

## NRS Advanced Technologies in Lung Research Symposium

**Date:** Friday March 31, 2023

**Location:** University of Utrecht – David de Wied Building

*Topics of interest 2023:* Lung-on-Chip, scRNA-seq, CyToF imaging, genome editing.

This yearly symposium will be an educational journey through exciting current developments in lung research focusing on novel powerful technology. The program includes lectures by internationally renowned experts and research presentations by advanced PhD students and post-docs.

Furthermore, there will be parallel workshops addressing how novel technological approaches can boost your scientific creativity and help you to answer specific research questions.

### PROGRAM OF THE DAY

<b>09:30-10:30</b>	<b>Reception with coffee</b>	
<b>10:30-13:00</b>	<b>Morning session</b>	
<b>10:30-10:40</b>	Opening-Introduction to the symposium	
<b>10:40-11:15</b>	Lung-on-Chip in a clinical perspective	Prof. Thomas Geiser
<b>11:15-11:50</b>	Novel tissue niche discovery in the lung by spatial multi-omics	Dr. Amanda Oliver
<b>11:50-12:25</b>	(Imaging) mass cytometry for detecting (disease-specific) immune profiles: what's in it for the lung?	Dr. Padmini Khedoe & Dr. Vincent van Unen
<b>12:25-13:00</b>	Cellular and Molecular Mechanisms of Alveolar Cell Fate Differentiation and Patterning in the Developing Human Lung	Dr. Kyungtae Lim
<b>13:00-14:00</b>	<b>Meet the speaker Lunch</b>	
<b>14:00-15:00</b>	<b>Workshop (parallel sessions)</b>	
	Session 1: CyToF	Dr. Padmini Khedoe & Dr. Vincent van Unen
	Session 2: Genome Editing	Dr. Kyungtae Lim & Prof. Rudi Hendriks
	Session 3: scRNA seq	Dr. Amanda Oliver & Dr. Martijn Nawijn
	Session 4: Lung-on-Chip	Dr. Anne van der Does & Brady-Rae Pinchen, UMCG
<b>15:00-15:30</b>	<b>Coffee break</b>	
<b>15:30-16:50</b>	<b>Junior session: View into the Future</b>	
<b>15:30-15:50</b>	Modelling mucociliary airway epithelial cells in submerged cultures	Dr. Gimano Amatngalim
<b>15:50-16:10</b>	The use of mass spectrometry imaging in research; molecular changes in malignant peripheral nerve sheath tumor (MPNST)	Rick Ursem
<b>16:10-16:30</b>	Primetime: The role of the Tumor Draining Lymph Node in Anti-Tumor Immunity	Mandy van Gulijk
<b>16:30-16:50</b>	Culture-independent diagnosis of lower respiratory infections	Dominic Fenn
<b>16:50-17:00</b>	Closing highlights/take home messages	
<b>17:00-19:00</b>	Dinner	

## Meet the Speakers



### Prof. Thomas Geiser

University Hospital Bern, Switzerland

Thomas Geiser is head of the Department of Pulmonary Medicine & Allergology and Director for Research and Teaching at the University Hospital in Bern, Switzerland. He trained in internal, pulmonary and experimental medicine at the Universities of Bern and Zurich, and completed his training at the University of California, San Francisco, CA, USA. He was a visiting professor at Université Diderot in Paris in 2018.

Professor Geiser's main interest are chronic lung diseases like asthma, emphysema and interstitial lung diseases (ILD) and he is involved in clinical, translational and experimental research projects. His research work, which is supported by the Swiss National Science Foundation, mainly focuses on the cellular and molecular mechanisms of pulmonary fibrosis and the development of novel personalised *in vitro* disease modelling systems like lung-on-chip and organoids to study precision medicine approaches in chronic lung diseases. Professor Geiser is member of the Swiss Academy of Medical Sciences (SAMW), was president of the Swiss Respiratory Society (SGP), Head of the Cellular and Molecular Biology Assembly and Treasurer of the European Respiratory Society (ERS).



### Dr. Amanda Oliver

Wellcome Sanger Institute

Amanda Oliver is a RESPIRE4 Marie Skłodowska-Curie post-doctoral fellow in the Teichmann lab at the Wellcome Sanger Institute where she is interested in studying mucosal immunology at single cell resolution. Her recent work in Nature Genetics used single cell and spatial transcriptomics across 5 locations of the human lung to reveal a novel IgA plasma niche in the airways. Amanda completed her PhD in lung tumour immunology at the Peter MacCallum Cancer Centre and her BSc Hons from the University of Queensland in Australia.



### Dr. Vincent van Unen

Leiden University Medical Center

As a PhD student in the group of prof. F. Koning at the Dept. of Immunology (then IHB) at LUMC, I was the first to apply mass cytometry to analyze the immune system in biopsy material from patients with inflammatory intestinal diseases (celiac and Crohn's disease). I was the first adopter of mass cytometry in the Netherlands. In this work, I have connected the biomedical field with computational scientists, which has resulted in the development of Cytosplore and Hierarchical Stochastic Neighbour Embedding (HSNE). These computational tools overcome the scalability limits of t-SNE, thus enabling the analysis of millions of cells.

My studies led to the identification of tissue- and disease-associated immune subsets in inflammatory intestinal diseases. Furthermore, several significant discoveries have been made possible by the computational pipeline I have developed through collaborations with Technical University Delft, covering multiple research fields: pathogen-immune interactions, tumor immunology,

autoimmunity, and pregnancy. I had the pleasure of collaborating with a diverse group of researchers. Moreover, these collaborations demonstrated that the computational immunology approach developed was versatile and readily applicable to various research topics.

To increase our understanding of inflammatory diseases affecting organs, it is crucial to gain better fundamental insight into the physiological development of the immune system. Therefore, I studied the cellular composition of the mucosal immune system in the developing human fetus with single-cell mass cytometry. We identified early-life compartmentalization of immune cells in fetal tissues, and extensive heterogeneity and multi-lineage differentiation trajectories of innate lymphoid cells in the fetal intestine. These analyses, along with single-cell RNA-seq, T cell receptor-seq and imaging-CyTOF, revealed the generation of memory CD4+ T cells in the fetal intestine, suggesting that the immune system before birth is far more mature than previously thought.

As a postdoctoral researcher at Stanford University (CA, USA), I continued my research on investigating the immune system in inflammatory intestinal diseases. In Mark Davis's lab, I gained significant experience applying a systems immunology approach to studying human disease. I worked on analyzing multiple single-cell techniques for an in-depth analysis of T cell populations. Moreover, I was a joint postdoc in Calvin Kuo's lab, which has developed the air-liquid interface (ALI) organoid system. I have extended this organoid technology and helped develop celiac disease and IBD organoids from human biopsies that preserve intestinal epithelium, supportive stroma, and native immune cells. When the pandemic struck, I was part of a research team where we generated human lung organoids and successfully infected them with SARS-CoV-2, identifying lung cell types amenable to infection.

My research experience has positioned me between computational sciences and immunology, which has resulted in discoveries that offer opportunities to determine cellular parameters that correlate with disease and predict response to treatment. My interests range from basic research on the immune system to direct clinical translational research of cohort studies and development of computational tools.

My key interests are

- Investigating human immune-mediated intestinal diseases (celiac, inflammatory bowel disease).
- Developing System Immunology approaches to study human disease.
- Performing fundamental research on the development of the immune system in the intestine.



## Dr. Padmini Khedoe

Leiden University Medical Center

I am a postdoctoral scientist at the Department of Pulmonology of the LUMC. I performed my PhD project on the link between COPD and cardiovascular disease and the potential of reparative/regenerative therapies in these diseases. After obtaining my PhD in 2017, I focused my research on developing human preclinical models (*e.g.* co-cultures, organoids) of lung repair that can be used to advance pulmonary regenerative medicine towards the clinic in emphysema and fibrotic lung disease. Currently, I am working on a translational project studying the regenerative potential of mesenchymal stromal cell (MSC) therapy in COPD patients with emphysema. In this project, we apply single-cell mass cytometry (scMC) and imaging mass cytometry (IMC) to profile immune cells upon MSC treatment in lung tissue and blood. Within this project, we study the interaction between immune cells and lung structural cells (*e.g.* epithelial, endothelial cells), and examine alterations in these cellular interactions in respiratory disease such as COPD and a subgroup of COPD patients with  $\alpha$ -1-antitrypsin deficiency, using spectral flow cytometry.



### Dr. KYUNGTAE LIM

The Wellcome Trust/Cancer Research UK Gurdon Institute, University of Cambridge, UK

I earned my PhD in Stem Cell Biology from Konkuk University in Seoul, South Korea, in 2016. I studied cellular mechanisms of reprogramming and differentiation of somatic and pluripotent stem cells<sup>4</sup>. Since November 2017, I have been a postdoc in Emma Rawlins' group at the Gurdon Institute, University of Cambridge. My research focuses on investigating alveolar fate differentiation mechanisms in the developing human lung using primary human fetal lung tissues and human lung progenitor-derived organoid culture systems. Using cutting-edge technologies such as CRISPR knock-out<sup>3</sup> (in the Rawlins group) and single-cell sequencing (in collaboration with the Sara Teichman group in Wellcome Sanger Institute, UK), I successfully addressed cellular and molecular mechanisms of alveolar cell fate differentiation and patterning in the developing human lung at a single-cell level and finally published these results in peer-reviewed journals, *Cell Stem Cell*<sup>1</sup> and *Cell*<sup>2</sup>. Currently, I am seeking a new job as a PI in South Korea and aiming to expand my previous knowledge and experience to further understand alveolar development and differentiation mechanisms from diverse angles using fetal lung-derived organoids and pluripotent stem cell platforms.



### Dr. Gimano Amatngalim

University Medical Center Utrecht

Dr. Gimano Amatngalim conducted his PhD training in the research laboratory of Prof. Dr. Pieter Hiemstra at the Department of Pulmonology at the Leiden University Medical Center, in which he studied airway epithelial cell innate immune defence in COPD. In his current position as a Post doc in the research group of Prof. Dr. Jeffrey Beekman, he is developing and using airway epithelial culture methods and assays for personalized disease modelling of the monogenetic diseases, cystic fibrosis and primary ciliary dyskinesia.



### Rick Ursem

Leiden University Medical Center

My previous experiences have focused on mass spectrometry and the data analysis thereof, as well as the analysis and interpretation of various types of 'omics' datasets. I performed analysis of crosslinked peptides with ESI-FTICR-MS/MS in the group for Mass Spectrometry of Biomolecules at the Swammerdam Institute for Life Sciences (SILS) in Amsterdam. Later on, I gained experience in the analysis of large-scale lipidomics and (public) transcriptomics datasets as well as experience in the use of machine learning at the laboratory for genetic metabolic diseases in the Amsterdam Medical Center. Currently, as a third year PhD candidate at the Leiden University Medical Center (LUMC), my research takes places at the intersection of sarcoma research and mass spectrometry imaging (MSI). My goal is to extract the maximum amount of information from this rich high resolution spatial data and use this to gain new insights into sarcoma biology.





## Mandy van Gulijk

Erasmus Medical Center

Mandy van Gulijk is currently finishing her PhD training and starting as a Postdoctoral researcher in the research group of Prof. Dr. Joachim Aerts at the Erasmus Medical Center. Her research is mainly focused on the identification of the mechanisms underlying resistance to immune checkpoint blockade, primarily in lung cancer and mesothelioma. “My interests include translational preclinical research to identify therapeutic targets that can be used to improve the efficacy of immune checkpoint blockade in the clinic”.



## Dominic Fenn

,Amsterdam University Medical Centre

Dominic Fenn graduated from University College London with a medical degree in 2013 as well as a Bachelors in Speech Science and Communication before undertaking his clinical foundation training in London. He entered his paediatric training in 2015 and became a member of the Royal College of Paediatrics and Child health in 2018. Dominic started his PhD in 2020 at Amsterdam UMC under the supervision of Dr L.D.J Bos and Prof. A.H Maitland van der Zee focused primarily on the culture independent diagnosis of pulmonary infections. His interests and areas of research include the clinical application of microbiome (DOI:10.1186/s13054-022-04068-z , DOI:10.1016/j.jcf.2021.08.031) and volatile organic compounds (DOI:10.1183/23120541.00427-2022 , DOI:10.1093/cid/ciac859).

### **Organized by the NRS Advanced Technologies in Lung Research Committee**

Prof. Rudi Hendriks, Erasmus MC (chair)

Dr. Martijn Nawijn, University Medical Center Groningen

Dr. Anne van der Does, Leiden University Medical Center

Supported by

Dr. Michelle Yang, NRS

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