Expression analysis of human miRNA - mRNA interactome

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miRNAs are short (~ 22nt) endogenous RNAs, which ensure an essential post-transcriptional regulation of gene expression. The miRTarBase provides information about 6,000 experimentally validated human miRNA - mRNA interactions, which were collected from the articles. While miRBase contains more than 2500 human miRNAs, and, therefore, a majority of their interactions with mRNAs remain unidentified.

The recent high-throughput techniques CLASH (crosslinking, ligation, and sequencing of hybrids) [1] and CLEAR (covalent ligation of endogenous Argonaute-bound RNAs)-CLIP [2] allow to revealed miRNAs ligated to their endogenous mRNA targets: more than 18,000 high-confidence miRNA-mRNA interactions in HEK293 cell line and more than 40,000 interactions in human hepatoma cells respectively. Multiple survey of these datasets enable us to estimated errors of methods and to yielded insights into miRNA – mRNA interactions in cell. To accomplish this, we observed the associations of the expression level of miRNAs and mRNAs (from FANTOM5 and GEO) and the amount of interactions (from CLASH and CLEAR-CLIP).

Expression analysis of miRNA revealed two interesting groups: “specific” regulators expressed at high levels while forming only a few interactions with cognate mRNAs and “promiscuous” regulators expressed at low levels each forming more than 100 interactions with mRNAs. In normal cells, these “promiscuous” miRNAs are kept under tight transcriptional control that may be relaxed in pathophysiological states, thus forming an attractive pool of potential biomarkers, while the “specific” regulators may become candidates for therapeutic modulation.

Both of these miRNA groups are recognized as biomarkers associated with adverse prognostic features in cancer and other severe pathologies. Only about 1% of mRNAs are actively engaged in miRNA interactions. Furthermore, we identified several coding mRNAs with a substantial sponge effect, including AGO1, which function may reflect the competition and resultant coevolution of mRNAs and miRNAs.

1. A. Helwak et al. (2013) Mapping the human miRNA interactome by CLASH reveals frequent noncanonical binding, *Cell,* **153(3):** 654-665
2. M.J. Moore et al. (2015) miRNA-target chimeras reveal miRNA 3'-end pairing as a major determinant of Argonaute target specificity, *Nature communications,* **6**