**Influence of Distinct MicroRNAs on White and Brown Adipogenesis in Human**

While pharmacological treatments to fight obesity by reducing energy intake have repeatedly failed, increasing energy expenditure via thermogenesis in brown adipose tissue (BAT) constitutes a promising weight loss strategy. However, fat cell (adipocyte) development and physiology are still poorly characterized at the molecular level. This is most evident for non-protein-coding RNAs (ncRNAs), many of which have been discovered only a few years ago. MicroRNAs (miRNAs) are one such group of ncRNAs that direct post-transcriptional gene silencing via binding to complementary messenger RNAs (mRNAs), thereby dampening protein output. Using human and mouse in vitro model systems, the global miRNA expression profile during adipogenesis was analyzed. Subsequently, three candidate miRNAs were selected for functional characterization. First, miR-27b was found to decrease during adipogenesis, was identified as the first miRNA in human to negatively regulate adipocyte differentiation, and was shown to directly target the adipogenic key transcription factor PPARgamma. Second, miR-30c, which increased during human adipogenesis, was found to promote adipocyte differentiation and directly target the adipokine PAI-1 and the receptor ALK2. Interestingly, combined silencing of PAI-1 and ALK2 recapitulated the pro-adipogenic effect of miR-30c. Thereby, for the first time in the study of adipogenesis, a miRNA was revealed as a possible coordinator of two previously unconnected pathways. Third, another miRNA was found to increase during human adipocyte differentiation. Interestingly, overexpression of this miRNA promoted a brown gene expression program, most importantly a pronounced upregulation of UCP1, which ultimately resulted in enhanced metabolic activity. In line with this, the miRNA was induced in white adipose tissue (WAT) of cold-exposed mice, suggesting this transcript to be a physiological mediator of cold acclimation. Mechanistically, three known suppressors of the brown adipocyte phenotype were validated as direct targets of this miRNA. In sum, three miRNAs have been identified as novel players in human adipogenesis. Especially the discovery of the first miRNA promoting a brown phenotype might be of therapeutic impact to increase energy expenditure in fat for the purpose of weight loss.