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Driving innovation from discovery to access

Development of a human lung-liver-lymph node co-culture on a chip for the screening of tuberculosis vaccine candidates.

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Tuberculosis (TB) has long been one of the leading worldwide causes of death from a single pathogen. In addition, several studies have shown that vaccination with Bacille Calmette-Guérin (BCG), the only widely-accepted TB vaccine, does not efficiently prevent disease in the adult population. Therefore, new TB vaccine alternatives must be developed, but this is currently hampered by the absence of a truly predictive TB animal model, or of valid human correlates of protection for TB. Our objective is to develop a unique human lung-liver-lymph node co-culture on a chip system for the screening TB vaccine candidates.

First, we further adapted established HUMIMIC chip system to house the iPSC-derived three-organ co-culture. The lung compartment will enable both a human-like infection by airborne Mycobacterium tuberculosis (Mtb) in its air-exposed surface and a first line response of resident alveolar macrophages, dendritic cells and circulating monocytes in its liquid compartment. Then, the lymph node model, and circulating white blood cells within the chip, will support innate and adaptive immune reactions towards the pathogen. Finally, the human liver model will support a stable homeostasis of the co-cultures. In the meantime, we are setting up conditions for chip infection and in vitro vaccination. Alveolar macrophages, the first site of Mtb proliferation, will be included in the lung compartment. Bacterial proliferation, inflammatory response and epithelial barrier integrity will be assessed as infection readouts. Finally, chips will be inoculated with BCG as a gold standard, and subsequent changes to Mtb load, as well as the induction of an antigen-specific T cell response, will be evaluated. The ultimate goal of the project is to compare currently developed TB vaccine candidates with BCG in their capacity to induce protection against Mtb within the HUMIMIC chip, and provide predictive pre-clinical data to support promising candidates progressing to clinical trial

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Conflicts of Interest
None