Universitat Pompeu Fabra Barcelona

Master in Bioinformatics for Health Sciences

Master project 2021-2022

Personal Information

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Project

Computational genomics

Project Title:

Unraveling the intrinsic determinants of dynamic gene expression variability

Keywords:

Gene expression variability, single-cell RNA-seq, cellular stress

Summary:

Virtually all organisms interact with the environment. Sudden changes in the external environment, such as variations in nutrients, oxygen concentration or osmolarity, compromise cell fitness. To survive, cells have developed cellular responses ranging from metabolism tuning to gene expression reprogramming. Upon stress, Saccharomyces cerevisiae (yeast) undertakes a massive gene expression reprogramming involving at least 10 % of the genome. Despite being tightly regulated, gene expression changes differ between cells in a genetically homogeneous population, a phenomenon known as gene expression variability. This variability underlies relevant processes such as stress responsiveness, antibiotic and chemotherapy resistance or aging. The advent of single-cell RNA-seq (scRNA-seq) technologies allowed the quantification of gene expression variability at genome-wide level. Recently, we and others have developed a range of scRNA-seq methods (1-7) for interrogating single-cell yeast transcriptomes under several different conditions (e.g., oxidative, osmotic, and heat stress, galactose media, nitrogen limiting media or aging). For this project, we propose creating a yeast single-cell atlas (yscAtlas), a centralized resource comprising newly generated and published single-cell yeast datasets to profile the dynamics of gene expression variability. Leveraging on the yscAtlas, we will stratify all the yeast genes by their gene expression variability profile under changing environmental conditions. Based on this stratification, we will determine the biophysical and biochemical features associated with specific gene expression variability dynamics. To link specific gene features with gene expression variability dynamics, we will use state-of-the-art scRNA-seq data integration methods (e.g., MNNs, CCA), visualization methods (e.g., tSNE, UMAP), a set of complementary gene expression variability metrics and data modelling approaches.

References:

1. Gasch, A. P. et al. Single-cell RNA sequencing reveals intrinsic and extrinsic regulatory heterogeneity in yeast responding to stress. PLoS Biol. 15, e2004050 (2017). 2. Nadal-Ribelles, M. et al. Sensitive high-throughput single-cell RNA-seq reveals within-clonal transcript correlations in yeast populations. Nat. Microbiol. 4, 683–692 (2019). 3. Saint, M. et al. Single-cell imaging and RNA sequencing reveal patterns of gene expression heterogeneity during fission yeast growth and adaptation. Nat. Microbiol. 4, 480–491 (2019). 4. Zhang, Y. et al. Single-cell RNA-seq reveals early heterogeneity during ageing in yeast. BioRxiv (2020) doi:10.1101/2020.09.04.282525. 5. Jariani, A. et al. A new protocol for single-cell RNA-seq reveals stochastic gene expression during lag phase in budding yeast. elife 9, (2020). 6. Tsuyuzaki, H. et al. Time-lapse single-cell transcriptomics reveals modulation of histone H3 for dormancy breaking in fission yeast. Nat. Commun. 11, 1265 (2020). 7. Jackson, C. A., Castro, D. M., Saldi, G.-A., Bonneau, R. & Gresham, D. Gene regulatory network reconstruction using single-cell RNA sequencing of barcoded genotypes in diverse environments. elife 9, (2020).

Expected skills::

We are looking for an enthusiastic master student to work in our group with basic knowledge of any programming language (preferably R or Python) and interest in functional genomics.

Possibility of funding::

To be discussed

Possible continuity with PhD: :

To be discussed