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[Medicine] NCKU Research Team Discovers New Mechanism of Tabacco Induced Lung Cancer, Selected as Cover Story of 2010 February 《JCI》

[Medicine] NCKU Research Team Discovers New Mechanism of Tabacco Induced Lung Cancer, Selected as Cover Story of 2010 February 《JCI》(Chinese Version)

NCKU Realtime News (2010/02/11), Merit Times (2010/02/09), Awakening News Networks & China Times E-paper (2010/02/08) A research team from NCKU (National Cheng Kung University), led by Professor Yi-Ching WANG of the Department of Pharmacology, College of Medicine, and supported by the National Research Program for Genomic Medicine, discovers a new mechanism of tobacco induced lung cancer. The achievement brings forth new clues for cancer prevention and treatment; it is also selected as the cover story of the 2010 February Issue of the Journal of Clinical Investigation.

In addition to the known carcinogenesis mechanism of gene mutation induced by the tobacco-specific carcinogen NNK in lung cancer, the team of NCKU Professor Yi-Ching WANG discovers a new carcinogenic mechanism, viz., the inhibition of the tumor suppressor genes' performance due to the abnormal accumulation of the DNA methytransferaese (DNMT) in nucleus induced by NNK. DNA methyltransferase 1 (DNMT1) catalyzes DNA methylation and is overexpressed in many human diseases, including cancer. The tobacco-specific carcinogen NNK also induces DNA methylation. However, the role of DNMT1-mediated methylation in tobacco carcinogenesis remains unclear. The team adopts human and mouse lung cancer samples and cell lines to determine a mechanism whereby NNK induced DNMT1 expression and activity. The cell-based experiments show that the tobacco-specific carcinogen NNK activates AKT signaling, inhibiting GSK3β function and thereby attenuating DNMT1 degradation and prolonging DNMT1 protein stability. Besides, NNK is also found to induce βTrCP translocation to the cytoplasm via the heterogeneous nuclear ribonucleoprotein U (hnRNP-U) shuttling protein, resulting in DNMT1 nuclear accumulation and hypermethylation of the promoters of tumor suppressor genes. This result directly proves the significant correlation between NNK and the occurrence of lung cancer.

However, different from the irreversibility of genetic mutation, the team also shows that as long as blocking the tobacco-specific carcinogen NNK, the protein activity of DNMT1 will decrease and the function of tumor suppressor gene will be recovered, increasing the survival rate.

Related Websites:
JCI linkage: http://www.jci.org/articles/view/40706
Professor Yi-Ching WANG's personal page: http://www.ncku.edu.tw/~pharma/pharmacology/index.html

Further Information:
NCKU Realtime News 2010/02/11 (Chinese)
Merit Times 2010/02/09 (Chinese)
Awakening News Networks 2010/02/08 (Chinese)
China Times E-paper 2010/02/08 (Chinese)

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