



**Offer:** MD Scholarship for doctoral thesis  
**Starting Date:** 01.08.2024  
**Institute:** Institute of Lung Health and Immunity at Helmholtz Munich  
**Working Group:** Immunopathology of COPD (Yildirim Lab and Funk Lab)

### **Exploring the impact of airborne toxins and viral infections on COPD progression**

The incidence of chronic lung diseases increases with age. Among them, chronic obstructive pulmonary disease (COPD) is one of the most important age-related chronic inflammatory lung diseases and represents a major health and socio-economic burden. Age-related symptoms in the lung that are relevant to COPD pathophysiology include chronic inflammation of the airways and a reduced ability of the lung epithelium to regenerate.

As the airway epithelium is also the first site to be exposed to toxic airborne pollutants and viruses, epithelial homeostasis and thus the integrity of the epithelial barrier is a critical site for the development of COPD. The airways of COPD patients show an increase in immune-primed basal stem cells compared to healthy controls (Conlon *et al*, 2020; Funk *et al*, 2023; Lee *et al*, 2023), however their role in disease development and progression is still unclear. Importantly, these disease-specific cell states are partially recapitulated in three-dimensional organoid cultures derived from COPD patient samples. This fact validates the organoid model and places it as a powerful tool to study the contribution of disease-specific cell states, including immune-primed basal stem cells, to the pathology of COPD, including reduced stem cell capacity, and chronic inflammatory states of the lung.

In this project, we will use patient samples to investigate the response of the COPD airway epithelium to recurrent and combined toxic particle exposures and viral infections. To this end, we will use human organoid models from samples of COPD patients and healthy controls. The analysis will focus on immune-primed basal stem cells, the changes in their response during viral and environmental insults in healthy and COPD human organoids and assess their regenerative capacity. The results of this project will ultimately help to determine the role of immune-primed basal stem cells in the development and progression of COPD in response of exacerbation to viral infections and exposure to toxic particles. In addition, it will evaluate disease-specific epithelial cell states as potential preventive and therapeutic targets in COPD and associated exacerbations.

#### **Literature:**

Conlon TM, John-Schuster G, Heide D, Pfister D, Lehmann M, Hu Y, Ertuz Z, Lopez MA, Ansari M, Strunz M *et al* (2020) Inhibition of LTbetaR signalling activates WNT-induced regeneration in lung. *Nature* 588: 151-156

Funk MC, Gleixner JG, Heigwer F, Vonficht D, Valentini E, Aydin Z, Tonin E, Del Prete S, Mahara S, Throm Y *et al* (2023) Aged intestinal stem cells propagate cell-intrinsic sources of inflammaging in mice. *Dev Cell* 58: 2914-2929 e2917

Lee W, Lee S, Yoon JK, Lee D, Kim Y, Han YB, Kim R, Moon S, Park YJ, Park K *et al* (2023) A single-cell atlas of in vitro multiculture systems uncovers the in vivo lineage trajectory and cell state in the human lung. *Exp Mol Med* 55: 1831-1842



## **MANDATORY EVENTS**

As holder of this scholarship you are a member of the **Research Training Group (RTG) GRK 2338 “Targets in Toxicology”**. The GRK represents a truly international program and benefits from an excellent scientific environment and a state-of-the-art research infrastructure.

As member of the RTG you have to participate in the lecture series “Toxicology of the lung” (once a month) and the annual Research Retreat (once a year). All other courses offered by the GRK can be attended optionally. For more information about the RTG GRK 2338 please visit the following website: <https://www.grk2338.med.uni-muenchen.de/index.html>

## **FUNDING**

The scholarship will be given for 12 months, a minimum of 8 months full-time in the laboratory is required. The monthly scholarship payment is 1.037 €. In addition, a total amount of 395 € in lab consumables per month is available.

## **REQUIREMENTS**

Medical student

## **APPLICATION**

If you want to apply for this scholarship, send an application (CV, motivation letter and certificates) to [S.Resenberger@lmu.de](mailto:S.Resenberger@lmu.de) by **10<sup>th</sup> May 2024**. For project-specific questions please contact Prof. Dr. A. Önder Yildirim ([oender.yildirim@helmholtz-munich.de](mailto:oender.yildirim@helmholtz-munich.de)) or Dr. Maja Funk ([maja.funk@helmholtz-munich.de](mailto:maja.funk@helmholtz-munich.de)).