Summary

Adipose tissue (AT) is a complex organ specialised in safe storage and release of energy as lipids. The adipose organ is therefore essential for the maintenance of energy homeostasis. The prototypical cells of AT are adipocytes, emerging from the precursors in a process called adipogenesis. Adipogenesis itself is tightly connected with lipogenesis, i.e. with the synthesis of fatty acids and triglycerides. Various stimuli can disturb adipocyte differentiation and lipogenesis and thus contribute to AT dysfunction and development of associated metabolic diseases.

This thesis was focused on the investigation of lipogenesis in the context of endoplasmic reticulum stress (ERS), calorie restriction and aging.

In **Project A**, we showed that exposition of adipocytes to high acute ERS inhibits expression of lipogenic genes and glucose incorporation into lipids. Moreover, chronic exposure of preadipocytes to ERS impaired both, lipogenesis and adipogenesis. On the other hand, chronic low ERS had no apparent effect on lipogenesis in adipocytes. These effects of ERS could therefore contribute to the worsening of AT function seen in obesity.

The capacity of AT to store lipids decreases in aging, possibly due to the accumulation of senescence cells or higher ERS. In **Project B**, we investigated lipogenic capacity of human AT in relation to senescence and markers of ERS. AT and adipose cells from young and elderly women were investigated. While mRNA expression of major senescent markers was increased in AT from the elderly compared to young individuals, mRNA expression of lipogenic enzymes and chaperones was decreased in AT from elderly individuals. These results were also partly observed *in vitro* in differentiated adipocytes from AT of the same individuals suggesting the reduced capability to cope with ERS in aging.

Very-low calorie diet (VLCD) is first line lifestyle intervention to achieve rapid weight loss. The improvement of whole body insulin sensitivity can be seen as soon as after 2 days of VLCD. However, little is known about AT metabolic changes in those early days. Thus, in **Project C**, we compared metabolic and inflammation-related characteristics of subcutaneous AT in the early (2 days) and later (28 days) phase of a VLCD. In the early phase of VLCD, the expression of lipolytic genes was increased, whereas the expression of lipogenic genes was suppressed. The inflammatory markers remained unchanged in AT. The changes in AT gene expression in the early phase of VLCD could not explain the effect of short calorie restriction on

the improvement of insulin sensitivity. At the later phase, expression of genes involved in lipogenesis and β-oxidation was markedly suppressed, whereas the expression of inflammatory markers was increased. Thus, we found that the early and later phases of VLCD differ with respect to metabolic and inflammatory responses in subcutaneous AT.

In **Project D**, we compared and defined the effects of moderate calorie restriction on preadipocytes and *in vitro* differentiated adipocytes in two groups of obese men: juniors and seniors. We did not observe any effect of the intervention on metabolism of preadipocytes in either group. However, we observed an intervention-driven improvement in adipocyte metabolism selectively in the group of seniors. Therefore, our data suggest that moderate calorie restriction could initiate positive changes in metabolism of adipocytes in seniors.

In conclusion, this thesis brought several pieces of evidence that lipogenesis in human AT can be inhibited by ER stress, severe caloric restriction and aging.