**Understanding miRNA roles in breast cancer through enrichment networks**

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Abstract:Deregulation of microRNAs (miRNAs) has been increasingly implicated in cancer. Several miRNAs have aberrant expression profiles in breast cancer and the expression of some has been correlated to specific clinical features of breast cancer.  miRNA dependent regulation is mediated through changes in mRNA levels and function, and miRNA/mRNA interaction in the context of breast cancer highlights clinically relevant pathways.

In this study we present and analyze data derived from expression profiling of 799 miRNAs in 100 primary human breast tumors, along with genome-wide mRNA profiles and extensive clinical information. We investigate the relationship between these molecular components, in terms of their effect on clinical characteristics and cellular processes. We identify statistically significant differential expression of miRNAs between molecular intrinsic subtypes, and between samples with different levels of proliferation.

We introduce a systems biology approach to examine the correlative relationship between miRNA and mRNAs using statistical enrichment methods and generate a miRNA-GO association network. We show that several cellular processes, such as proliferation, cell adhesion and immune response, are strongly associated with certain miRNAs. For example, we observe a strong association of the miR-17/92 family with proliferation. We validate the role of miRNAs in regulating proliferation using high-throughput lysate-microarrays on cell lines including a direct effect of miR-19a.

This study provides a comprehensive dataset as well as methods and system-level results that jointly form a basis for further work on understanding the role of miRNA in primary breast cancer.