MiRNA Biomarkers as Targets for Downstream Regulation of Tumoregenic Genes

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Introduction

Approximately 400,000 Americans that are living today have been diagnosed with lung cancer (World Health Organisation). Despite extensive research, not much is known about the genetic causes of the disease. MicroRNA, abbreviated miRNA, are small non-coding RNA molecules that function in the post-transcriptional regulation of gene expression. When an miRNA is upregulated, the gene it modifies is downregulated, but when the miRNA is downregulated, the gene is upregulated.

Methods

This study used the GSE61741 dataset (NCBI), which analyzed blood profiles from patients that had different diseases, with suitable controls in place for the analysis. Of the 1049 samples, expression values were collected from 73 lung cancer samples, and 94 control samples through microarray. The study focused on all 167 samples. Bayesian analysis was performed using GEO2R, a statistical analysis tool provided by NCBI, and samples with a log fold change (logFC) of less than -1.72 were discarded. The target genes of the remaining miRNAs were located. These target genes were then input to the String Database, and compared to their modifiers to see which genes were modified by more than one miRNA.

Results

After comparing miRNAs with their target genes, we determined that the genes CDH2, CD44, EGFR, ERG, and HSPA5 were all modified by the miRNAs hsa-miR-199a-5p, hsa-miR-145-5p, hsa-miR-574-3p, and hsa-miR-30a-5p. The functions of these genes relate to cell adhesion and migration, proliferation and apoptosis, which are all functions that can affect cell growth, motility, and therefore, the progression as well as malignancy of a cancer.

Conclusion

Based on this research, we determined that the miRNAs hsa-miR-199a-5p, hsa-miR-145-5p, hsa-miR-574-3p, and hsa-miR-30a-5p modify multiple genes that have been previously correlated with cancers. For instance, mutations in the gene EGFR have been proven multiple times to be linked to lung cancer, and this gene was downregulated by both hsa-miR-145-5p and hsa-miR-574-3p. Therefore, we conclude that identifying miRNA modifiers that act on multiple genes can suggest downstream approaches to control the actions of tumoregenic genes.