CALIFORNIA STATE SCIENCE FAIR
2017 PROJECT SUMMARY

Name(s)

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Project Number

S0825

Project Title

Identification of Diagnostic Biomarkers and Therapeutic Targets across Adenocarcinomas Using DNA Methylation Analyses

Abstract

Objectives/Goals

Adenocarcinomas are complex tumors that form in mucus-secreting glands. Their formation and progression are associated with DNA methylation alterations. Methylation, the process of adding methyl groups to DNA, plays a vital role in gene expression. The objective of this study is to identify diagnostic biomarkers and therapeutic targets across adenocarcinomas using methylation analyses.

Methods/Materials

I addressed the limitations of cancer methylation studies by studying more gene regions for differential methylation. I also accounted for biases via appropriate preprocessing methods. Further, I analyzed lung, pancreatic, and rectal cancers, the three most common adenocarcinomas accounting for 42% of cancer deaths in the US in 2016 alone, to find similarities. In my research, I analyzed the Illumina HumanMethylation450K datasets. I applied preprocessing methods of probe filtration, intra-sample normalization, and batch effect removal to each dataset. Next, I identified the differentially methylated loci (DMLs) that distinguish between tumor and normal samples. I clustered the tumor samples into methylation-based subgroups and identified the DMLs that distinguish between the clusters. Finally, I conducted gene-set enrichment analysis using the two sets of loci for each adenocarcinoma.

Results

I found 604 DMLs distinguishing between tumor and normal samples across the adenocarcinomas, 64% of which are outside the gene promoter region. I identified four common proteins and pathways involved in adenocarcinoma progression: Polycomb-group proteins, extracellular matrix proteins, G protein-coupled receptor signaling, and epidermal growth factor signaling.

Conclusions/Discussion

With wet laboratory experiments for validation, the common DMLs can be used as blood-based diagnostic biomarkers. Adenocarcinoma therapeutic drugs can be developed to target the common proteins and pathways and help reduce the high risk of recurrence. My pipeline can also be extended to sarcomas, melanomas, and lymphomas.

Summary Statement

I identified diagnostic biomarkers and therapeutic cancer targets for the three deadliest adenocarcinomas, cancers of the lung, pancreas, and rectum, using genome-wide DNA methylation analyses.

Help Received

I received project guidance and research paper feedback from Dr. Andrew Beck at Harvard Medical School, Mr. Benjamin Glass at Harvard Medical School, and Dr. Tim Triche at USC Norris Comprehensive Cancer Center.