PhD project No. 17, Prof. Hruz

Scientific Area	Innate and adaptive immunity
Two project titles	A) TCR γδ cells in Inflammatory Bowel Disease B) MR-1 restricted T cells in chronic intestinal inflammation
Host country	Switzerland
Supervisor, institution	Prof. Petr Hruz, University of Basel, Switzerland
Co-Supervisor, institution	A) Prof. Gennaro De Libero, University of Basel, Switzerland B) Prof. Peter Hasselblatt, University of Freiburg, Germany
Mentor, institution	A) and B) University of Basel, Switzerland and Medical Center - University of Freiburg, Germany.
Secondment institution	Dr. M. Bscheider, Pharma Research and Early Development Roche Basel, Switzerland

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

Inflammatory Bowel Disease (IBD) is a chronic inflammatory condition of the gut with relapsing-remitting episodes associated with mucosal lesions and dysregulated immune response against commensal microbes. In chronic intestinal inflammation, the loss of epithelial barrier integrity determines an increased influx of microbial products within the mucosa, including small metabolites. We will investigate the role of T cells specific for small metabolites and activated upon sensing local microenvironmental changes in the gut.

Topic description, including techniques to be used

Project A)

We aim to investigate T cells expressing a TCR γδ and responding to butyrophilins (BTN) expressed by gut epithelial cells and to products of microbial flora. Our research plan focuses: i) on identification and analysis of the functional capacity of TCR γδ cell populations involved in IBD with chronic relapsing inflammation and remitting episodes, and ii) on dissection of the microbial relevance in stimulating TCR γδ cells.

Techniques: multiparametric flow cytometry, single-cell transcriptomics, T cell cloning, cell culture

Project B)

A novel population of human MR1-restricted T cells has been identified in the laboratory of G. De Libero and have been defined as "MR1T" cell. They use a TCR αβ and are polyclonal. These cells recognize MR1-expressing tumor cell lines and also stressed epithelial cells. Our aim is to assess the role of these T cells in the pathogenesis of chronic inflammatory disorders of the gut including their functional capacity to react to epithelial cells expressing MR1.

Techniques: multiparametric flow cytometry, single-cell transcriptomics, T cell cloning, cell culture, organoids generation and analysis

Recommended applicant's training (technical expertise and knowledge)

Techniques: Cell culture, flow cytometry, gene cloning
Knowledge: Basics of TCR biology, antigen presentation, T cell functions

Maximum two relevant publications

M. Lepore et al., 2017, Elife **6:** Functionally diverse human T cells recognize non-microbial antigens presented by MR1.
M. Schmaler et al., 2018, Mucosal Immunol 11: Modulation of bacterial metabolism by the microenvironment controls MAIT cell stimulation.

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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