Role of Perilipin 5 phosphorylation in the development of liver disease

Summary

Guenter Haemmerle, Institute of Molecular Biosciences, University of Graz

Supervisor: Prof. Dr. Günter Hämmerle
Availability: This position has been occupied.
Offered by: Medical University of Graz
Application deadline: Applications are accepted between August 01, 2016 00:00 and September 30, 2016 23:59 (CEST)

Description

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Background: The prevalence of non-alcoholic fatty liver disease is steadily increasing and correlates with the prevalence of obesity and type 2 diabetes. However, the underlying molecular mechanisms await further clarification.

Aims/Hypothesis: Lipid droplets (LDs) are enriched with proteins from the perilipin family including the presence of Perilipin 5 (Plin5) on LDs derived from liver and muscle tissue. We could previously show that Plin5-enriched LDs are resistant towards adipose triglyceride lipase (ATGL)-mediated lipolysis [1]. This lipolytic barrier could be resolved upon Protein Kinase A-mediated Plin5 phosphorylation [2]. Notably, mice overexpressing Plin5 in the liver develop hepatic steatosis but are protected from lipotoxicity paralleled by increased hepatic insulin sensitivity [3,4]. This project aims to unravel the role of PKA-mediated Plin5 phosphorylation in the regulation of hepatic lipid and energy metabolism.

Methodology: Generating recombinant adenovirus expressing wildtype and mutant Plin5 (harboring an amino acid exchanged in the proposed PKA phosphorylation side). Mice will be infected with recombinant adenovirus which will lead to increased hepatic expression of wildtype and mutant Plin5, respectively. The impact of increased Plin5 expression on liver and whole body TG homeostasis and energy metabolism will be examined. Cultivation and transfection of mammalian cell lines and applying tracer isotope techniques. Mouse handling and phenotypic characterization (collecting blood samples and organs, enzymatic assays, tissue uptake studies, RNA isolation and qRT-PCR).

References:


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