Project 9.3 Biological control and pharmacological regulation of RNAs implicated in aetiology of Parkinson's disease (NCN/OPUS)

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www: https://shorturl.at/AHPW3

Background:

Parkinson's disease (PD) is an incurable neurodegenerative disorder affecting all age groups, with the highest prevalence in the elderly (over 1% of the population above 60 years). By 2050, the elderly population is expected to increase by 2.1 billion, resulting in 21 million PD cases in individuals over 60 years. PD is caused by the accumulation of alpha-synuclein (alpha-Syn) protein in the brain. Reduction of alpha-Syn levels may benefit patients, and this is being investigated in current clinical studies.

Studies have shown that small non-coding miRNA-7 and miRNA-153 negatively regulate alpha-Syn production, and reduced levels of these miRNAs in PD lead to overproduction of alpha-Syn. The protein HuR naturally inhibits miRNA-7 production, increasing alpha-Syn levels. Our research suggests that targeting HuR RNA interactions may decrease alpha-Syn levels, offering a potential PD therapy (Zhu S., et al., NAR 2021). Additionally, *C. elegans* nematodes are a promising model for research, possessing the HuR homolog, exc-7, and exhibiting a PD phenotype when producing human alpha-Syn. Moreover, our preliminary data suggests that blocking miRNA-153 production in neuronal cells could be an additional regulatory mechanism for alpha-Syn levels.

Aim:

The main goal of the project is to investigate and potentially regulate the RNA regulatory processes that control the expression of alpha-Syn, a key protein associated with PD pathology. The research program aims to address three main questions: 1) What are the factors and mechanisms regulating the biogenesis of miRNA-153, which controls alpha-Syn in human cells? 2) Can HuR and its ortholog exc-7 regulate alpha-Syn expression in human dopaminergic cells obtained through iPSC technology and in the *C. elegans* PD model? 3) Is it possible to control alpha-Syn expression by inhibiting the formation of RNA-protein complexes? These studies will contribute to a deeper understanding of the regulatory networks involved in PD and may open new therapeutic perspectives focused on alpha-Syn expression.

Requirements:

- Master's degree in biology, biotechnology, biochemistry, genetics, or related fields,
- proficiency in molecular and cellular biology,
- fluent English language skills in both speech and writing,
- excellent interpersonal skills, initiative, good organizational abilities, and strong collaboration skills,
- practical experience in laboratory work,

Previous experience in the following techniques will be an advantage (but is not required):

- cell cultures (cell lines, induced pluripotent stem cells (iPSC), iPSC-derived neurons, cell line modification techniques based on CRISPR),
- *C. elegans* cultivation,
- methods for studying RNA-protein interactions,
- quantitative RNA analyses (RNAseq, qRT-PCR),
- mass spectrometry, proteomics

Number of positions available: 2

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