

# Gut-liver bile acid signaling in healthy and diseased metabolism

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## 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 February 04, 2019 00:00 and March 31, 2019 23:59 (Europe/Zurich)

## Description

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### Background:

Bile acids (BAs) function as signaling molecules that greatly influence metabolism under physiological (healthy) and pathophysiological (diseased) conditions. Their metabolic action is versatile and depends on the activation of nuclear hormone (FXR) - and G protein-coupled receptors (TGR5) in the liver and intestine and is also indirectly mediated by fibroblast growth factor-15 that is secreted from the gut to regulate metabolism in the liver. We have identified a novel mechanism whereby FXR regulates metabolism via a post-transcriptional mechanisms and vice versa signaling pathways that maintain a healthy metabolic status by regulating FXR and TGR5.

### Hypothesis and Objectives:

Identify and characterize regulators within this vicious circle that are involved in the interplay between the gut and the liver in the regulation of metabolism by bile acids signaling. Within this research project the candidate will use both in vivo and in vitro models to determine the impact of BAs on gut/liver (patho)-physiology.

### Methodology:

The applicant will use state-of-the-art molecular/cellular techniques combined with pre-clinical genetic models and diet-induced models for metabolic diseases (e.g. high fat/cholesterol diet, within the fasting-refeeding transition, and by treating animals with endogenous and semi-synthetic BAs). The in vitro part includes mainly cell culture work with mouse and human immortalized hepatocytes mimicking the in vivo situation (e.g. fatty acid / cholesterol loading of cells, treatment with endogenous and synthetic ligands, siRNA or CRISPR/Cas9-System to knockdown/delete potential targets). Moreover, the interactions between the host and bile acid-converting bacteria in the gut will be studied. This part of the project includes experiments in vitro (e.g. anaerobic cultivation of gut bacteria) and in vivo (mouse models e.g. under antibiotic treatment).

### We offer:

a very dynamic and interdisciplinary environment with state-of-the art laboratories and equipment.

Your profile: The candidate holds a Master degree (or equivalent) in Molecular Biology or Biochemistry. You are open-minded. Good command of the English language (oral and written) is expected. The student will be involved in developing methods and contribute to the research progress with his own ideas.

### References:

1. Shapiro H, et al. Bile acids in glucose metabolism in health and disease. *J Exp Med.* 2018 Feb
2. Wahlström A et al. Intestinal Crosstalk between Bile Acids and Microbiota and Its Impact on Host Metabolism. *Cell-Metab.* 2016
3. Guo GL, Xie W. Metformin action through the microbiome and bile acids. *Nat Med.* 2018

4. Morris A. Metabolism: New insights into the BAT-liver-gut axis. Nat Rev Endocrinol. 2017



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