

LS24-035 - Sounds of Silence: Codons and Chaperones in the Protein Folding Concert

Zusammenfassung

The MYOSYN project employs an integrative approach to address the molecular mechanisms underlying tissue-specific biogenesis of myosin, the motor protein driving muscle contraction. Central to our project is a myosin folding reporter that will be used to track protein maturation in the native environment of the cell. By incorporating a split fluorescent protein (split-FP), we can perform quantitative and high-throughput Fluorescence-Activated Cell Sorting (FACS) experiments to study protein folding. Harnessing the power of synthetic cDNA libraries, our team will first probe the impact of codon usage on myosin biogenesis in muscle cells. By analysing folding profiles from over 30,000 myosin variants through machine learning algorithms, we aim to obtain a protein atlas describing the impact of single amino acids and the genetic code on myosin folding. Based on our preliminary results, we are particularly excited to study how subtle genetic variations, exemplified by synonymous codons, can alter protein folding efficiencies. In parallel, we will use our split-FP folding reporter in genome wide CRISPR screens to identify and characterize molecular chaperones, co-factors and regulators involved in myosin maturation. Of note, current tools have not allowed for a detailed analysis of synonymous codons and chaperone networks. The MYOSYN project will provide the necessary toolkit to explore these important aspects, enabling a deeper understanding of myosin (mis)folding and paving the way for new treatment approaches for related protein disorders.

Wissenschaftliche Disziplinen:

Molecular biology (40%) | Computer aided design (CAD) | Genomics (30%)

Keywords:

Synonymous Codon Usage Co-translation protein folding Genomic CRISPR screens Myosin folding

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Status: Vertrag in Vorbereitung

Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter

<https://wwtf.at/funding/programmes/ls/LS24-035/>