

PostDoc Kaja Plucinska

Place of enrolment: University of Copenhagen, Center for Basic Metabolic Research
Principal investigator: Brice Emanuelli, Center for Basic Metabolic Research, University of Copenhagen

Title of project: Thermo-adipokines: Novel Brown Fat Enriched Secreted Factors as Potent Regulators of Metabolic Homeostasis.

ABSTRACT

Fat tissues play a critical role in the pathogenesis of metabolic disorder, due to altered secretion of essential hormones (collectively termed adipokines), lipid 'spill-over' from white adipose tissue (WAT) and impaired thermogenic activity of brown adipose tissue (BAT). The healthy impact of the calorie-burning BAT on whole-body metabolic homeostasis holds a strong anti-diabetic potential, yet, novel strategies are required for activation of BAT in obese individuals. Up to date, BAT research has largely focused on UCP1-related thermogenesis; it has only recently become apparent that, similarly to white fat, BAT may secrete regulatory endocrine factors. Since brown fat enriched adipokines are known to facilitate BAT activity and metabolic homeostasis, there is an urgent need to further uncover *brown fat secretome* and test its therapeutic potential in metabolic disease. To address this gap, I recently discovered 210 novel brown fat enriched adipokines (*thermo-adipokines*) via RNA-sequencing of adipose tissue from mice exposed to chronic cold (5°C, major thermogenesis inducer). These *thermo-adipokines* are likely involved in maintenance of BAT activity and healthy energy balance *in vivo*. My preliminary data further suggest that several of these novel players are involved in BAT impairment during obesity. This fellowship aims to functionally test 4 lead *thermo-adipokine* candidates against metabolic disorder using CRISPR-mediated gene manipulation in high-fat diet challenged mice. A potential ground-breaking outcome of this project is a preclinical validation of circulating factors that modulate energy homeostasis, appetite and/or body weight, which may become of particular interest for diagnostic or therapeutic purposes in human metabolic disease.