Cologne Evolution Colloquium

SFB 680 Molecular Basis of Evolutionary Innovations

Ofer Biham

Hebrew University, Jerusalem

Competition-induced interactions between distant miRNAs and targets in post-transcriptional regulatory networks

miRNAs play a fundamental role in post-transcriptional regulation. Due to the stoichiometric nature of the miRNA-mRNA interaction, the regulation is bi-directional, namely in addition to the effect of the miRNA regulators on their targets, the transcripts affect the activity of their miRNA regulators. This implies that there should be cross-talk between mRNAs that share a miRNA regulator as well as between miRNAs that share common targets, which is mediated by the shared regulators and targets, respectively. We have analyzed a recently published, experimentally-determined human miRNA-mRNA interactome and found that it is a dense, intertwined network, suggesting that the effect of an expression change in a single mRNA or miRNA could propagate along paths in the network, affecting non-adjacent regulators and targets. Through computational modeling we determined the parameters governing the magnitude of this propagation and support the model by analysis of experimental perturbation data. Our results provide a new view of post-transcriptional regulatory networks, expanding the concept of ceRNAs (competing endogenous RNAs), implying significant cross-talk within the network with far-reaching consequences for perturbation effects.

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