"Identification of microRNAs that Predict Metastatic Relapse and Sensitivity to Chemotherapy in Human Colorectal Cancer"

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Abstract: Colorectal cancer is a highly prevalent and aggressive disease. Despite surgical resection of primary tumors, many patients will ultimately develop metastases to distant organs and succumb to their disease. Chemotherapy can reduce the likelihood of metastatic relapse in patients who are deemed at "high risk" based on conventional pathologic staging methods. Unfortunately, current pathologic methods fail to identify thousands of patients who will subsequently develop metastatic disease. Recently, we have identified a set of microRNAs for which expression is lost in primary breast cancers of patients who ultimately go on to develop metastatic disease. These 'metastasis suppressor microRNAs' identify breast cancer patients at high risk for metastases and can therefore guide clinical decision-making. These microRNAs also act as strong inhibitors of metastatic dissemination in an animal model of human breast cancer metastasis. Through a systematic approach employing *in vivo* selection of colon cancer cells in mice, global microRNA profiling of human colorectal cancer cells with diverse metastatic activities, and validation of putative 'metastasis prognostic miRNAs', we propose to identify microRNAs that will enable clinicians to identify high risk subsets of colorectal cancer patients whose treatment with chemotherapy could prove life-saving. We will furthermore test the ability of these microRNAs to predict clinical tumor responses to modern chemotherapies in ongoing trials. The identification of such miRNAs will not only be of tremendous clinical diagnostic value, but will lay the foundation for future mechanistic studies aimed at generation of novel therapeutic agents for the prevention of colorectal cancer metastasis.