

Master thesis project II – development of an *in silico* approach to predict the impact of genetic perturbation on longevity

Background

Slowing down the pace of aging could have a major impact on human lifespan and healthspan, but we still lack a deep understanding of the aging process. A reason for that is the long duration and cost of lifespan screens *in vivo*, which prohibit researchers from deeply exploring the molecular basis of the regulation of longevity. While many whole-body lifespan screens have been conducted in *C. elegans*, a widely used model for aging research, almost no *in silico* methods have been developed to date.

Project aims and description

In this project, we propose to develop an innovative approach to predict the lifespan changes induced by the knockout, knockdown, or overexpression of transcription factors in a given tissue in *C. elegans*. This approach will rely on the recently published CellOracle method, which can predict the impact of genetic perturbations on a given dynamic process. We will apply the CellOracle method to a large single-cell RNA-seq dataset of *C. elegans* worms of different ages to estimate the impact of perturbing various transcription factors on the age of cell types and tissues. Then, we will use our new model to systematically generate tissue-specific knockdowns and overexpressions to explore the landscape of genetic perturbations influencing lifespan *in silico*.

Perspectives

Biologists in our group will experimentally validate the effect of genetic perturbations with the highest predicted lifespan changes. We expect our project, if successful, to drastically accelerate the pace at which discoveries of aging regulatory mechanisms in *C. elegans* can be made, provide a better understanding of the tissues regulating longevity, and lead to the identification of interventions to slow down aging in mice and humans.

Contact

If this sounds of interest to you, don't hesitate to contact:

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