microscale phenomena dominate at the cellular level. This thesis describes 4 microsystems that take advantage of microtechnology and when integrated can form an 'artificial alveoli' microchip to study VILI. The first microsystem is a series of individually programmable cell stretching microwell arrays where cell alignment in response to applied cyclic strain can be quantified. In the second, cells cultured in wells can be stretched using an air-liquid interface to show increasing damage to epithelial cells. For an on-chip analysis of the biochemical responses of cells to cytokine exposure, the third device is a self-contained microfluidic immunoassay system where liquid flow is controlled using the pins of a Braille display. The fourth is a multi-width multi-depth microchannel network to generate biomimetic vasculatures. The first two and the fourth microsystems are technical device-oriented projects, while the third is used to probe a unique unexplored biological theory that the structural damage of the alveolar epithelium found in VILI is largely due to the stretching of alveoli using an air-liquid interface during ventilation.