## Summary

Balancing fluctuations in availability and requirements of metabolic energy is vital for life. Adipocytes are central players in this equation and disturbances in adipocytes lipid storing capacity lead to a plethora of human diseases. The recent upsurge in adipocyte biology research coincident with the onset of the obesity epidemic, and for the first time in human history the global burden of overnutrition outpaces that due to undernutrition. Give its central role in energy homeostasis adipocytes have become of great interest and an important therapeutic target. The primary aim of this thesis is to dissect the transcriptional network controlled by lipolysis in adipocytes.

The work in this thesis is split into four different parts. **In Part 1**, we used a novel compound that activate adipose triglyceride lipase (ATGL)-mediated lipolysis independent of receptor- and PKA-mediated activation to study the effects of lipolytic products on transcription in brown adipocytes. We provide evidence that acute activation of lipolysis resembles β-adrenergically-induced browning, indicating that lipolytic signals are crucial mediators of the β-adrenergically-induced thermogenic program. Using a machine-learning tool to identify transcriptional mediators of acute lipolysis activation, we showed that lipolysis initiates highly interconnected transcriptional networks involved in peroxisome proliferator-activated receptor (PPAR) signaling, unfolded protein response (UPR) and circadian rhythm.

**In Part 2**, we identified the G protein-coupled receptor 3 (GPR3) to be the most regulated GPCR in a lipolysis-dependent manner in mouse brown adipocytes. We uncover a parallel mechanism whereby cold exposure increases the expression of the constitutively active receptor, *Gpr3*, to modulate cAMP levels and thermogenic output independently of a ligand. Transcriptional control of *Gpr3* affords the brown adipocyte the ability to non-adrenergically sustain lipid oxidation throughout cold or diet-induced adaptive thermogenesis.

**In Part 3**, we utilized a novel 3D culturing system of mature *in vivo* differentiated adipocytes to show that basal lipolysis maintains PPAR signaling in a lean state. Importantly, our results reveal that obesity changes the signaling properties of the adipocytes leading to a differential transcriptomic response to basal lipolysis. However, this needs further validation.

**In Part 4**, we determined the effects long chain ω3-polyunsaturated fatty acids (ω-3 PUFAs) on the transcriptome of human adipocytes. We show that treatment of human adipocytes with ω-3 PUFAs leads to a pro-inflammatory transcriptional response and down regulation of adipocyte identity genes, and leverage serum normalization to overcome the pro-inflammatory effects of ω-3 PUFAs allowing for investigation of mechanistic and functional effects *in vitro*.