



RNA modifications - Design principals and biological functions

Aldema Sas-Chen

Tel Aviv University, Israel

Background: The epitranscriptome defines over 170 chemical modifications of RNA molecules, which affect the structure and function of both coding and non-coding RNAs. Efforts are directed at developing methods for high resolution mapping of the epitranscriptome, which facilitate the investigation of the roles of specific RNA modifications and the enzymes that catalyze them.

Methods: Using next-generation sequencing based technologies, we have developed and employed methods for high-throughput detection of RNA modifications at single base resolution. We focused on the profiling of RNA acetylation, 2'-O-methylation and pseudouridylation and elucidating mechanisms that support their formation on ribosomal RNA, tRNA and mRNA.

Results: We have identified an evolutionary conserved mechanism for RNA acetylation, which contributes to thermostability of the molecules. We have identified that the methyltransferase MRM2 methylates mitochondrial rRNA, and its absence abrogates mitoribosome assembly and mitochondrial homeostasis. We have uncovered design-principals that allow snoRNAs, which usually mediate rRNA modification, to target mRNA for pseudouridylation.

Conclusion: Overall our findings uncover effects of the three RNA modifications on molecular and cellular processes, and, in the context of pseudouridylation, offer 'design rules', constraints and consequences of snoRNA-mediated pseudouridylation of mRNAs.