PhD Student Anne Lundager Madsen
Place of enrolment: University of Copenhagen, Faculty of Health and Medical Science
Principal supervisor: Torben Hansen, The Novo Nordisk Foundation Center for Basic Metabolic Research, Section for Metabolic Genetics

Title of project: Unravelling mechanisms related to glucose stimulated beta-cell function – A systematic genetic examination of measures of oral glucose stimulated insulin secretion

ABSTRACT

Background and purpose

The scientific literature use different measures for estimating insulin secretion by the beta cells after an oral glucose stimulation.

The aim of the project is to examine if different estimates for insulin secretion by the beta cells in pancreas capture different aspects of the biological mechanisms behind the glucose stimulated insulin secretion, i.e. beta cell function (BCF). A detailed genetic examination of BCF estimates will provide novel insights into diabetes and other diseases related to dysregulated glucose homeostasis.

Methods

Genetic variants associated with several glucose-stimulated BCF estimates will be identified by genome-wide association analysis (GWAS) with approx. 31,600 individuals from Nordic cohorts. The heritability of each BCF estimate will be investigated and the genetic correlations of the BCF estimates will be calculated. Finally, genetic variants located in enhancer regions mapped to regulate specific beta cell genes will be associated to the various BCF estimates to elucidate the functional consequence of the genetic variant.

Significance of the project

A better understanding of how to use the various BCF estimates through a systematic approach is crucial to the field of metabolic research. Knowledge about the factors involved in the regulation of BCF is essential in the prevention and treatment of diabetes and its related diseases.

ABSTRAKT

Baggrund og formål

I den videnskabelige litteratur anvendes forskellige metoder til at estimere beta-cellens evne til at secernere insulin efter indtag af sukkervand kaldet beta-celle funktions-estimat (BCF-estimat).

Formålet med projektet er at undersøge om de forskellige estimater for insulin sekretion fra beta-cellerne i pancreas giver forskellig viden om de biologiske mekanismer bag BCF. En detaljeret genetisk undersøgelse af de enkelte BCF-estimaterne vil give bedre indsigt i diabetes og sygdomme, der er relateret til forstyrrelser i BCF.

Metode

Genetiske varianter associeret med forskellige BCF-estimater vil blive identificeret ved *genome-wide* associationsanalyser (GWAS) i et studie af ca. 31.600 individer. Arveligheden af de enkelte BCF-estimater vil blive undersøgt og den genetiske korrelation mellem BCF-estimaterne vil blive udregnet. Endeligt vil genetiske varianter lokaliseret i *enhancer* regioner, som er blevet kortlagt til at regulere specifikke beta-celle gener, blive associeret til BCF-estimaterne. Dette vil belyse den funktionelle betydning af den genetiske variant yderligere.

Projektets signifikans

En bedre forståelse af forskellige BCF-estimater vil være afgørende for en dybdegående forståelse af beta-cellens funktion og vil tillade en mere systematisk tilgang til forskning i beta-cellen. Viden om faktorerne, der er involveret i regulering af BCF er essentiel for forståelsen af progression og behandling af diabetes.