DEVELOPMENT OF IMMUNE MICROPHYSIOLOGICAL SYSTEMS (IMMUNE SYSTEMS ON A CHIP) FOR MCM TESTING

Axorgan-on-chip Technology asa Model for Early Detection of Human Lung Toxicity

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We have all heard the term 'the canary in the coal mine'—a historical reference to how canaries were used to detect toxic gases in mines, serving as an early warning system for miners' safety. Today, at AlveoliX, we have transcended this early detection method with a revolutionary technology: the artificial Lung-on-Chip. This cutting-edge device operates continuously (mimicking the breathing motion), around the clock, directly predicting potential organ damage to lung cells either from airborne substances that are inhaled or when systemically administered.

Our focus at AlveoliX is on leveraging this technology to enhance our understanding of how drugs interact with the lung tissue and its immune system. In this abstract, we are applying our innovative Lung-on-Chip technology to study the systemic effects of two specific cancer drugs, IL-2 and FOLR1-TCB.
By closely monitoring how these substances affect lung health, we are paving the way for safer and more effective treatments, ensuring a future where drug therapy is as secure as it is potent.

Organs-on-Chip help bridge the gap between the standard in vitro assays and the clinics by providing human-relevant results. Here we evaluated the risk of lung toxicity induced by FOLR1-T Cell Bispecific antibody and Interleukin-2 (Proleukin®). Notably, FOLR1-TCB, toxic in cynomolgus monkeys, showed no toxicity in mice due to a different target expression profile. Our AXLung-on-Chip model indicated that both molecules induce lung injury, namely tissue barrier disruption and vascular leak.

Our toxicity assessment involved trans-epithelial-endothelia-resistance (TEER) measurement on our AXLung-on-Chip, immune cell activation and screening of potential relevant biomarkers (transcriptomics and proteomics).

We present the use case of the AXLung-on-Chip system for safety testing of oncotherapeutics with the examples of IL-2 and a bispecific T cell engaging antibody (FOLR1-TCB), respectively associated with side effects in a subset of patients or concerns for on-target/off-tumour pulmonary toxicity (FOLR1-TCB, Geiger et al. 2020, Kerns et al. 2021).
Upon treatment with IL-2, our patient-derived immune competent model matched the donor-to-donor variability in the response therapeutics. In comparison, the FOLR1-TCB antibody, exhibited alveolar cell death and secretion of proinflammatory triggers due to T-cell specific activation. These effects resulted in increased immune cell recruitment and disruption of the epithelial layer, suggesting that our patient-derived model holds the promise of being predictive of clinically relevant safety.

Our data supports the value of AXLung-on-Chip technology as an early prediction method for human lung toxicity of systemically administered therapeutics.

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