Overexpression of Mitosis-Regulating Genes Observed in Smokers with Adenocarcinoma

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Introduction

Making up nearly 40% of lung cancer cases, adenocarcinoma starts in early versions of cells that normally secrete substances such as mucus and is usually found in outer parts of the lung. It occurs mainly in current or former smokers, but is also the most common type of lung cancer in nonsmokers. Tobacco smoking is responsible for over 90% of lung cancers, yet the specific molecular alterations induced by smoking that develop into lung cancer remain unclear. This study aimed to find significant genetic differences between smokers and nonsmokers who got lung cancer. I focused on AURKA, a cell-cycle regulator gene overexpressed in smokers with adenocarcinoma. My hypothesis is that the upregulation of AURKA in nonsmokers with lung cancer would slow the progression of the cancer.

Methods

A publically available dataset, GSE 10072, was obtained from a gene expression analysis of 135 tissue samples of adenocarcinoma and healthy lung tissue from current, former and never smokers. This study compared 42 samples of tumor tissue from smokers with 16 samples of tumor tissue from nonsmokers. T-tests were conducted and the top 274 most significantly differently expressed genes (p-values < 0.001) were selected for analysis of gene-gene interactions and gene ontology. Finally, correlations between faulty mitotic regulation and lung cancer were researched.

Results

Among the 274 genes found to have significantly different expressions between the smoker and nonsmoker cancer samples, 234 genes were identified as directly interacting. AURKA, a gene involved in mitotic spindle formation (during chromosome separation), was selected for further study and found to be upregulated in the smokers' tumor tissue, with a t-test p-value of 0.00003091 and a fold change value of 0.693052. AURKA was found to code for a cell-cycle regulated kinase protein and to be involved in many mitotic processes such as the formation of microtubules (major constituents of mitotic spindles) and stabilization at the spindle pole during chromosome separation. Finally, links between faulty mitotic regulation and tumor development were observed.

Conclusion

My research is only based off of one dataset, nonetheless, the data is consistent with previous studies that show that the very mitotic genes involved in cancer development seem linked to smoking and affect survival. All cell cycle genes, particularly those involved in mitotic spindle formation, were strongly differentiated in lung tumors between smokers and nonsmokers. AURKA codes for protein kinases which can become mutated and stuck in the "on" position. It also directly interacts with NEK2 and TTK, two genes that were associated with a three-fold increased risk of mortality from lung adenocarcinoma in smokers. Overexpression or malfunction of AURKA and related genes may cause unregulated cell division and tumor growth. Therefore, these genes are candidate targets for the treatment of lung cancer in smokers and their down-regulation might slow cancer development. Future experiments could determine the significance of AURKA and its role in the pathogenesis of lung cancer in nonsmokers.