Universität Basel

Research Project

Regulation of mRNA translation and its relationship with disease

Third-party funded project

Project title Regulation of mRNA translation and its relationship with disease
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Organisation / Research unit
Departement Biozentrum / Bioinformatics (Zavolan)
Department
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Protein synthesis is at the core of cellular life. Consequently, a vast proportion of a cell's resources is dedicated to this process, which is reflected in the ribosomes taking up a large fraction of a cell's mass. Proliferative states are associated with a further increase in the fraction of the cellular mass dedicated to the translation machinery. The translation process is targeted by many antibacterial agents which exploit the fact that bacterial ribosomes differ from those of eukaryotes. Moreover, a global reduction in translation by means of inhibiting the RNA polymerase I is being explored as a therapeutic possibility in cancers. In recent years, novel mechanisms for modulating the rate, efficiency or site of translation, either globally or for specific transcripts, in relation to the cellular state have been uncovered. Among these are condition-specific alterations in transfer RNA abundance, expression of particular ribosomal proteins in specific disease states, the change in the RNA-binding protein interactome of transcripts through alternative polyadenylation, and RNA modifications such as the 1 or 6-methyladenosine. Nevertheless, the relative importance of translation and transcription regulation for gene expression is highly debated and the breadth and mechanisms underlying dynamic changes in translation are not well understood. Evidence has started to emerge that dynamic sub-cellular structures that are organized in part by multivalent RNAs and in part by proteins with intrinsically disordered domains play a role.

The aim of the project proposed here is to characterize the role of specific mechanisms that we have uncovered in our previous work, in modulating mRNA translation in relation to normal and disease states. Thus, we would like to investigate the impact on mRNA translation of systematic changes in 3'UTR lengths as a result of changes in cell state (e.g. cell differentiation) or in the expression of regulators of 3'UTR length. Having already identified systems in which the aforementioned behaviors can be studied, we would now like to undertake their molecular characterization and evaluate their relevance for cell differentiation, development and cancer. Succinctly, the work outlined in this proposal aims to elucidate cell type-specific translational programs that are rooted in specific regulators and could open new avenues for engineering cellular behaviors. At the same time, we hope that through a nuanced understanding of how translation is regulated in different conditions we will enable targeted manipulations of the process for therapeutic applications.

Keywords pre-mRNA 3' end processing, mRNA translation, 3'UTR length, cleavage factor I
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Add publication

Published results

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Specify cooperation partners

ID	Kreditinhaber	Kooperationspartner	Institution	Laufzeit - von	Laufzeit - bis
3721944	Zavolan, Mihaela	Jeker, Lukas	DBM, University Hospital Basel	01.01.2015	31.12.2025
4235372	Zavolan, Mihaela	Heissmeyer, Vigo	Helmholzzentrum Munich	01.01.2017	31.12.2035