Summary

Adapting metabolism in response to environmental alterations is one of the most prevalent mechanisms promoting survival and ensuring balanced growth for all organisms. Over the course of time, nutritional stress in the form of starvation has induced evolutionarily conservation of such mechanisms across many different species. Even though starvation is not a common health issue in the Western World today we can still greatly benefit from understanding the nutrient-derived responses induced by starvation. Obesity is the nutritional stress posing a threat to our health today, causing metabolic syndrome and diabetes among others. The increasing prevalence of obesity has especially made lipid metabolism a high-profile target for understanding the metabolic cues leading to this condition. Importantly, lowering caloric intake has several beneficial effects on metabolic diseases brought on by diet-induced obesity in addition to numerous other physiological benefits including aging. Therefore, expanding the knowledge of the underlying molecular mechanisms regulating metabolism in response to nutritional alterations is of great importance.

This thesis approaches the different aspects of the starvation response in the nematode C. elegans. The first study presented investigates the starvation response in a temporal manner by applying proteomics and transcriptomics. This multi-omics analysis reveals that the transcription factor HLH-30/TFEB regulates lipid stores through specific lipid transporters called vitellogenins and that this regulation is crucial for surviving starvation. The second study further investigates the regulatory role of HLH-30/TFEB in the starvation response from a different angle. Here a combination of metabolomics and lipidomics shows that HLH-30/TFEB is important for maintaining mitochondrial functions specifically in upholding β-oxidation during starvation. Furthermore, a novel mechanism for peroxisomal β-oxidation in the starvation response is revealed as the removal of the peroxisomal assembly factor PRX-5 impairs the survival of the C. elegans mutant lacking functional hlh-30 during starvation.

Collectively, these studies have assessed the starvation response in a global manner and thereby provided several interesting findings contributing not only to the common knowledge of the starvation response on molecular level but to the continuing efforts of finding new ways of improving healthy living and even healthy aging.