

miRNA-mRNA integrated pathway analysis: an application to colorectal cancer

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Motivations

In recent studies, it has been argued that small noncoding microRNAs (miRNAs) can contribute to development and progression of cancer and show a differential expression between normal and neoplastic tissues. To date, it is still not completely clear the functional role of miRNAs in human solid tumors both in terms of changes of expression profiles and in terms of changes of their regulatory activities. Our analysis aims to enlighten the specific contributes of miRNAs in cancer by identifying miRNA-driven pathways deregulated in tumor onset and progression.

Methods

We present a strategy to infer biological processes potentially altered in tumor development by analyzing the expression of multiple microRNAs as well as by evaluating the cooperative miRNA regulatory activities on them. Our scoring algo-

rithm is based on the inference of pathways in terms of miRNAs determined by tissue-specific and condition-specific correlations evaluated on paired expression levels of human miRNAs and mRNAs. An enrichment analysis of the resulting miRNA pathways allows to identify pathways associated with differentially expressed miRNAs and pathways enriched for different miRNA regulatory activities by using tissue-specific and condition-specific measures, respectively.

Results

Our novel approach integrates miRNA and mRNA expression data for the understanding of complex pathologies. The application of this approach to colorectal cancer highlights many biological pathways enriched of oncogenes and tumor suppressors that traditional mRNA pathway enrichment analyses were not able to reveal.