Weighted Gene Co-expression Network Analysis Reveals Different Gene Profiles in Lung Cancer Current and Never Smoker Patients'

P-35-088


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Although 85-90% of LUAD malignacies have been attributed directly to tobacco smoking, little is known regarding the epigenetic changes of the molecular mechanisms involved in epithelial to mesenchymal transition (EMT). LUAD patients with a smoking history have low E-cadherin levels with even further reduced levels in smokers, thus indicating a poor prognostic factor. Cigarette smoking plays a vital role in promoting EMT and is associated with poor survival, cell migration and invasion in non-small cell lung cancer (NSCLC) through the deregulation of E-cadherin. Almost 25% of all lung cancer cases worldwide have been found in never smokers (NS), with environmental tobacco being a relatively weak carcinogen.

In our analyses we used miRNASeq expression and clinical data downloaded from The Cancer Genome Atlas (TCGA). Weighted gene correlation network analysis (WGCNA) was used for the association of constructed gene modules and clinical traits. Gene set enrichment analyses (GSEA) was used to analyse global gene expression differentiation between groups of current smokers (CS) and NS. The differentially expressed genes were analyzed by Gene Ontology (GO), then Cytoscape to construct a co-expression network of hub differentially expressed genes mediated pathways.

LUAD in CS and NS patients shows clear differentiation of gene profiles. In addition, we found that differentially expressed genes are responsible for important functions such as replication and EMT with a higher expression in CS. Our results highlight the potential difference in biological mechanisms of cancer development due to tobacco smoking.

According to our results, there are significant differences between the gene expression profiles in CS and NS. The overexpression of certain genes involved in cell cycle, EMT and replication in current smokers seems to be key drivers in LUAD progression.

Acknowledgment: This work was supported by the Medical University of Lodz grant number 503/0-078-02/503-01-004.

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