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Title of project: Identification of Metabolic and Lifespan Biomarkers Regulated by Dietary Intervention Mimetics Across Species

ABSTRACT

Identification of Metabolic and Lifespan Biomarkers Regulated by Dietary Intervention Mimetics Across Species

Dietary intervention (DI) without malnutrition extends lifespan across species from yeast to primates. It is well established that restricting food intake by 25-40% can extend the lifespan of rodents and protect from metabolic diseases such as diabetes and obesity, as well as cancer, cardiovascular disease and other age-related complications. Evidence of similar benefits in primates (including humans) is mounting, but more studies are required to define safety and efficacy of DI in humans. **This project aims to discover and compare new molecular networks involved in the lifespan and metabolic health benefits promoted by DI and its mimetics within and across species.** In order to achieve this, we have designed a pipeline to determine biologically relevant pathways affected by these interventions. We took advantage of the multidisciplinary expertise of our team to explore the effects of dietary interventions [i.e., (DI), dietary methionine restriction (MR) and nicotinamide riboside (NR) supplementation] in various animal models and in humans. In brief, we have sequenced and are currently analyzing the transcriptome and metabolome of samples obtained from *C. elegans*, as well as adipose tissue and serum from mice and humans (healthy and/or type 2 diabetics) following NR treatment as well as in conditions of MR or DI. In addition, we performed metagenomics sequencing and analyses of the microbiota of mice and humans since changes in the microbiome have been associated with the effects of DI. We will correlate these findings with lifespan and/or metabolic profiling using data integration through genome-scale modeling approaches in order to identify evolutionarily conserved pathways that are commonly affected by DI, MR and NR treatments. The relevant pathways will then be scrutinized using gain- or loss-of-function models in *C. elegans*, mice and mammalian preadipocyte cell lines. Collectively, this project will provide novel insights into how these dietary interventions affect health span in multiple organisms, including humans.