

Master of Science Thesis Position

Duration: 9-12 months (start: as soon as possible)

Laboratory of Prof. Dr. Burkhard Becher, Institute of Experimental Immunology, University of Zürich.

Supervisor: Dr. Fernando Canale

Research Topic: Screening of transcriptional regulators of cytokines production by human T cells.

Cytokine production by T cells plays a critical role in regulating immune responses, influencing the balance between immunity and tolerance. In chronic inflammatory diseases and autoimmunity, dysregulated cytokine production can perpetuate inflammation and tissue damage. Well-known cytokines like IL-17, IL-4, and IFN- γ are induced by specific transcription factors such as ROR γ t, GATA3, and T-bet, respectively, in human T cells. These cytokines have clear pathways of induction and regulation. However, other cytokines, have less understood regulatory mechanisms. For example, GM-CSF production by CD4 T cells has been shown to be particularly important in animal models of experimental autoimmune encephalomyelitis (EAE), a model for multiple sclerosis (MS), where it drive inflammation and disease progression. However, the conditions in which it is induced and further regulated are not clear.

We will focus on the design, optimization and application of a CRISPR screening workflow developed in the laboratory of Prof. Adriano Aguzzi. **The objective** is to identify and validate regulators of T cell 's cytokines production. **The challenge** consists in the adaptation of such workflows to primary human CD4 T cells, to test a library of 1634 plasmids containing each 4 sgRNAs targeting transcription factors and test different approaches for readouts and analysis pipelines. The project also will involve validation of hits by orthogonal approaches, knock-out/overexpression and in vitro assays using primary human T cells and/or cell lines.

Aims:

- Design, optimization and testing of conditions to adapt primary human T cells to an arrayed or pooled CRISPR/Cas9 screening system to evaluate transcriptional regulators of cytokines production.
- In vitro manipulation of primary T cells and cell lines to evaluate potential candidates. Involving plasmids design, construction, cloning. Lentivirus production. Transfection of cells and readout by standard techniques such as flow cytometry, ELISA, proteomics, etc..
- Data analysis.

We offer:

- Becoming part of an exciting research project.
- A dynamic young and international team in a thriving research environment at the Institute of Experimental Immunology, University of Zurich.
- Training and application of cutting-edge methods (Spectral flow cytometry, molecular biology, cell culture, data analysis, etc.).
- Weekly group meetings, journal flow and scientific seminars.

Requirements:

- Interest in Immunology, oriented to human research.
- Highly motivated and open to flexibility regarding prioritization of project aims, tasks and objectives.
- Experience in molecular biology, BSL2 cell culture and data analysis in R, is a plus.

Applications:

Please send your CV and a brief statement of research interest to canale@immunology.uzh.ch