Post-transcriptional regulatory networks in neurodegenerative diseases

https://neurodegenerationresearch.eu/survey/post-transcriptional-regulatory-networks-in-neurodegenerative-diseases/

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Country

Slovenia

Title of project or programme

Post-transcriptional regulatory networks in neurodegenerative diseases

Source of funding information

SLOVENIAN STATE RESEARCH AGENCY (ARRS)

Total sum awarded (Euro)

€ 58,962

Start date of award

01/08/2013

Total duration of award in years

3

Keywords
Research Abstract
The recent years have seen an explosion of new methods employing high-throughput sequencing (HTS) to understand the functions of RNA-binding proteins (RBPs). The resulting data requires customized computational tools for its interpretation. Here we propose to develop such tools, with the overarching goal to increase the understanding of the mechanistic principles underlying RNA-dependent regulation of gene expression. Therefore, we aim to drive forward the
research in bioinformatics, and provide the tools required by the experimental scientists to study the systems biology of RNA. The project will develop new data mining and artificial intelligence

tools, and embed them into an intelligent web-based assistant for explorative analysis of these data. These tools will significantly advance the data-intensive computational studies of protein-RNA interactions and gene expression. Importantly, these tools will be capable of deriving new hypotheses, which will serve as a starting point for further experiments in the Ule group, aimed at understanding how the defects in the regulatory mechanisms contribute to neurodegenerative diseases. Specifically, we will achieve the following (objectives): 1) Build a computational pipeline to map, quantify and visualize the protein-RNA interactions and model the post-transcriptional regulation of gene expression. 2) Develop a new descriptive language and efficient heuristics to integrate and model the relations among different post-transcriptional regulatory stages and infer new hypotheses explaining the molecular functions of RNA binding proteins and global mechanistic regulatory patterns. 3) Infer predictive models through machine learning and implement an intelligent, web-based interface for explorative analysis that will direct the researcher to the critical regulatory sites and will reveal the regulatory mechanisms unique to each protein. 4) Integrate the data of state-of-the-art high-throughput sequencing methods in order to dissect the molecular mechanisms of the two RBPs associated with neurodegenerative diseases: TDP-43 and FUS.The Zupan group (FRI), University of Ljubljana, Faculty of Computer and Information Science, Ljubljana, Slovenia has a proven track record in the analysis and visualization of next-generation sequencing data, machine learning and software development. Members of the Zupan group will be working closely together with members of the Ule group (LMB), MRC Laboratory of Molecular Biology, Cambridge, UK, which are developing new experimental methods and have expertise in genomics and studies of protein-RNA interactions. Both groups will collaborate with Rogelj group (IJS), Jožef Stefan Institute, Ljubljana, Slovenia who has expertise in neurobiology and is building resources to study the signaling pathways upstream of the RBPs. The three groups have successfully collaborated in the past and have already produced significant joint research results and publications, which warrant success of the proposed project.

Further information available at:

Types:
Investments < €500k

Member States:
Slovenia

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A