CALIFORNIA STATE SCIENCE FAIR
2013 PROJECT SUMMARY

Name(s)

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Project Number

S0518

Project Title

Advancing Precision Medicine: MicroRNA Prognostic Signatures and Prediction Models for Breast Cancer

Abstract

Objectives/Goals

MicroRNAs (miRNAs) have the ability to regulate large gene networks and are estimated to regulate 50% of the human genome. The primary objective of my project is to investigate the role miRNAs play in mediating growth, invasiveness, and metastasis of breast cancer cells. This project comprises of the two components: (1) in-silico discovery of miRNA signatures predictive of distant metastasis-free survival in breast cancer, and (2) experimental validation to assess the role of prognostic miRNAs in regulating in-vitro metastatic characteristics of breast cancer cells.

Methods/Materials

A super series microarray dataset of matched miRNA and mRNA data was downloaded from the Gene Expression Omnibus. A novel computational method was proposed and developed to identify miRNA prognostic signatures predictive of breast cancer metastasis. The workflow consists of integrative analysis of mRNA and miRNA expressions with the aid of a miRNA knowledge-based tool and survival analysis. miRNA expressions in breast cancer cell lines used for validation were measured using qPCR. In-vitro characterization assays (Transwell invasion and migration assays and MTT proliferation assay) were conducted to assess metastatic potential.

Results

MicroRNA prognostic signatures in the prediction models were identified. The ER+/ER- signatures consist of 14 and 12 miRNAs, respectively. The accuracy of the prediction models were cross-validated using independent patient samples, supporting the prognostic value of the models. In the experimental validation of ER- signature, correlation between detectable expressions and in-vitro metastatic potential was confirmed for the highly metastatic cell line, according to model prediction. Experimental work to investigate the impact of modulated miRNA expressions on metastatic characteristics also supports the role of the miRNAs in regulating metastasis.

Conclusions/Discussion

This study has identified 17 known miRNAs that have been implicated to breast cancer, according to published literature. This study also identified 9 novel miRNAs, which have not been previously linked to breast cancer. The experimental validation of the ER- signature showed excellent correlation between detectable miRNA expressions and metastatic characteristics according to model prediction. The study also identified miR-210 as a potential independent indicator of metastatic potential.

Summary Statement

I proposed and developed an in-silico miRNA discovery flow to identify prognostic signatures predictive of breast cancer metastasis; experimental studies were performed to correlate miRNA expressions and in-vitro metastatic characteristics.

Help Received

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