



FUNCTIONAL ANALYSIS OF MICRORNAS AS REGULATORS OF SECRETORY MEMBRANE TRAFFICKING

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MicroRNAs (miRNAs) are small non-coding RNAs emerging as important translational gene expression regulators in animals and plants. It is thought that miRNAs modulate as many as 60% of protein-coding genes in mammals. miRNAs affect a multitude of biological processes such as developmental transition, cell proliferation and apoptosis. Alteration of miRNA expression pattern leads to the tumorigenesis, diabetes, neuropsychiatric diseases and many other diseases.

In the present study, we demonstrate an integrative approach to identify miRNAs and their target genes potentially involved in the regulation of secretory membrane trafficking. By applying (i) molecular biology, (ii) fluorescence microscopy, (iii) statistical data analysis, (iv) bioinformatics and (v) expression profiling methods we are enabled to identify miRNAs of interest. A high-throughput screening of oligonucleotides mimicking 470 human precursor miRNAs led to the identification of 44 miRNAs with an effect on the model cargo protein secretion rate. In parallel, a genome-wide library of 875 miRNA inhibitors is being screened to determine the function of individual miRNA by inhibiting endogenously expressed species. The primary data is being validated by additional cellular assays, e.g., Golgi complex integrity assay. For some of the hit miRNAs we have identified relevant gene targets.

In perspective, the results of detailed analysis of identified miRNAs and their target genes will allow us to model the posttranscriptional miRNA regulatory networks and to understand how these networks coordinate the activity of secretory membrane trafficking as a global adaptive response system.

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