Prediction of human targets for viral encoded microRNAs by thermodynamics and empirical constraints

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Ferro Alfredo[1,2], Forte Stefano[1,2], Giugno Rosalba[1], Lagana' Alessandro[1,2], Pulvirenti Alfredo[1], Barbagallo Davide[2], Di Pietro Cinzia[2], Majorana Alessandra[2], Purrello Michele[2], Ragusa Marco[2], Bonci Desiree[3], De Maria Ruggero[3,4], Pagliuca Alfredo[3]

[1]Dipartimento di Matematica e Informatica, Università di Catania

[2]Dipartimento di Scienze Biomediche, Università di Catania

[3]Istituto Superiore di Sanita', Roma

[4]Fondazione Istituto Oncologico del Mediterraneo, Catania

Motivation

MicroRNAs (miRNAs) are small RNA molecules that modulate gene expression through degradation of specific mRNAs and/or repression of their translation. miRNAs are involved in both physiological and pathological processes, such as apoptosis and cancer. Their presence has been demonstrated in several organisms as well as in viruses. Virus encoded miRNAs can act as regulators of viral gene expression, but they may also interfere with host gene expression. In particular, viral miRNAs may control cell proliferation by targeting cell-cycle and apoptosis regulators in host cells: accordingly, they could be involved in the pathogenesis of cancer.

Computational prediction of miRNA/target pairs is a fundamental step in these studies.

Methods

Here we describe the use of miRiam, a novel program based on both thermodynamics features and empirical constraints, to specifically predict viral miRNAs/human targets interactions. More precisely, miRiam exploits target mRNA secondary structure accessibility and interaction rules, inferred from validated miRNA/mRNA pairs. A set of genes involved in apoptosis and cell-cycle regulation was identified as target for our studies, a choice supported by the knowledge that DNA tumor viruses interfere with these processes in humans. miRNAs were selected from two cancer related viruses, Epstein-Barr Virus (EBV) and Kaposi-Sarcoma Associated Herpes Virus (KSHV).

Results

The results of our prediction show that several of the mRNAs we analyzed (such as BID, BAX, CASP3, CASP10, TP53) possess good binding scores to these miRNAs. This suggests that besides the protein based host regulation mechanism, a post transcriptional level interference may exist. Future work will be aimed at providing the experimental validation of these computational predictions.

Email: ferro@dmi.unict.it