Control of metabolic diseases: Gut/liver –adipose tissue communication through mTORC1

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:

Calories refer to the energy our body gets from food, starting by the absorbance through the small and large intestine. In mammals, the synthesis and storage of energy occurs largely in two organs: liver and adipose tissue. The adipose tissue acts as a caloric reservoir, stores nutrients in the form of neutral lipids, and delivers energy to other tissues through lipolysis. The liver, facing nutrients directly from the intestine orchestrates anabolic and catabolic processes to maintain its own and systemic energy homeostasis. Therefore, metabolic flexibility is tightly controlled by a nutrient sensitive network that is centered on the mammalian target of rapamycin complex 1 (mTORC1), acting as a metabolic 'rheostat'. Bile acids (BAs), steroid hormones, improve the metabolic profile of obese animals through its actions on adipocytes e.g. via the GPCR (TGR5) and improve fatty liver disease e.g. via the nuclear hormone receptor (FXR). BAs therefore act as signaling molecules that greatly influence metabolism under physiological (healthy) and immuno-metabolism under pathophysiological (diseased) conditions.

Hypothesis and Objectives:

The main goal of our laboratory is to investigate the involvement and underlying molecular mechanisms by which intracellular nutrient sensors, in particular mTORC1, regulate the metabolic and inflammatory phenotypes associated with the above-mentioned immuno-metabolic diseases, including liver cancer. Specific emphasis will be put on how mTORC1 is integrated into the FGF19/FGF21 signaling network; both hormones have been used to improve the metabolic profile of various animal models and are currently studied in phase clinical II trials.

The thesis: will focus on signaling pathways controlling cellular and whole body glucose and lipid homeostasis in cell-based and animal models. To accomplish our goals, you will perform:

a) large-scale analysis of gene, lipid and protein expression profiles in cells and tissue;

b) experiments of gain and loss of function of proteins of interest (AAV- vectors and genetically modified mice); and

c) *in vivo* and *in vitro* functional analysis of metabolic and inflammatory pathways.

The results of these research aims will allow us to better define the molecular and physiological mechanisms by which BAs, and dietary compounds, affect glucose tolerance and insulin sensitivity.

We offer: a highly dynamic and interdisciplinary environment in collaboration with departmental, institutional and international colleagues as well as state-of-the art laboratories and equipment.

Your profile: The candidate holds a Master degree (or equivalent) in Molecular Biology or Biochemistry. Good command of the English language (oral and written) is expected.

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