Project 9.1 Poly(A) tails - central hubs of mRNA stability control

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WWW: https://bit.ly/3wPZLfy

Background:

Gene expression is regulated at multiple levels. Our lab is interested in the regulation of mRNA stability, especially through the modifications of poly(A) tails.

Recently, we have shown that the addition of untemplated uridines to the 3' end of LINE1 retrotransposons precludes their propagation (Warkocki et al. Cell 2018). Moreover, we have identified a family of poly(A) polymerases TENT5, which reside in the cytoplasm and enhance the expression of mRNAs encoding secreted proteins (Moczek et al. Nature com. 2017; Bilska et al. Nature com. 2020; Gewartowska et al. Cell reports 2021). Those enzymes are differentially expressed in tissues and organs, affecting several aspects of animal physiology. TENT5C is an onco-suppressor in multiple myeloma and control immunoglobulin expression in B cells. TENT5A is essential for collagen secretion, and its mutations lead to congenital bone disease

To study the dynamics of poly(A) tails genome-wide, we have implemented a Direct RNA sequencing Nanopore methodology. It is now widely used in our projects, and we also collaborate with other laboratories interested in post-transcriptional gene expression regulation (for instance, Scheer et al. Nature com. 2021). Moreover, we use Direct RNA sequencing to look globally at the regulation of poly(A) tails (Tudek et al. Nature com., under revision).

In the future, we will continue to study the role and mechanism of action of TENT5 poly(A) polymerases, analyze global control of poly(A) tail lengths and develop bioinformatics tools for Direct RNA sequencing. Finally, we are planning to translate our knowledge out poly(A) tails for the design of mRNAs, which are more stable and better translated, which will be very valuable for mRNA-based therapeutics such as mRNA vaccines.

Aim:

The exact nature of the project will depend on the skills, predispositions, and interests of the selected PhD student. It may focus on:

- functional analysis of the TENT5A poly(A) polymerases in transgenic mouse models generated in-house using CRISPR/Cas9 methodology.
- mastering of the DRS methodology in either the experimental part or bioinformatic analysis.
- analysis of principles of mRNA stability control and design of more efficient mRNA based therapeutics

Requirements:

- Master's degree in biology, biochemistry or related field
- Eligibility for PhD studies in Poland
- Highly talented individuals who are passionate about research and are full of scientific curiosity
- Experience in either: molecular biology/transcriptomics, animal models, bioinformatic analysis of transcriptomic data, will be a clear benefit
- Written and spoken fluency in English
- Willingness to learn and take new challenges, ability to work independently, analytical thinking
- Good interpersonal skills and a collaborative attitude.

Number of positions available: 2
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