PhD Student **Ellen Gammelmark, BSc**

Place of enrolment: University of Southern Denmark, Faculty of Science

Principal supervisor: Professor Susanne Mandrup, University of Southern Denmark, Department of Biochemistry and Molecular Biology

Title of project: Adipose Tissue Plasticity and Cellular Crosstalk at Single-Cell Resolution during Regression of Obesity

ABSTRACT

Obesity and its co-morbidities constitute a major challenge to human health worldwide. There is increasing evidence that changes in adipose tissue function constitute key drivers of the development of obesity co-morbidities. One of the biggest challenges in the management of obesity is the prevention of weight regain after successful weight loss. It is still largely unknown to what extent the obesity-induced changes in different adipose tissues are reversed by weight loss, or whether there is a molecular or cellular "memory" of the obese state that affects the function and health of adipose tissues after weight loss. The overarching aim of this project is to understand adipose tissue plasticity and crosstalk between adipocytes and macrophages at single-cell resolution during regression of obesity. I will use mouse models to map adipose tissue plasticity at single-cell resolution during regression of obesity. Furthermore, I will identify key transcriptional drivers involved in adipose tissue plasticity during regression of obesity by investigating epigenomic changes at single-cell resolution. Based on single-cell transcriptomics and epigenomics, I will infer crosstalk between different cell types during regression of obesity, with a particular focus on different subtypes of adipocytes and macrophages. Specifically, I will in international collaboration with Dr. Nicolas Venteclef test the hypothesis that fatty acids released by lipolysis signals to macrophages, and I will investigate the mechanisms involved. In collaboration with my clinical co-supervisor Assoc. Prof. MD Mette Enok Munk Lauridsen, I will analyse changes in human abdominal subcutaneous adipose during regression of obesity, using biopsies from patients undergoing bariatric surgery. I will do this by applying a combined bulk RNA and single-cell transcriptomics approach to determine major changes in cellular composition as well as changes in the transcriptome of specific cell types. The mechanistic understanding from mouse tissues will then be used to infer molecular and cellular aspects of adipose tissue plasticity during regression of obesity in humans. With this PhD project, I expect to gain completely new insight to the plasticity of adipose tissue in response to regression of obesity, which may aid in the development of effective strategies to prevent weight regain after successful weight loss.