A Systematic Analysis of Epigenetic Genes across Different Stages of Lung Adenocarcinoma

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Introduction: Epigenetic refers to the reversible functional modifications of the genome that do not correlate to changes in the DNA sequence. Hence identifying these epigenetic targets contributing to the cancers and modifying them might provide a new approach to successful drug therapies. The aim of our study is to understand DNA methylation patterns across different stages of lung adenocarcinoma (LUAD). **Method:** An integrative system biology approach was developed to combine gene-expression, DNA methylation and protein-protein interaction data to obtain the targets for LUAD. The expression and methylation data was downloaded from TCGA. Statistical analysis was performed to further obtain the differentially expressed and significant methylated genes. An integrated network of these significant genes was constructed using BioGRID. Seed and expand approach was then used to identify and analyze epigenetically relevant subnetworks. **Results:** Our study identified 72, 93 and 170 significant methylated genes in Stage I, II and III respectively of LUAD. Variable methylation patterns were found for the significant genes across the different stages. Chromosomal analysis discovered that most of the methylated genes were distributed across chromosomes 7, 8, and 7 for Stage I, II and III respectively. Functionally conserved subnetworks of DNA methylation were obtained and compared across stages. This comparison showed a pattern of seven functionally conserved genes, mostly belonging to the KRAS pathway. Validation of the results was based on literature review which identified NEFM (beta value 0.36), NMUR2 (beta value 0.28), NEUROG1 (beta value -0.26) and IVL (beta value -0.26) as novel methylated LUAD genes. **Conclusion:** A distinct methylation pattern exists across stages which can help to characterize LUAD. Several tumor oncogenes and transcription factors were identified in the epigenetically relevant subnetworks, indicating that methylation affects the tumor progression. Methylated genes identified in this study can be further evaluated for their use as potential drug targets.

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