Development of a Novel Exosomal miRNA Biomarker Panel for Treatment and Rapid Identification of Lung Cancer by Blood Tests Utilizing Next-Generation Sequencing, Computational, and in vitro Analyses

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Lung cancer is the leading cause of cancer death worldwide. Diagnostic methods including CT-scans are expensive and time-consuming. miRNAs participate in gene-silencing, and can be dysregulated in cancer. Extracellular Vesicles (EVs) circulate our bloodstream and participate in cell-cell communication within tumor microenvironments during metastasis. This project developed a novel exosomal miRNA biomarker panel for various lung cancer histologies and stages, for point-of-care testing. Small RNA libraries of patients' plasma were quantified by qRT-PCR, underwent next-generation sequencing, and pre-processed. Novel miRNAs with their default parameters and their abundance changes were identified. A heat-map (biomarker panel) displayed the expression of miRNAs with p-values <0.05 and fold-changes >1.5, for Stages I-III of SCC, LUAD, and SCLC. miR-1306-5p, miR-374a-5p, and miR-374b-5p were selected for qRT-PCR validation of the biomarker panel in LUAD EVs. PCR confirmed that miR-374a-5p and miR-374b-5p were downregulated in advanced stages of LUAD patient plasma samples. Hundreds of LUAD patient data were extracted from TCGA. miR-374a and miR-374b were downregulated in LUAD tissue samples, while miR-1306 was upregulated. Low levels of miR-374a-5p and miR-374b-5p and high levels of miR-1306-5p resulted in LUAD patients having a lower probability surviving over a period of time. Discovery of these novel, circulating EV miRNAs can be used for rapid identification of various lung cancer types and their specific stages via simple blood extraction tests, while miR-374a-5p and miR-374b-5p can be utilized as therapeutics for LUAD.

Awards Won: