Master Position

Principal Investigator: Dr. Bojana Müller-Durovic

Project Title: *Decoding the Role of Kynurenine Metabolism in Rheumatoid Arthritis Monocytes and Macrophages*

Project Description:

Immune cell metabolism is a central driver of inflammation and immune regulation in autoimmune diseases such as rheumatoid arthritis (RA). Recent studies highlight the importance of the **kynurenine pathway**, the primary route of tryptophan catabolism, as a critical immunometabolic axis that influences monocyte and macrophage function. Dysregulation of this pathway has been linked to altered immune responses, chronic inflammation, and disease progression in RA.

In our group, we have generated multi-omics datasets (transcriptomic, proteomic, and metabolomic) from peripheral blood monocytes of RA patients and matched healthy controls. These datasets reveal a distinct kynurenine pathway signature, including altered expression of IDO1 and kynureninase (KYNU), as well as changes in the meetabolites kynurenine and 3-hydroxyanthranilate. We are also integrating data from synovial tissue macrophages and single-cell RNA-seq analyses from joint biopsies to understand tissue-specific metabolic reprogramming.

The overarching aim of this Master's project is to investigate how kynurenine metabolism is altered in monocytes and macrophages in the context of RA, and how it contributes to inflammatory immune phenotypes.

Specific Objectives:

To characterize kynurenine pathway activity in monocytes and macrophages from RA patients.

Analyze transcriptomic, proteomic, and metabolomic datasets to assess the expression and regulation of key enzymes in the kynurenine pathway. Compare peripheral blood monocytes and synovial macrophages from RA patients and healthy controls.

To explore the functional consequences of kynurenine pathway modulation.

Perform metabolic flux analyses and mass spectrometry-based metabolite quantification.

Use CRISPR-based genetic perturbations and pharmacologic inhibitors of IDO1 and other key pathway enzymes in in vitro monocyte/macrophage cultures. Assess the impact of pathway modulation on cytokine production, polarization and activation markers in macrophages.

Training Opportunities: The project offers training in immune cell culture, CRISPR-Cas9 gene editing, Western blotting, flow cytometry (FACS), and immunometabolism assays. Candidates will also gain experience with metabolomics, mass spectrometry, and omics data interpretation. Prior experience in bioinformatics is not required; existing datasets have already undergone preliminary analysis.

Requirements: We are seeking a motivated and curious MSc candidate with a strong interest in immunometabolism and translational immunology. A background in biochemistry, pharmaceutical sciences, molecular biology, or a related field is desirable. Strong analytical skills and the ability to work collaboratively in a multidisciplinary environment are important.

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