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## The Molecular Mechanisms of Tobacco in Cancer Pathogenesis

Elaheh Nooshinfar<sup>1, 2</sup>, Davood Bashash<sup>3\*</sup>, Mahnaz Abbasalizadeh<sup>3</sup>, Ava Safaroghli-Azar<sup>3</sup>, Parisa Sadrazami<sup>3</sup>, Mohammad Esmail Akbari<sup>1</sup>

1. Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2. Department of Basic Sciences, Faculty of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3. Department of Hematology and Blood Banking, Faculty of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

### Abstract

**Introduction:** Studies have shown that cancer is a multi-factorial disease that in its pathogenesis, in addition to genetic disorders, the effect of environmental factors can also be pointed. Among all environmental factors, tobacco that is considered as the leading cause of respiratory and cardiovascular disease plays a key role in cancer pathogenesis and progression. More than 5,000 chemicals and 62 carcinogens have been detected in tobacco, which could contribute to tumorigenesis through activating oncogenes, inhibition of tumor suppressor genes, genetic and epigenetic changes, alteration of growth pathways, angiogenesis and metastasis.

**Evidence Acquisition:** To access the articles, we used from valid external and internal databases. In order to set the search formula with maximum collectivity, at the first step, the main keywords were characterized and then equivalent terms were identified using various sources. In order to retrieve the last research papers, searches were conducted constantly from 1970 until 2015. The obtained results were screened in terms of relevance and quality indicators such as proper research design, control groups, inclusion and exclusion criteria, and also the statistical analysis. Accordingly, 150 articles were obtained and finally 64 articles which were eligible and having high relevance to the topic, were selected and reviewed.

**Results:** This review will explain the association between tobacco smoking and the incidence of different human cancers; also it will focus on molecular mechanisms through which carcinogenic chemicals in tobacco smoke promote cancer progression. Among multiple components of tobacco smoke, three carcinogens, including polycyclic aromatic hydrocarbons (PAH), nicotine and nicotine-derived nitrosamine ketone (NNK) convincingly play major roles in the pathogenesis of a wide range of cancers. In fact, these toxic and carcinogenic agents alter the expression of



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oncogenes, tumor suppressors, DNA repair, and last but not least, apoptosis-related genes through several mechanisms, such as point mutations, deletions, translocations and gene recombination. Moreover, implication of different tumorigenic signal transduction pathways, such as PI3K/AKT, STAT3, ERK1/2 and COX-2 in tobacco-induced tumorigenesis should not be underestimated.

**Conclusion:** Although many facts about the carcinogenic character of tobacco are yet unknown, understanding the molecular mechanisms of cancer development associated with smoking, could be promising for early detection, treatment, and reducing metastasis of tobacco-related cancers.

**Key words:** Cancer, Molecular mechanisms, Tobacco