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:

Small-RNAs in neurodegenerative diseases: identification of deregulated species as potential biomarkers and therapeutic targets

Keywords:

small RNA, extracellular vesicles, neurodegenerative disaese, deregulation patterns, biomarkers

Summary:

Background: Neurodegenerative diseases (ND) are debilitating and largely untreatable conditions, whose prevalence dramatically increases in late life. Thus, early diagnosis, patient's stratifications and identification of presymptomatic individuals at higher risk of developing dementia represent important unmet needs. Transcriptional deregulation in ND occurs long before clinical symptoms and pathological hallmarks become evident, and circulating, extracellular RNA (exRNA) has been revealed as a new source of little invasive biomarkers. Our preliminary data show that plasma sub-fractionation provides specific patterns of distribution of protein brain markers and exRNAs in extracellular vesicles (EVs) and non-EV compartments. These results highlight the possibility that both plasma EVs and/or non-EVs compartments are informative layers in biomarker discovery. Moreover, diverse data including our most recent findings suggest that exRNA influence the homeostasis and signaling pathways in brain cells. Objective: The objective of this project is to analyze the exRNA transcriptome and identify new deregulated species in neurodegenerative diseases using small-RNA-seq data. We will evaluate the performance of specific pipelines generated in the lab in comparison with another commonly used analytical platform. Methods: We will use data generated in the lab and/or publicly available data. Transcripts mapping will be performed using STAR toolkit. Quantification and annotation will be carried out using in-house bioinformatic tools: Seqbuster (Pantano et al, 2010) and seqcluster pipelines (Pantano et al, 2011) as well as the exceRpt processing toolkit of the NIH Extracellular RNA Communication Consortium (ERCC) (Rozowsky et al., 2019; doi:10.1016/j.cels.2019.03.004). The integration of the different pipelines will allow us to better characterize the profiles of different small RNA (sRNA) types, such as microRNA, tRNA, snoRNA, piRNA or circularRNA. Differential expression of each sRNA between cases and controls will be carried out using negative binomial generalized linear models through DESeq2 bioconductor R package. Machine learning approaches such as Random Forest or Suport Vector Machines will be performed to evaluate weather global patterns of sRNA types can discriminate disease versus control condition. Functional Genomics of Neurodegenerative Diseases group: Applicants will be integrated into the research group "Functional Genomics of Neurodegenerative diseases" (P.I. Eulàlia Martí), that belongs to the Institute of Neurosciences. We are based at the Department of Biomedical Sciences (Universitat de Barcelona, Campus Clinic), with multidisciplinary research teams tackling different aspects of Neurosciences. This very friendly environment provides a number of different theoretical skills and experimental expertise as well as it gathers many young and successful research leaders. Non-coding RNAs (ncRNAs) generally act as gene expression regulators; and are particularly abundant and diverse in the brain, showing highly dynamic and specific expression patterns. The accurate expression pattern of ncRNAs is fundamental for the correct function of the nervous system and deregulation of ncRNA pathways underlies human disease. Our hypothesis is that the ncRNA profiles reflect in a very precise manner fine-tuned changes in neuronal sates. Our lab has been working for more than 10 years in the understanding of disease-driven deregulation of ncRNAs and their role in neuronal dysfunction. Major challenges in translational biomedicine that are the core research of the lab are (i) to evaluate the potential of ncRNAs as disease-specific, peripheral non-invasive biomarkers and (ii) to understand the functional and pathogenic relevance of these species, which may help to unravel disease mechanisms and identify therapeutic targets. We perform these activities using state-of-the art functional genomics approaches, in mouse models and cell cultures. We have also strong expertise in RNA-seq data mining algorithms to detect candidate ncRNA species. We develop these activities in a network of national and international collaborations to address multidisciplinary aspects of RNA biology in Neurosciences.

Expected skills::

basic bash programming and R programming language knowledge

Possibility of funding::

No

Possible continuity with PhD: :

To be discussed