Universitat Pompeu Fabra Barcelona | Master in Bioinformatics for Health Sciences

Master project 2021-2022

Personal Information

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Project

Computational systems biology

Project Title:

Defining the molecular landscape of premature aging disease through biological networks

Keywords:

Networks, systems biology, graph theory, clustering, premature aging disease.

Summary:

Premature aging (PA) syndromes, also called Progeroid syndromes, are a group of rare genetic disorders that phenotypically recapitulate some of the aspects of physiological aging at an early age. These syndromes are clinically and genetically heterogeneous (Navarro et al., 2006). They are usually monogenic, i.e., caused by mutations in single genes, but can affect few or many tissues, different loci can lead to similar diseases, and, contrarily, the phenotypes and severity can vary considerably across individuals carrying the same mutations. Genes and proteins do not act isolated in cells but rather interact with each other to perform their functions in molecular complexes, pathways, and other biological processes. Mutations in genes and proteins will thereby affect their interactions and consequently the biological processes in which they are involved (Zhong et al., 2009). Diseases hence arise from network perturbations, and studying the complex biological networks in which genes and proteins participate is a first step towards better understanding the genotype to phenotype relationships in diseases (Schadt, 2009). Biological interaction data are accumulating since the development of experimental techniques allowing their identification on a large-scale. These interactions are usually represented as large networks in which the nodes correspond to the genes or proteins, and the edges represent their physical or functional interactions. Biological networks are usually organized in communities, i.e. structured around groups of nodes more densely connected with each other than with the rest of the network. These groups of tightly connected nodes, usually called modules, contain genes/proteins likely to be involved in the same cellular functions or processes in cells (Hartwell et al., 1999). The accurate extraction of these modules is promising in biomedicine because studying the modules in which the mutated genes/proteins are involved can reveal the cellular and molecular mechanisms underlying diseases (Furlong, 2013). We propose a project in which we aim at systematically identifying the modules associated with the different PA diseases and their causative genes. We hypothesized that those modules would i) reveal the biological processes perturbed in these diseases, but also ii) define a comprehensive landscape of biological processes perturbed in PA disorders. These results may provide a better understanding of the disease molecular mechanisms and reveal their links with physiological aging processes. During the internship, the student will get familiar with biological networks and graph theory. He/She will apply different methods from this field, such as random walks or community identification. He/She will also get his/her hands on the different types of biological networks, which can better describe the complexity of biological systems, like multiplex or heterogeneous networks. Moreover, the selected candidate will apply the acquired knowledge to a concrete biological question: obtaining new insights about premature aging diseases. Therefore, the student will learn about these syndromes and their potential links with physiological aging. Our group has extensive experience in the development of computational methods to extract the knowledge contained in biological networks (Didier et al., 2018; Novoa-del-Toro et al., 2020; Valdeolivas et al., 2019). We are based in the Faculty of Medicine, located next to the University Hospital of Marseille, La Timone. We work in close collaboration with medical doctors and this hospital which is a European reference in the treatment of rare disease and, in particular, of premature aging diseases. We therefore believe that the selected candidate will have a suitable environment to develop the proposed project. The selected candidate will work in close collaboration with Ozan Ozisik (PostDoc in AB team) and Alberto Valdeolivas (Roche, Switzerland).

References:

Didier, G., Valdeolivas, A., & Baudot, A. (2018). Identifying communities from multiplex biological networks by randomized optimization of modularity. F1000Research, 7, 1042. Furlong, L. I. (2013). Human diseases through the lens of network biology. Trends in Genetics: TIG, 29(3), 150–159. Hartwell, L. H., Hopfield, J. J., Leibler, S., & Murray, A. W. (1999). From molecular to modular cell biology. Nature, 402(6761 Suppl), C47–C52. Navarro, C. L., Cau, P., & Lévy, N. (2006). Molecular bases of progeroid syndromes. Human Molecular Genetics, 15 Spec No 2, R151–R161. Novoa-del-Toro, E.-M., Mezura-Montes, E., Vignes, M., Magdinier, F., Tichit, L., & Baudot, A. (2020). A Multi-Objective Genetic Algorithm to Find Active Modules in Multiplex Biological Networks. In Cold Spring Harbor Laboratory (p. 2020.05.25.114215). https://doi.org/10.1101/2020.05.25.114215 Schadt, E. E. (2009). Molecular networks as sensors and drivers of common human diseases. Nature, 461(7261), 218–223. Valdeolivas, A., Tichit, L., Navarro, C., Perrin, S., Odelin, G., Levy, N., Cau, P., Remy, E., & Baudot, A. (2019). Random walk with restart on multiplex and heterogeneous biological networks. Bioinformatics , 35(3), 497–505. Zhong, Q., Simonis, N., Li, Q.-R., Charloteaux, B., Heuze, F., Klitgord, N., Tam, S., Yu, H., Venkatesan, K., Mou, D., Swearingen, V., Yildirim, M. A., Yan, H., Dricot, A., Szeto, D., Lin, C., Hao, T., Fan, C., Milstein, S., … Vidal, M. (2009). Edgetic perturbation models of human inherited disorders. Molecular Systems Biology, 5(1), 321.

Expected skills::

Programming skills in Python or R are necessary. Familiarity with network science and/or omics data analysis is a plus. Fluency in English is required. The candidate should have a background in one of the following domains: Biology, Medicine, Biochemistry, Biotechnology, Pharmacy, Veterinary studies, engineering studies, Chemistry, Physics or Mathematics or related degrees, complemented by basic knowledge in the other domains.

Possibility of funding::

Yes

Possible continuity with PhD: :

To be discussed