25th November, 2019

The biological effects of rare mutations in autoinflammatory diseases

Master's thesis research project opportunity (3-6 months) in the research group of Prof. Timo Hautala, Unit of Biomedicine, Faculty of Medicine, University of Oulu.

Prof. Hautala's newly established research group is the first one at the University of Oulu that focuses on revealing the genetic and biological bases of rare ***autoimmune and autoinflammatory conditions***. His research focuses on Finnish population which is relatively sparse and isolated - hence providing a unique genetic makeup to study diseases. Moreover, the findings will offer new knowledge on the function of immune system in general.

Background of the project: Patients with certain rare mutations, e.g. in the genes affecting ***NF-κB pathway***, display varying symptoms, for example those typical for autoinflammatory syndromes. Autoinflammatory syndromes are defined as conditions caused by an exaggerated innate immune response and results in episodes of spontaneous inflammation affecting multiple organs. Some patients show autoinflammatory symptoms without any potential mutation that could explain their state. NF-κB participates in regulating the function of ***inflammasomes***, cytosolic multiprotein oligomers of the innate immune system that activate inflammatory responses. Activation and assembly of the inflammasome is crucial for transcription, activation and secretion of pro-inflammatory cytokines, such as interleukin 1β (IL-1β). In neutrophils, NF-κB participates in degranulation and induction of oxidative burst to destroy internalized pathogens. Deregulated NF-κB activation is a hallmark of chronic inflammatory diseases. Understanding of the mechanisms that underlies NF-κB activation and its functions in inflammation is highly important for development of novel therapeutic strategies in the treatment of inflammatory diseases.

Research aims and expected results: The research utilizes patient blood samples to examine the effects of various mutations (most in the genes affecting NF-κB pathway, recently identified by our group) on the function of inflammasome. Depending on the results, the role of some mutations can be further studied in neutrophils' phagocytotic function and oxidative burst. We expect this study to reveal (dysfunctional) novel genes causing autoimmune/autoinflammatory syndromes and uncover previously unknown functions of factors in the immune system.

Methodology to be used in the project: In this project, you will learn various laboratory techniques used in the field of biomedicine and immunology. You will master the isolation of human peripheral blood mononuclear cells (PBMC) from whole blood, cell culture and differentiation techniques as well as collection of conditioned media and protein/RNA extraction from the cells. Moreover, you will learn to perform PCR, ELISA and Western blot. Depending on the results, you might also use fluorescent-activated cell sorting (FACS) and immunocytochemistry to further study the role of most potential genes on cell functions.

Contact: If you are interested in the project, please contact post-doctoral researcher Pirjo Åström (pirjo.astrom@oulu.fi / 050 4331827) for more details.