PhD project No. 25, Prof. King

Scientific Area	Immune-related diseases
Two project titles	A) Pulmonary macrophage heterogeneity and mycobacteria infection B) Functional impact of antibodies during mycobacteria infection
Host country	Switzerland
Supervisor, institution	Carolyn King, University of Basel
Co-Supervisor, institution	Susan Chan, University of Strasbourg
Mentor, institution	Elisabetta Traggiai, Novartis
Secondment institution	University of Strasbourg

Short description of the supervisor's lab with introduction to the topic

The King lab has a long-standing interest in pulmonary infection and the development of immune cell memory. We recently examined the transcriptional regulation of lung resident and lymphoid CD4 T cells during influenza, defining a "universal" residency signature which is conserved across multiple tissues and infection models. Ongoing work in the lab builds on these findings to investigate the metabolic constraints on lymphocytes in the lung as well as trained immunity – a form of memory among innate cells which have no immunoglobulin antigen receptors.

Topic description, including techniques to be used

Project A)

The role of airway macrophages as the initial site of mycobacteria infection is well established. On the other hand, very little is known about the impact of pulmonary vaccination on macrophage remodeling or imprinting. In this project we will assess how vaccination route influences macrophage heterogeneity, using targeted interventions in a mouse model to assess the dynamics, function and intercellular niche of distinct macrophage subsets.

Techniques: mouse models, mycobacteria infection, cell culture, high-dimensional flow cytometry, single cell RNA-seq, ATAC-seq and spatial-seq

Project B)

The importance of antibody responses during mycobacterial infection remains unresolved. Recent studies in mice and humans have implicated a protective effect of serum antibody responses on bacterial containment. It is unclear if mucosal antibodies in the lung show a similar protective effect. This project will focus on understanding the impact of mycobacteria-specific monoclonal antibodies on alveolar versus peripheral monocyte uptake of bacteria, and antibody mediated effects on bacterial fitness and oxidative stress. The student will additionally investigate the therapeutic potential of monoclonal antibodies in a mouse model of mycobacteria challenge.

Techniques: mouse models, mycobacteria infection, high-dimensional flow cytometry, cell culture, monoclonal antibody generation, development of bacterial reporter strains, immunofluorescence microscopy

Recommended applicant's training (technical expertise and knowledge)

Techniques: flow cytometry, cell culture, microscopy

Knowledge: immunology, microbiology, bioinformatics (or interest in learning!)

Maximum two relevant publications

Swarnalekha et al., 2021, Science Immunology: T resident helper cells promote humoral responses in the lung

Künzli et al, 2020, Science Immunology: Long-lived T follicular helper cells retain plasticity and help sustain humoral immunity

The EURIdoc programme has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement number 101034170.

Ethics description

1. Humans	
This research involves human participants.	YES ☐ / NO ☒
This research involves physical interventions on the study participants.	YES ☐ / NO ☒
2. Human Cells /Tissues	
This research involves human cells or tissues, such as blood.	YES ☐ / NO ☒
3. Personal Data	
This research involves personal data collection and/or processing.	YES ☐ / NO ☒
This research involves further processing of previously collected personal data (secondary use).	YES ☐ / NO ☒
4. Animals	
This research involves animals, such as mice.	YES ☒ / NO ☐

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