

The role of the positional cloned Ncf1 gene; Impact of oxidation on antigen presentation function of macrophages

The positional cloned *Ncf1* gene has been shown to control chronic inflammatory diseases such as arthritis and encephalomyelitis both in rats and mice. Ncf1 is a part of the NADPH oxidase complex, which functions as electron donor in the oxidative burst process. The mutated form of Ncf1 has been found to induce lower burst than the wild type form, and this, surprisingly, leads to enhanced autoimmunity.

The aim of this project is to characterize the role of macrophages in this process. Macrophages can be divided in two subgroups: those that are pro-inflammatory are called type I macrophages and those that counteract inflammation are called type II macrophages. The phenotype of macrophages is very much dependent on their differentiation status as a response to recent *in vivo* or *in vitro* conditions. It is believed, that the type I macrophages secrete both inflammatory cytokines (like TNF- α) and reactive oxidative species (ROS), while the type 2 macrophages that differentiate in response to Th-2 cytokines express scavenger receptors such as mannose receptor (MR) and CLEVER-1. Interestingly, macrophages that are deficient in making an oxidative burst (i.e. lack functional Ncf1) activate the T cells and may in fact prime them in similarity with dendritic cells.

CLEVER-1 is a newly identified molecule expressed not only on high endothelial venules, but also on lymphatic endothelial cells and on a subset of type 2 macrophages. CLEVER-1 promotes transmigration of lymphocytes into inflamed tissues from the blood stream and also from lymph vessels into the lymph nodes. In this project we will address the role of CLEVER-1 and MR on macrophage function and also study the role of oxidative burst in cell trafficking to lymph nodes.