Interaction between diets, bile acid metabolism and gut microbiota: Common mediators in inflammatory bowel & fatty liver -disease (IB/FL- D)

Summary

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Supervisor:	Prof. Dr. Peter Fickert
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between July 15, 2019 00:00 and September 15, 2019 23:59 (Europe/Zurich)

Description

Background:

Inflammatory bowel disease (IBD) and non-alcoholic fatty liver disease (NAFLD) affect mainly epithelial cells (enterocytes / hepatocytes) within the enterohepatic cycle. The role of diets in the prevention and treatment of diseases within the gut/liver axis has become evident as nutrient uptake, conversion and sensing of microbial metabolites and elimination of toxic dietary components have been proven to be therapeutic targets in the treatment of IB/FL-D. Intriguingly, increased levels of intestinal bile acids (BAs) are a risk factor for colorectal cancer; whereas increased hepatic BAs are associated with liver cancer. Several studies indicate an important participation of intracellular nutrient sensing pathways in the control of metabolism and inflammation within both diseases. Nuclear hormone receptors (NHRs), highly expressed in both tissues are endocrine sensors of these metabolites and control cellular homeostasis of epithelial cells as well as immune-metabolism in the gut and liver, respectively.

Hypothesis and Objectives:

a) Identify and characterize common regulators in IB/FL-D (e.g. microbial fermentation products, ligands for GPCRs, hormones);

b) study the interaction between the gut microbiome and gut/liver-resident immune cells (immune cell metabolism),

c) the role of bile acids and autophagy in maintaining epithelial cell integrity and enterohepatic homeostasis.

Within this research project, the candidate will use both *in vivo* and *in vitro* models to determine the impact of “signaling molecules” on gut/liver (patho)-physiology.

Methodology:

The applicant will use molecular/cell biology techniques combined with pre-clinical genetic/dietary mouse models susceptible to IB/FL-D (e.g. chemical/antibiotic induced colitis). The *in vitro* part includes mainly cell culture work with mouse and human immortalized cells (liver & intestine), as well as organoid cultures that greatly mimicking the *in vivo* situation. Moreover, the interactions between the host and (bile acid/metabolite -converting) bacteria in the gut will be studied. This part of the project includes *in vitro* experiments (e.g. anaerobic cultivation of gut bacteria) and *in vivo* donor fecal transplant into various knockout mouse models susceptible to IB/FL-D (e.g. after high fat diet and antibiotic treatment). We offer a very dynamic and interdisciplinary environment with great laboratory infrastructure and equipment.

Your profile: The candidate holds a Master degree (or equivalent) in Molecular Biology or Biochemistry, be open-minded and has good command of the English language. The student will be involved in developing methods and contribute to the research progress with his own.

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