

Project 1 – Why does obesity cause Type 2 diabetes?

Background

Due to the growing obesity epidemic, the number of people with type 2 diabetes (T2D) is predicted to rise to over 750 million in 2045. Notably, the undiagnosed number of people with T2D is significant, partly because the progression of diabetes is silent and can be present for many years before diagnosis. T2D is multifactorial, involving the interaction of genes and environmental-behavioural risk factors. Over the last years, treatment options have improved, but there is still a great need for the discovery of novel treatment concepts.

One specific research topic that our group is interested in is the **link between obesity and type 2 diabetes**. Why is obesity associated with an increased risk of diabetes? Moreover, why does obesity surgery that leads to weight loss cause marked improvements in metabolism, not found/above what is found with diet-induced weight loss alone? In this context, we identify novel genes in human adipose tissue associated with the link between obesity and insulin resistance. In order to elucidate potential molecular mechanisms for these candidate genes, we use CRISPR-Cas9, a pioneering genome-editing technique, to generate loss-of-function cell models. Phenotyping of the knock-out cells is focused on metabolic measures, such as glucose and lipid metabolism and fat cell development, as well as changes in gene and protein expression.

Another specific research topic is the **link between inflammation, the immune system, and metabolism**. Anti-inflammatory approaches have attracted much interest as a means to treat T2D during the last decades. Conversely, some pharmacological agents with anti-inflammatory properties, such as glucocorticoids and antipsychotic drugs, can induce metabolic syndrome and diabetes. Our previous studies suggest that multiple mechanisms seem to be involved in inflammation-associated diabetes, including fibrosis. This project is a continuation of previous work where we plan to answer different questions: How do inflammation and associated fibrosis contribute to adipose tissue insulin resistance? Which circulating and adipose tissue factors are markers of insulin resistance in metabolically healthy or unhealthy obese? Does adipose tissue function, including adipocyte metabolism and immune cell profile, shape the response to pharmacological treatment? Adipose tissue pharmacotherapy is an experimental model for understanding the biology of this critical metabolic tissue.

These projects have a strong translational focus, ranging from experimental studies explored in clinical cohorts and cell models to observational studies to support target validation. There is the potential for publication in high-impact journals.

Methods

The student can use techniques such as tissue and cell culture, histology, immunofluorescence, gene and protein expression, glucose uptake, lipolysis and lipogenesis, and CRISPR-Cas9 gene editing. Apart from the tasks above, the student will also have the possibility to get acquainted with several methods related to handling human adipose tissue obtained from human biopsies.

Are you interested in our work? Looking for a MSc project?

We are always looking for creative and motivated students who want to work in our lab. You will be part of a highly interactive group and profit from the group's experience in experimental and theoretical work. You will get to familiarise yourself with this exciting research area, work experimentally under supervision, learn to handle pre-clinical data in a structured way, make the calculations and present the results in a report and/or article. We hope this independent work leads to a continued interest in metabolism and kidney medicine, patient-related research, and graduate education.

If interested, please contact us for more information:

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