Metabolic Network Analysis for Understanding the Biology of Ageing

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Ageing is a complex process, marked by a progressive functional and physiological decline that results in increased morbidity and culminates in death. Ageing is one of the major risk factor of a plethora of human diseases such as cancer, cardiovascular and neurodegenerative diseases, thus drawing significant fraction of government spending in industrialized countries. Without a concomitant or faster increase in the length of healthy life, longer lifespan would translate to higher health care spending. In this regard, a better understanding of the biology of ageing has the potential to delay the onset of age-related diseases, extend healthy life expectancy, and thus reduce the socioeconomic burden of a greying population.

The biology and mechanism of ageing is still poorly understood and the role of ageing in causing or predisposing individuals to diseases with varying pathologies remains largely unknown. The complexity of the ageing process has motivated applying a systems-oriented approach to ageing research in the last decade, involving the creation and analysis of network of biological interactions among cellular components. The close connection between ageing and metabolism is well documented, but the specific metabolic pathways that are involved in the ageing process are still hazy. In this study, we analyzed human transcriptomics data from the Genotype-Tissue Expression (GTEx) project. In particular, we employed the linear mixed effects model to determine age-related gene expression changes across different human tissues. Subsequently, we projected the age-related gene expression changes onto human genome scale metabolic model based on the constraint-based modeling of flux balance analysis. By doing so, we were able to show specific age-related alterations in metabolic pathways across different tissues. In our continuing work, we will use this knowledge to identify potential metabolic targets whose regulation may reverse the changes during ageing, and validate these targets using *Caenorhabditis elegans.*