Modelling the lung in vitro

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PROPOSITIONS – STELLINGEN

Modelling the lung *in vitro*

1. Organoid-based expansion of epithelial progenitor cells is a valid method to establish epithelial cell cultures from healthy and patient-derived samples with low cell numbers (This thesis).

2. Next steps in developing a patient-specific *in vitro* model of the human alveolus should include primary human alveolar epithelial cells or human iPSC-derived alveolar epithelial cells, and the possibility to stretch the membrane on which these cells are cultured (This thesis).

3. The response of alveolar epithelial cells to activation of WNT signalling is determined in part by the extracellular matrix. (This thesis).

4. M-CSF and GM-CSF polarized macrophages stimulate airway epithelial wound repair through different pathways (This thesis).

5. A clear definition of which aspects of the disease are to be studied is a prerequisite for the selection of an *in vitro* model (Hiemstra et al, ERJ 2019; 54: 1900742).

6. Human iPSC-derived alveolar type 2 cells cultured at the air-liquid interface are a suitable model to study the pathogenesis of peripheral lung injury in patients with severe COVID-19 (Huang et al, Cell Stem Cell 2020; 27:962-973).

7. Single cell RNA sequencing is a powerful tool in lung biology, but results in underrepresentation of fragile cell types such as airway or alveolar epithelial cells, suffers from a loss of spatial registration and therefore fails to capture the complexity of cell-cell interactions (Raredon et al, Sci Adv 2019; 5:eaaw3851).

8. Their ability to capture genetic variation in the human population and their suitability for genome editing, makes human iPSC- or progenitor cell-based organoids an excellent platform for studies in personalized medicine (Chen et al, Nature Cell Biology 2021; doi: 10.1038/s41556-021-00721-x. Online ahead of print).

9. 'COVID-19 is challenging all human beings. Tackling this epidemic is a long-term job which requires efforts of every individual, and international collaborations by scientists, authorities and the public.' (Hu et al, Nature Reviews Microbiology 2021; 19:141–154).

10. "The saddest aspect of life right now is that science gathers knowledge faster than society gathers wisdom." Isaac Asimov, Isaac Asimov's Book of Science and Nature Quotations, 1988