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Role of protein tyrosine phosphatases in the regulation of innate immune functions and gut inflammation

Variations within the gene loci encoding protein tyrosine phosphatases (PTP)N2 and PTPN22 have been associated with chronic inflammatory diseases, e.g. inflammatory bowel disease (IBD), rheumatoid arthritis or type-1-diabetes. PTPN2/22 regulate innate (e.g. inflammasome activation) and adaptive immune responses. We will study how genetic PTPN2/22 variations affect immune cell function in vivo using well-established mouse colitis models in mice being either PTPN2/22-wildtype, PTPN2/22-deficient or overexpressing the PTPN22 altered-function gene variant. We will determine the effects of altered PTP function on NLRP3 inflammasome and investigate whether PTPN2/22 regulate inflammatory effects of the food additive and NLRP3 inflammasome activator titanium dioxide in vivo. Using cells and tissue samples from PTPN2/22 genotype-matched patients from the Swiss IBD Cohort and healthy volunteers, we will analyze, whether different genetic backgrounds influence inflammasome activation and immune cell functions in the human intestine. Our studies will help characterizing the role for PTPN2/22 in regulating human immune responses.