Summary

Being able to respond metabolically to stressful situations, such as acute starvation, is of great importance to the survival of all organisms. Although, not common in the Western World today, the human species did indeed evolve under the omnipresent threat of hunger. While metabolic syndrome and diabetes are more present threats to our health today, we can certainly benefit from knowledge of the metabolic machinery that sets in when nutrients are scarce; introducing periods of reduced calorie intake can help cure metabolic diseases and have numerous other beneficial effects, including delayed aging. ½

In this thesis, the different aspects of starvation responses are approached from multiple angles in the nematode *C. elegans*; in the first study discussed, a multi-omics starvation time series approach revealed that regulation of the lipid stores by the transcription factor HLH-30 through the lipid transporters, the vitellogenins, is crucial for survival under acute starvation. The role of HLH-30 was further investigated in an unpublished study, revealing that orthologs of DAP1 is commonly up-regulated under acute starvation and in the sterile mutant *glp-1*, in an HLH-30 dependent manner. Being an inhibitor of the intracellular degradation process autophagy, DAP1 likely keeps this process in check and is possibly important for the shared phenotypical traits of starved and sterile animals.

In the second study, regulation of autophagy was investigated by phosphoproteomics and a series of drugs, including inhibitors of mTORC1, thus simulating nutrients scarcity. These studies led to the finding of multiple candidate proteins conserved from nematodes to humans, and evaluation of the importance of specific phosphosites for regulation of autophagy.

In total, these studies give a detailed, multi-omics representation of the response to starvation, describe vitellogenins as potential HLH-30 targets crucial for survival under starvation, reveal important phosphosites for regulation of autophagy, and elaborate the previously suggested connection between sterility and reduced calorie intake. Moreover, by applying a multi-omics approach, we emphasize the importance of describing novel molecular mechanisms at multiple levels as the different levels of regulation do not necessarily correlate.