Master thesis project I – Prediction of lifespan from chromatin accessibility and gene expression data

Background

The past decades have seen a multitude of aging-preventive interventions being developed by many research groups across the world. However, evaluating the efficacy of these interventions for slowing down the aging process, improving health and delaying the appearance of aging-associated diseases is often a very long and tedious process. Therefore, the aging field has seen a huge interest in the development of so-called "aging clocks" that allow to predict the relative health of individuals. These clocks typically predict chronological age from various types of measurements, including different omics data. The difference between predicted and true age can be used as a proxy of the health of an individual as compared with other individuals of the same age. The most promising clocks of aging have so far been developed from DNA methylation data. However, they suffer from high experimental cost and the difficult interpretation of the methylation site selected by the models.

Project aims and description

Our group found that a chromatin remodeler regulates longevity in the model organism Caenorhabditis elegans (see Riedel 2013). This result made us wonder if chromatin remodelers are key regulators of longevity in general. We addressed this question by evaluating the regulation of lifespan of multiple chromatin remodelers in different long-lived C. elegans strains using a two-step RNAi screen. Several chromatin remodelers were found to regulate lifespan. To characterize the molecular mechanisms that provide the longevity phenotypes of these factors, we did ATAC-Seq and mRNA-Seq measurements for each of them. The resulting data was preprocessed using an in-house developed analysis pipeline. The selected master thesis student will now be in charge of addressing the question of whether accessibility and transcription of specific loci are associated with age and / or can be used to make accurate age predictions. In addition, the student will explore the general impact of the chromatin remodelers on the chromatin accessibility landscape and how this relates to the described longevity phenotype.

Contact

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

Staff Scientist: Jerome Salignon, jerome.salignon@ki.se

Group Leader: Christian Riedel, christian.riedel@ki.se

Master thesis project II – Big data analysis for the discovery of new aging-preventive factors

Background

Big datasets are becoming increasingly available in biology. This accumulation of data permits the development of predictive models of unprecedented accuracy. In the field of aging, this has led to the advent of "aging clocks" that can predict individuals ages – usually from various types of omics data. Another recent trend in the aging field is the prediction of aging-preventive or even rejuvenating compounds (also known as geroprotectors). However, in silico approaches for either of these purposes are still in their infancy and there is still plenty of room for innovative approaches that combines different datasets in an elegant way to discover promising aging preventive compounds and health promoting interventions.

Project aims and description

Our laboratory has developed methods to predict drugs or genetic interventions that modulate aging by shifting the cells to a younger state. In this project, we propose for interested students to continue in this line of research by helping to further improve our current method, by refining it and including also yet other datasets (i.e. Swedish registry data, single cell omics data, etc…).

Contact

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

Staff Scientist: Jerome Salignon, jerome.salignon@ki.se

Group Leader: Christian Riedel, christian.riedel@ki.se