CSC-RUB PhD Project Proposal

**Title:** Identification of signaling pathways to treat obstructive lung disease

**Sector of research:** Dr.rer.nat. (PhD)

**Degree awarded:** Biosciences

**Keywords:** lung function, lung physiology, asthma, ovalum-induced asthma, inflammation, respiration, respiratory system, bronchomotor tone, bronchoalveolar lavage, collagen, goblet cell hyperplasia, airway smooth muscle, allergy, bronchial hyperreactivity, pharmacotherapy, animal research, experimental research, medicine and health, human health and disease, endocannabinoids, isometric force measurements, precision-cut lung slices, flexivent, Western Blotting, ELISA, cytokines, qPCR, immunostainings

**Supervisor of PhD project:**
Prof. Dr. med. Daniela Wenzel, Department of Systems Physiology, Faculty of Medicine, Ruhr University Bochum, e-mail: daniela.wenzel@ruhr-uni-bochum.de

**Research focus of supervisor:**
Our lab focuses on lung and cardiovascular physiology. Hereby, we are interested to identify signaling molecules in common diseases with the long-term goal to develop new therapeutic approaches. We are applying various standard methods from cell culture techniques to molecular biology, immunostaining and microscopy. In addition, we use a variety of ex vivo and in vivo approaches for the investigation of mouse tissues such as isometric force measurements of vessels and airways, precision-cut lung slices, the isolated perfused lung model, whole body plethysmography, flexivent spirometry and pressure-volume catheter measurements. These techniques are also applied in mouse disease models for lung injury, asthma bronchiale, pulmonary hypertension, COPD, heart hypertrophy, atherosclerosis and aortic aneurysm. Thus, we cover a wide spectrum of experimental methods to investigate the mechanisms of lung and cardiovascular diseases that are major health problems worldwide.

**Publications:**
53 publications (original research articles in peer-reviewed international journals), H index 26

1x Nature, 1x Circulation, 1x Cell Stem Cell, 1x Cell Metab, 2x Sci Transl Med, 1x Circulation Research, 2x Neuron, 1x Mol Cell, 1x ACS Nano, 1x Nat Commun, 2x PNAS, 2x Hypertension


**Second Supervisor of PhD project:**
Prof. Dr. Andreas Reiner, Cellular Neurobiology, Ruhr University Bochum
**Background:** Chronic obstructive lung diseases are among the most common causes of death worldwide. They represent an important global public health challenge that will even increase in the next decades. Despite various established treatment approaches with beta adrenergic agonists, corticosteroids or antibodies, there are still patients that do not respond well to available treatment regimens. Therefore, the identification of new molecular targets for the therapy of obstructive lung diseases are urgently needed.

**Study objective:** In a previous study we could show that endocannabinoids (cannabinoid-like compounds that are endogenously produced within the body) regulate the tone of pulmonary arteries (Wenzel et al. PNAS 2013). Therefore, we are now interested in the role of endocannabinoids in airway function. In an experimental approach using different pharmacological compounds and transgenic mouse lines, we will identify new molecular targets for the treatment of obstructive lung diseases. For that purpose, various ex vivo and in vivo methods will be applied. Students will be trained in experimental techniques, they will learn to interpret the results in the context of lung (patho)physiology, they will generate high-quality scientific presentations and they are introduced to scientific writing.

**Expected Results:** We hypothesize that signaling molecules of the endocannabinoid system could be new target molecules for the treatment of obstructive lung diseases. The molecular mechanisms of how endocannabinoids contribute to the regulation of lung function will be investigated, this should result in the development of new pharmacological treatment options. The experimental results will be published in high-ranking international peer-reviewed scientific journals.

**Methods:** Airway tone of mouse will be analyzed in isometric force measurements in a wire-myograph and in precision cut lung slices bronchoconstriction ex vivo. For in vivo analyses acute and chronic asthma mouse models (ovalbumin-induced asthma, house dust mite-induced asthma) will be applied. Airway hyperresponsiveness will be analyzed by the gold-standard flexivent method in vivo. Immune cell infiltration will be determined in broncho-alveolar lavage, collagen deposition and goblet cell metaplasia will be investigated in histological lung sections. Cytokines and endocannabinoid-related enzyme expression will be investigated by ELISA, PCR, qPCR, Western Blotting and immunostainings.

**Candidate Requirements:** The candidate should be highly motivated and able to work independently. In addition, a collaborative spirit and enthusiasm are highly desirable. A MSc degree in life sciences is required. Very good English language skills and the willingness to work with mice are prerequisites. Experience with animal experiments is welcome.

**Motivation for CSC application:** Students will be trained in experimental techniques and they will learn to interpret the results in the context of lung (patho)physiology. Furthermore, they will generate high-quality scientific presentations and they are introduced to scientific writing. The successful candidate will be enrolled in the International Graduate School of Biosciences at the Ruhr-University Bochum to expand his/her interdisciplinary experience.