Institute of Molecular Genetics
of the Czech Academy of Sciences

Regular Wednesday IMG seminar

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"IL-17 signaling in Paneth cells protects the host from ileal pathology"

One of the outstanding questions of intestinal biology is the regulatory circuit(s) that control the homeostatic balance between microbiota, host intestine, and host immune system. Paneth cells (PCs), which through the secretion of AMPs, control the composition of microbiota and display transcriptional differences which are associated with increased AMP production along the duodenum-to-ileum axis. While Interleukin 17 (IL-17) is known to regulate AMP production on epithelial surfaces, its effect on PCs and the underlying mechanism has been addressed only indirectly and accompanied by controversy. The premise of our study is that among all intestinal epithelial cells, PCs express high, if not the highest levels of surface IL-17 receptor (IL-17R). Using mice with targeted ablation of IL-17R in PCs and executing RNA sequencing of isolated PCs as well as whole ileal tissue, we have shown that PCs are directly stimulated by IL-17 in vivo, that IL-17R signaling controls PC numbers and regulates defense response to bacterium pathways, in which the expression of α-defensins seem to be of critical importance. The lack of IL-17 signaling in PCs translates to the upregulation of ileal inflammatory pathways which is manifested by ileitis, accompanied by ileal dysbiosis. Remarkably, a sub-cohort of patients with Crohn's disease which displayed low PC numbers in the ileum and diminished levels of serum IL-17 was accompanied by symptoms of severe ileitis, a phenotype that was observed in mice with disrupted IL-17 responsiveness. Thus, our data provides insight into the function IL-17 signaling in the intestine as an essential regulator of PC functions that contribute to ileal homeostasis, acting via the prevention of dysbiosis.

The seminar will be held

on Wednesday 25th May 2022 at 15:00

in the Milan Hašek Auditorium at IMG

(Institute of Molecular Genetics of the Czech Academy of Sciences, Vídeňská 1083, Prague 4)