PhD Student, **Amalie London**, MD.

Place of enrolment: University of Copenhagen, Faculty of Health and Medical Sciences

Principal supervisor: Professor **Bente Kiens**, University of Copenhagen, Department of Nutrition, Exercise and Sports Sciences

Title of project: Targeting liver fat accumulation by dietary interventions

ABSTRACT

Hepatic accumulation of triacylglycerol (TG) is a key factor in the pathophysiology of the metabolic syndrome, and there is a linear relationship between the degree of hepatic TG accumulation and the occurrence and severity of several of the components of the metabolic syndrome (elevated concentrations of circulating glucose, insulin and TG) which seems to be closely linked to impairments in hepatic insulin action and clearance. Moreover, excess hepatic TG seems to induce resistance for the effect of glucagon on hepatic amino acid metabolism leading to increased concentrations of circulating amino acids (AAs) and glucagon. The molecular regulatory mechanisms linking hepatic TG accumulation to these metabolic disturbances are, however, not completely understood.

Reducing hepatic TG content is an appealing therapeutic goal since it will target both the metabolic disturbances (impaired glucose tolerance/type 2 diabetes and dyslipidemia) as well as the risk of progressive liver disease (non-alcoholic steatohepatitis and NASH-cirrhosis). Currently, weight loss is the recommended treatment for patients with liver steatosis and metabolic syndrome, and weight loss inducing drugs (including GLP1 receptor agonists) are currently evaluated for liver effects. However, it may be possible to target liver TG content in a more specific way by dietary interventions not solely focusing on energy content but also on macronutrient composition as well as timing of intervals between eating and fasting.

It is the aim of this PhD study to evaluate the metabolic effects of dietary interventions designed to target liver TG preferentially and thereby to increase the knowledge about the regulatory mechanisms linking hepatic TG accumulation to impairments in hepatic gluco- and lipid regulation including the effects on insulin action and clearance. Two short term human dietary intervention studies will be performed to evaluate the acute effects of 1. Manipulation of dietary carbohydrate and fat availability and 2. Intermittent fasting (5+2 diet) compared with daily caloric restriction. The hypothesis is that liver TG and liver glucose and lipid metabolism respond rapidly (i.e. within days) in response to targeted dietary interventions.