

Award plan

If I would receive the NRS Mid-Career award, the budget of €10.000 would be spent on the development of a novel human lung tissue model. The most used standard tissue model, the precision cut lung slice (PCLS) model, provides challenges when working with diseased tissue. For example, when using emphysematous tissue, the agar to solidify the tissue before cutting, leaks out quite quickly, hampering the slicing of the tissue for culture. Furthermore, the cell culture medium for the PCLS does not facilitate viability of all cell-types and thereby the tissue degrades rapidly during culture. The proposed novel tissue model, inspired by a culture model published by Prof. Kuo's group (PMID:37205380) developed to study SARS-CoV-2 infection, overcomes these challenges. This group developed an air-liquid interface organoid model from tissue fragments that preserves the immune compartment, besides the epithelial and stromal compartments after 40 days in culture. We aim to reproduce this model in-house to ultimately use this culture platform to study epithelial-immune interactions in (severe) emphysema and lung fibrosis. We performed pilot experiments with 2 donors, optimizing tissue fragment size and culturing the fragments up to one month. Analysis is currently underway assessing viability of the cells. The budget would be used to assess -in depth- the tissues in culture, repeat in multiple donors and validate these tissue cultures against data directly derived from human tissue. For this we will compare scRNA seq data obtained from the tissue cultures with that of the Human Lung Cell Atlas with help of R scripts. We furthermore will perform imaging mass cytometry on paraffin-embedded tissue cultures and stain these using a recently in-house optimized lung panel, including all major cell-types, and compare these data to already obtained data from control human tissues.

Outlook: This model will be stimulated with disease-relevant mediator cocktails (fibrotic cocktail and emphysema cocktail; latter currently in development) and disease-specific outcomes will be assessed. Using the 'healthy' and disease models, we can add one extra step toward patient level in the animal-free preclinical phase. This is essential to translate the findings in our other models (e.g. insert, organoid or Lung-on-Chip), to tissue level outcomes and increase the predictive value of our findings.

Budget

Type	Price
Cell culture (media, hydrogel, inserts, plastics, stimuli)	€2.000
scRNA seq (€1.000 per sample, 6 donors)	€6.000
Imaging mass cytometry (€250 per sample, 6 donors)	€1.500
Outreach (patient participation costs and science day stand costs)	€500

Societal Outreach: The results of our validation study will be discussed with our patient participation panel, and communicated to the general public via in-person meetings and social media (LinkedIn), respectively. We will furthermore discuss with the Lung Foundation Netherlands if we could provide information during an LED meeting, or webinar on our models, including the newly developed model. We will furthermore participate in the Science family day of the LUMC with activities for children and their parents related to our models. The Dutch Society for the Replacement of Animal Testing will furthermore be contacted to write a blog on our models or support other activities for which our model would suit the outreach activity.