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miRNA and proteomic dysregulation in non-small cell lung cancer in response to cigarette smoke

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Abstract

Dysregulation of miRNAs is well associated with the development of non-small cell lung cancer (NSCLC). It is imperative that dysregulation of miRNAs by cigarette smoke will affect the expression of their targets, either leading to the activation of oncoproteins or suppression of tumor suppressor proteins. In this study, we have carried out miRNA sequencing and SILAC-based proteomics analysis of H358 cells chronically exposed to cigarette smoke condensate. miRNA sequencing resulted in the identification of 208 miRNAs, of which 6 miRNAs were found to be significantly dysregulated (fold change ≥ 4, p-value ≤ 0.05) in H358-smoke exposed cells. Proteomic analysis of the smoke exposed cells compared to the parental cells resulted in the quantification of 2,396 proteins, of which 681 proteins were found to be differentially expressed (fold change ≥ 2). Gene ontology based analysis of target proteins revealed enrichment of proteins involved in biological processes driving metabolism and a decrease in expression of proteins associated with immune response in the cells exposed to cigarette smoke. Pathway analysis using Ingenuity Pathway Analysis (IPA) revealed activation of ERK/MAPK and integrin signaling and repression of RhoGDI signaling in H358 smoke exposed cells. We also identified 5 novel miRNA in H358 smoke exposed cells using unassigned reads of small RNA-Seq dataset. In summary, this study indicates that chronic exposure to cigarette smoke leads to widespread dysregulation of miRNAs and their targets, resulting in signaling aberrations in NSCLC. The miRNAs and their targets identified in the study need to be further investigated to explore their role as potential targets and/or molecular markers in NSCLC especially in smokers.

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