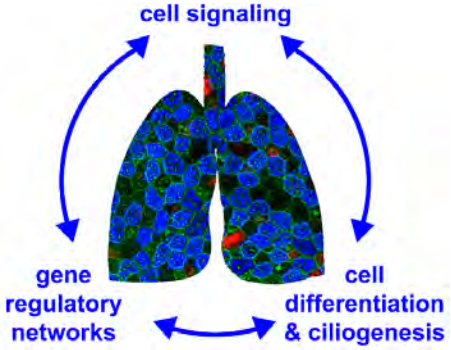
Two fully funded PhD Positions in cell, developmental and systems biology

at the Universitätsklinikum Freiburg, Germany

The Walentek lab studies the molecular mechanisms of mucociliary development, regeneration and disease. Mucociliary epithelia line the embryonic epidermis as well as the respiratory tract of many animal species, and provide an important first line of defense against pathogens for the organism. We are particularly interested to elucidate the interactions between cell signaling, transcriptional and post-transcriptional regulation of gene regulatory networks, and the morphogenetic processes at the cellular and tissue-wide levels, which facilitate complex tissue formation and function. Our work aims to provide crucial insights into the logic of self-organization in biological systems as well as into the molecular mechanisms underlying chronic lung diseases.

Two PhD positions will be available starting October 2017 (or later). The group is supported through the Emmy-Noether-Program by the DFG, which provides fully funded PhD positions (65%). We offer a great environment to perform cutting-edge science at the interface between basic biology and translational medical studies. The Walentek lab is affiliated with the excellent Freiburg Medical Center (Universitätsklinikum Freiburg) and situated in the multidisciplinary research building of the ZBSA (Center for Biological Systems Analysis). This setting provides access to state-of-the-art core facilities and collaborations, including advanced light and electron microscopy, proteomics, computational biology, mathematical modeling and genetics/genomics. PhD students will have the option to participate in the Spemann Graduate School of Biology and Medicine and benefit from advanced training and mentoring opportunities.

Prior experience in cell/developmental biology, genetics/ genomics, or (bio)informatics is highly desired. Interested students should apply with a cover letter stating their motivation, a CV (incl. list of publications if applicable), and contact information for two scientific references to applications_walenteklab@gmx.de .



UNIVERSITÄTS KLINIKUM FREIBURG

zbsa zentrum für biosystemanalyse

SGBM SPEMANN GRADUATE SCHOOL OF BIOLOGY AND MEDICINE

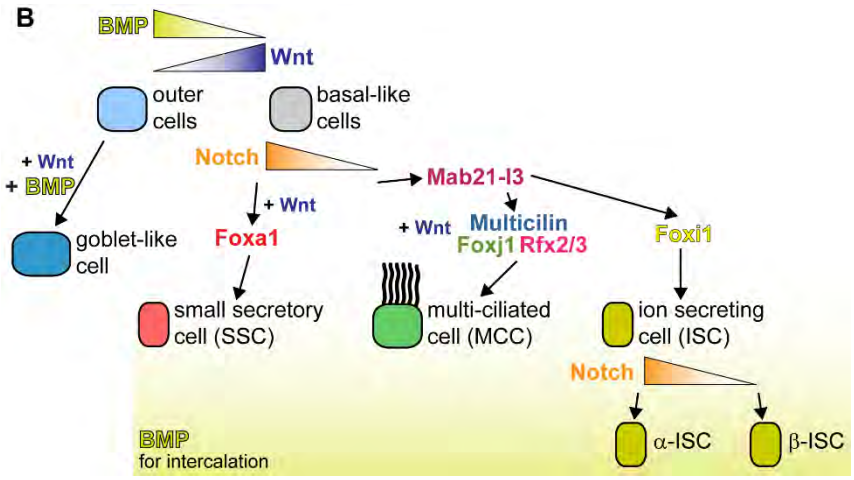
Emmy Noether-Programm
Deutsche Forschungsgemeinschaft DFG

We put special emphasis on providing equal opportunities to all applicants, independent of gender, age, race, sexual orientation/ identity, or disabilities, and strive to increase diversity in the STEM field.

Project descriptions:

(1) Analysis of Wnt/β-catenin dependent gene regulatory networks (GRNs) in airway epithelial development, regeneration and chronic lung diseases.

Project 1 aims to comprehensively investigate the evolutionarily conserved Wnt/β-catenin-dependent GRNs in vertebrate mucociliary epithelia and their specific functions in the different cell types over the course of development and regeneration. We will take advantage of a set of **models ranging from *Xenopus* embryos to mice and human stem cells**, and characterize spatiotemporal Wnt/β-catenin signaling dynamics *in vivo* and *in vitro*, and analyze the effects of signaling manipulations during key stages of development/regeneration at the morphological, genomic and transcriptomic levels. Using **RNA- and ChIP-seq in combination with bioinformatic data analysis** will help us to determine the evolutionarily conserved GRN modules to gain insight into the logic of signaling-dependent gene regulation and disease mechanisms. The system-wide investigations will be followed up by experiments elucidating the functions of **novel regulators of stem cells, cell type specification and morphogenesis** in mucociliary epithelia. This work will exploit the experimental advantages of the different models as well as **cutting-edge methods in systems, cell and developmental biology, including next generation sequencing, genome editing, as well as super-resolution and live-cell imaging**. The results from this project will not only uncover novel gene functions and elucidate the Wnt-dependent GRNs in mucociliary epithelia, but also greatly enhance the comparability of experimental results generated in different systems, establish an efficient experimental pipeline for future studies of other signaling pathways, and provide crucial information on the mechanisms contributing to mucociliary remodeling in chronic lung disease (e.g. COPD).



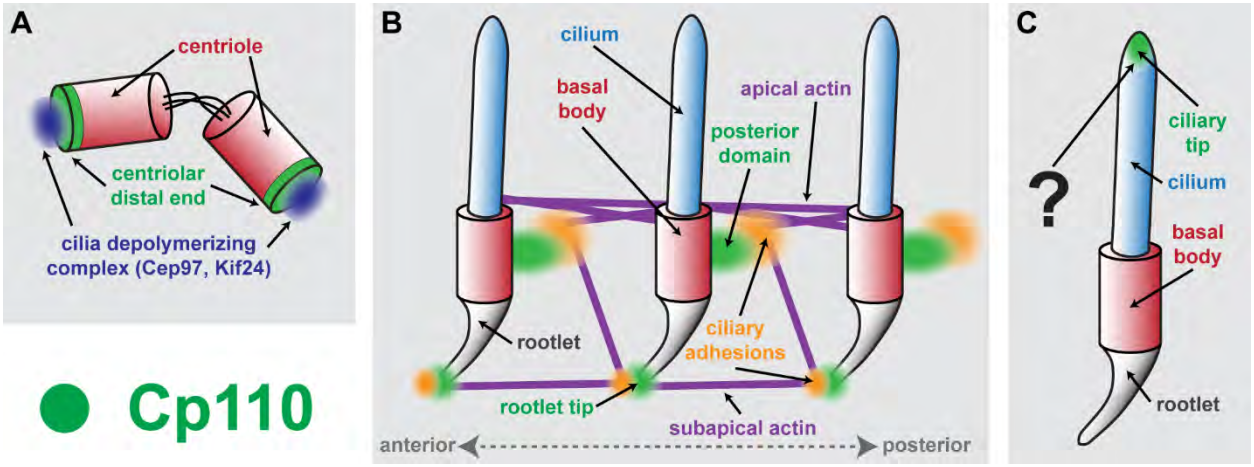
Further reading:

What we can learn from a tadpole about ciliopathies and airway diseases: Using systems biology in Xenopus to study cilia and mucociliary epithelia.
(Walentek & Quigley, 2017, **Genesis**) https://www.ncbi.nlm.nih.gov/pubmed/28095645

ATP4a is required for development and function of the Xenopus mucociliary epidermis - a potential model to study proton pump inhibitor-associated pneumonia.
(Walentek et al. 2015, **Dev. Biol.**) https://www.ncbi.nlm.nih.gov/pubmed/25848696

(2) Elucidating the versatile roles of Cp110 in cilia formation, function and signaling.

Project 2 aims to elucidate mechanisms of signaling, cilia formation and function by investigating novel cilia-related roles of Cp110, which has emerged as **key player in fundamental aspects of centriole and cilia biology**. **Using a proteomics approach**, we will first identify Cp110-interacting protein complexes specifically participating in different aspects of cilia function. Rapid functional **screening using CRISPR/Cas9 in *Xenopus* in combination with semi-automated high-throughput imaging analysis** will reveal Cp110 interaction partners involved in cilia formation, cytoskeletal organization, and cell polarity signaling. The molecular functions of novel Cp110 interaction partners will be studied in detail using **signaling manipulations, and structural and biochemical studies** in *Xenopus*, followed by validation of results in human airway stem cells. Additionally, we will carry out experiments to understand Cp110's role in cilia length control and resorption, analyze **spatiotemporal localization dynamics by advanced light microscopy, study molecular mechanisms in gain- and loss-of-function experiments**, and determine the hierarchical position of Cp110 in ciliogenesis and cilia-dependent signaling. These studies will reveal novel mechanisms of cilia and centriole regulation, shed light on the mechanistic basis for reciprocal influences between cilia and Wnt/PCP signaling, and inform about the structure/function relationship of distinct centriolar and basal body protein complexes in the formation, function and resorption of cilia. These data will enhance our understanding of higher-order complexes in biological systems, uncover the functions and regulation of new cilia-associated factors, and broaden our knowledge about ciliopathies, which affect airway clearance and increase susceptibility to lung infections.



Further reading:

Ciliary transcription factors and miRNAs precisely regulate Cp110 levels required for ciliary adhesions and ciliogenesis.
(Walentek et al. 2016, **eLife**) https://www.ncbi.nlm.nih.gov/pubmed/27623009

miR-34/449 miRNAs are required for motile ciliogenesis by repressing cp110.
(Song, Walentek, Sponer et al. 2014, **Nature**) https://www.ncbi.nlm.nih.gov/pubmed/24899310