

Master Degree Projects at Karolinska Institutet: Studying Human Lung Immunity in vivo



Dr. Tim Willinger's research group studies immune responses in mucosal tissues in health and disease (<http://ki.se/en/medh/tim-willinger-group>). The research group is based in the Center for Infectious Medicine (CIM) at the Department of Medicine, Huddinge. CIM has excellent expertise in human immunology and provides a stimulating and collaborative environment.

We have two exciting projects available, which will give the Master's student the opportunity to participate in cutting-edge research in the field of lung immunology. The projects aim to lead to fundamental new insights that are relevant to common and important lung diseases in humans, such as asthma, chronic obstructive airways disease, and influenza infection.

Project 1: Origin and Development of Human Alveolar Macrophages

The lung has a large number of macrophages that reside in alveoli, so-called alveolar macrophages. Due to their strategic location within the airways, alveolar macrophages are critical for healthy lung function and barrier immunity. They phagocytose inhaled material and initiate protective immunity against pathogens, while preventing excessive inflammatory responses. Despite their importance, the development of human alveolar macrophages is poorly understood due to the lack of suitable experimental systems.

We have developed a novel humanized mouse model to study the development of human alveolar macrophages in vivo (PNAS 108:2390, 2011; Nat Biotechnol 32:364, 2014). This cutting-edge model expresses human cytokines through gene knock-in (Trends Immunol 32:321, 2011), which allows the reconstitution of a complete human monocyte-macrophage compartment in the mouse. Our unique model will be used to characterize human alveolar macrophages derived from hematopoietic stem cells, to identify the progenitor of human alveolar macrophages, and to investigate the origin of human alveolar macrophages during lung inflammation.

Project 2: Human Innate Lymphoid Cells in Lung Inflammation

Innate lymphoid cells (ILC) are a recently discovered immune cell type that carries out tissue repair, lymphoid tissue formation, and host defence in mice. Human counterparts of ILC have been described, but the in-vivo function of human ILC is poorly understood due to the lack of suitable experimental systems.

To overcome this limitation, we have developed a novel humanized mouse model to study human ILC in vivo. This cutting-edge model expresses human cytokines through gene knock-in (Trends Immunol 32:321, 2011), which allows the reconstitution of a complete human innate immune system in the mouse (Nat Biotechnol 32:364, 2014). All types of human ILC develop in our unique model, which allows us to study their function in vivo, with a particular focus on the lung. Specifically, we aim to understand how ILC migrate during inflammation, how they are maintained in the inflamed lung, and how they contribute to lung inflammation.

The Master's student will have the opportunity to learn and apply several immunological techniques (purification of human hematopoietic stem cells from cord blood, isolation of immune cells from the lung, multi-color flow cytometry, immunohistochemistry to visualize alveolar macrophages in lung tissue sections, functional immunological assays). During the project, the Master's student will work closely together with the group leader, a PhD student, and a lab technician. Direct work with mice is not required.

Feel free to contact the group leader for more information: tim.willinger@ki.se