TITLE OF RESEARCH TOPIC: RNA-based therapy for genetic disorders

Summary:
PhD candidate will work towards designing novel gene therapy approaches for uncurable, rare neurodevelopmental disorders including CTNNB1 syndrome. Candidate will be focusing on the RNA-targeting strategies, particularly on the use of antisense oligonucleotides (ASO), short, single-stranded pieces of DNA, designed to bind RNA in order to alter its processing and expression and thus modulate transcription of genes associated with the disease or their regulatory counterparts. In addition, candidate will try to implement innovative modifications to improve ASO efficiency and ease of delivery. Candidate will actively participate in the establishment of a screening pipeline which will include computation-assisted selection of targets, rational ASO design, construction of reporter systems for ASO evaluation, assessment of the ASO effects by various biochemical assays as well as work with patient-derived induced pluripotent stem cells (iPSC), human organoids and disease-specific mouse models.

Research techniques used:
Throughout their PhD course candidate will be employing a host of biochemical techniques such as molecular cloning, cell culture sand organoid work, transfection of cells, transduction of cells, various literature-based and self-designed reporter systems and activity assays, protein detection by Western blot, luminometry, confocal microscopy, cytometry and quantitative PCR, histological sample preparation and data analysis with statistical tools.

The reason why the topic is innovative:
1. We intend to implement novel improvements to existing RNA-targeting approaches to increase their efficiency.
2. Our work on CTNNB1 syndrome approaches is expected to serve as the case-study for developing an approach pipeline that will allow us faster identification of applicable therapeutic strategies for other similar neurodevelopmental disorders.

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