Universitat Pompeu Fabra Barcelona | Master in Bioinformatics for Health Sciences

Master project 2020-2021

Personal Information

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Project

Computational genomics

Project Title:

The role of alternative splicing in the evolution of animal tissue diversity

Keywords:

Alternative splicing, microexons, exon-intron evolution, tissue-specific regulation, parallel evolution.

Summary:

Why evolution of alternative splicing? Alternative splicing (AS) is a molecular process allowing multiple transcripts to arise from the same gene. The power of AS in expanding the functional potential of a gene is well exemplified by the axon guidance receptor Dscam in Drosophila melanogaster. Dscam produces ~38000 distinct transcripts, which uniquely fine-tune the function of the gene in different neurons. AS contributes to functional diversity not only within cell populations but also between cell types/tissues. Our lab is currently investigating the role of AS in the evolution of animal tissue diversity: here we propose a parallel analysis of AS evolution in vertebrates and insects, two monophyletic clades in the bilaterian tree. Set up: we inferred exon orthology groups in a set of 20 bilaterian species (8 vertebrates, 8 insects and two pairs of relative outgroups) and we assembled a comprehensive RNA-seq dataset covering 8 homologous tissues in all species. We used the RNA-seq data to identify AS exons within each species and tissue. Experimental design: the project will be divided into three main parts: 1) We will investigate evolutionary patterns involving the entire tissue AS landscapes. Preliminary results show that neural and muscle AS networks seem to be well conserved in vertebrates but not in insects, suggesting different rewiring rates between the two clades. 2) We will focus on the exons specifically spliced within each tissue. Many tissue-specific exons have acquired tissue-specific regulation millions of years after their birth. An exciting perspective is the identification of a causal relationship between changes in exon regulation and simultaneous phenotypic innovation/adaptations. 3) We will explore the regulatory mechanisms underlying the rise of tissue-specific AS. The master project will be developed as part of this bigger project on exon evolution. The student will become familiar with the principles of alternative splicing and gene regulation, while getting hands-on experience with genome annotations, RNA-seq data analysis, comparative transcriptomics, and network reconstruction.

References:

- Torres-Méndez, A., Bonnal, S., Marquez, Y., Roth, J., Iglesias, M., Permanyer, J., Almudí, I., O'Hanlon, D., Guitart, T., Soller, M., Gingras, A.-C., Gebauer, F., Rentzsch, F., Blencowe, B.J.B., Valcárcel, J., Irimia, M. (2019). A novel protein domain in an ancestral splicing factor drove the evolution of neural microexons. Nature Ecol Evol, 3:691-701. - Marletaz, F., Firbas, P., Maeso, I., Tena, J.J., Bogdanovic, O., Perry, M., Wyatt, C.D.R., [+50 authors], Holland, P.W.H., Escriva, H., Gomez-Skarmeta, J.L., Irimia, M. (2018).

Amphioxus functional genomics and the origins of vertebrate gene regulation. Nature, 564:64-70. - 6) Burguera, D., Marquez, Y., Racioppi, C., Permanyer, J., Torres-Mendez, T., Esposito, R., Albuixech, B., Fanlo, L., D'Agostino, Y., Gohr, A., Navas-Perez, E., Riesgo, A., Cuomo, C., Benvenuto, G., Christiaen, L.A., Martí, E., D'Aniello, S., Spagnuolo, A., Ristoratore, F., Arnone, M.I., Garcia-Fernàndez, J., Irimia, M. (2017). Evolutionary recruitment of flexible Esrp-dependent splicing programs into diverse embryonic morphogenetic processes. Nat Commun, 8:1799.

Expected skills::

Ideally, experience on RNA-seq analyses and/or comparative genomics. Interest on genome evolution.

Possibility of funding::

To be discussed

Possible continuity with PhD: :

To be discussed