Investigating the role of N-acetyltransferase 8-like (NAT8L) in whole body energy metabolism and the consequences for the heart

Summary

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Supervisor: Prof. Dr. Juliane Bogner-Strauss
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

Background:
Imbalances in cellular energy homeostasis can lead to diseases such as type 2 diabetes, cardiovascular disease and cancer. The heart, which has to contract incessantly, is very sensitive to nutritional changes and requires optimal energy to fuel adjustment [1]. N-acetylaspartate (NAA) is one of the most abundant metabolites in brain [2] with yet unknown function. NAA is synthesized by mitochondrial N-acetyltransferase 8-like (NAT8L) and catabolized by cytoplasmic aspartoacylase (ASPA), building the so called NAA pathway [3–7]. Several studies linked NAA to neuronal osmoregulation, lipid synthesis and energy metabolism [8, 9]. We were the first to show that the NAA pathway functionally exists in (brown) adipose tissue [5]. Further, we demonstrated that manipulation of the NAA pathway impacts brown adipocyte lipid turnover (lipogenesis and lipolysis), brown marker gene expression, and cellular respiration in vitro [5] and in vivo, thereby impacting whole body energy metabolism (unpublished).

Hypothesis and Objectives: Until now we have discovered, that Nat8l-knockout mice show reduced body weight, reduced blood triglycerides, mild hypoglycemia and improved glucose tolerance. Most importantly for this work, we discovered that Nat8l-knockout mice die earlier than their littermates. They die especially in the time after weaning, where there is a nutritional change from high-fat containing mother’s milk to chow diet. The observation that Nat8l-knockout mice have increased heart weight upon cold exposure and trends to hypertension and increased heart rate made us hypothesize that the sudden death of these mice is linked to the heart. In this project, we seek to identify the molecular mechanism of how Nat8l influences whole body energy metabolism and how this impacts the heart.

Methodology: This project focuses on Nat8l and its influences on whole body energy metabolism. Candidates who are interested in this project should have basic experience in cell culture and molecular biology techniques, such as Western blot and real-time PCR. Since this project deals with the characterization of Nat8l-knockout mice, we are looking for candidates who are willing to work with laboratory animals and preferentially already have certain experience with mouse handling.

Research interest: https://www.tugraz.at/projekte/cellism/home/

Your experience: Ideally, you have a thorough background in cell culture, molecular biology techniques (cloning, RT-PCR, WB), and preliminary experience in mouse handling.

References:


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