A curated database of miRNA mediated Feed Forward Loops involving the MYC Transcription Factor as Master Regulator

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Motivation

In the last years, much interest has been attracted by the study of local connections between transcriptional and post-transcriptional (miRNA mediated) regulatory interactions. Among various possible ways to integrate together TF-mediated and miRNA-mediated interactions, Feed-Forward Loops (FFLs) play a prominent role, allowing a fine tuning of the expression level of target genes, and, in the case of incoherent FFLs, a careful control of fluctuations in the level of target proteins. We previously developed a computational framework for the genome-wide construction and functional study of mixed miRNA / Transcription Factors Feed-Forward Loops, which were identified through a bioinformatic pipeline, mainly based on an ab-initio sequence analysis of human and mouse genomes. In this poster, we focus our attention on the FFLs which have as master regulator the Myc Transcription factor which is one of the most intriguing oncogenes, involved in the regulation of a many targets and a broad range of miRNAs, which are likely to play key roles in cell proliferation and cancer. We made an in-depth study of the Myc/miRs cooperation in the regulation of common gene targets.

Methods

The work is divided in two different steps. In the first one, we screened and elaborated data belonging to freely available resources for the construction of a complete experimentally validated Myc-driven FFLs catalogue. In the second one, we used manual literature survey and bioinformatic functional databases to assess the biological role of the proposed mixed FFLs, having Myc as master transcription factor.

Results

We built a curate database of human mixed miRNA / TF FFLs having Myc as master regulator and characterized only by experimental supported regulatory connections at the transcriptional and post-transcriptional level. We found that these FFLs are statistically overrepresented in the global MYC/miRs network, with a wide implications in cell cycle and cancer diseases.

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