Project 1.7 The role of impaired autophagy and peroxisome function in NAFLD development and their targeted recovery for improved efficacy of n-3 fatty acids

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Background:

Excessive consumption of foods rich in saturated fats causes unhealthy fat accumulation in the liver, which is directly related to the increase in non-alcoholic fatty liver disease (NAFLD). NAFLD comprises a spectrum of metabolic states ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), cirrhosis, and finally hepatocellular carcinoma as an ultimate consequence. Despite the lack of complete knowledge, it is assumed that an additional insult is needed for NAFLD progression towards NASH, possibly involving increased cellular oxidative stress along with the failure of cellular quality control mechanisms. It seems, that development of NAFLD can be modulated by autophagy, one of the major quality control systems for the removal of oxidized molecules and damaged organelles. Failure of autophagy may cause the accumulation of dysfunctional organelles, which contributes to the induction of oxidative damage to the liver in NAFLD progression.

Aim:

The main goal of the project is to unravel the role of autophagy in NAFLD progression and to develop potential novel strategies to delay disease progression. Additionally, we aim to determine whether treatment with inducers of autophagy can increase the effectiveness of supplementation with n-3 polyunsaturated fatty acids (n-3 PUFA) towards the advanced stages of NAFLD, which is otherwise limited to the initial step in NAFLD (i.e., hepatic steatosis). We plan to uncover the exact role of autophagy and the associated metabolic disturbances. We will decipher how the inhibition of autophagy in HepG2 cells may contribute to the development and the progression of steatosis and which are the main cellular pathways affected. Moreover, we plan to investigate whether inducers of autophagy, may delay and/or reverse NAFLD development and what is their effect on cellular metabolism, fatty acid oxidation fluxes and the formation of ROS. Wit the use of a NAFLD mouse model, we will analyse the efficacy of various lipid forms of n-3 PUFA towards different stages of NAFLD and how this is related to changes in fatty acid metabolism, autophagy, and peroxisome function in the liver.

Requirements:

- A master's degree (or an equivalent) in biology, biochemistry, molecular biology, molecular biomedicine, medicine, genetics or biotechnology,
- good command of spoken and written English,
- knowledge of the standard biochemistry and molecular biology techniques,
- a strong motivation and ability to drive the project independently,
- well-developed collaborative skills,
- curiosity for discovery of biological processes,
- knowledge of statistics, experience of working with laboratory animals, documented scientific activity (e.g. publications, presentations at conferences, research internships, awards, scholarships) will be an additional advantage.