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Long-term exposure to extremely low-dose of nicotine and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) induce non-malignant breast epithelial cell transformation through activation of the α9-nicotinic acetylcholine receptor-mediated signaling pathway

Abdulfattah Salah Fararjeh and Yuan-Soon Ho
Taipei Medical University, Taiwan

Breast Cancer (BC) is the most common cancer affecting women worldwide and has been associated with active tobacco smoking. Low levels of nicotine and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), have been detected in cases of Second-Hand Smoke (SHS). However, the correlation between SHS and BC risk remains controversial. In this study, we investigated whether the physiological SHS achievable dose of nicotine and tobacco specific nitrosamine, NNK act together to induce breast carcinogenesis using an *in vitro* breast cell carcinogenesis model. Immortalized non-tumorigenic breast epithelial cell line, HBL-100 used for a time-course assay, was exposed to very low levels of either nicotine or NNK, or both. The time-course assay consisted of 23 cycles of nitrosamines treatment. In each cycle, HBL-100 cells were exposed to 1 pM of nicotine and/or 100 femtM of NNK for 48 hours. Cells were passaged every 3 days and harvested after 10, 15 and 23 cycles. Our results demonstrated that the tumorigenicity of HBL-100, defined by soft agar colony forming, proliferation, migration and invasion abilities, was enhanced by co-exposure to physiologically SHS achievable doses of nicotine and NNK. In addition, α9-nAChR signaling activation, which plays an important role in cellular proliferation and cell survival, was also observed. Importantly, an increase in stemness properties including the prevalence of CD44+/CD24- cells, increase NANOG expression and mammosphere-forming ability were also observed. Our results indicate that chronic and long-term exposure to environmental tobacco smoke, may induce breast cell carcinogenesis even at extremely low doses.

Biography

Abdulfattah Salah Fararjeh has his expertise in Molecular biology and Human Genetic and is pursuing his PhD in Cancer Biology and Drug Discovery with focusing on the molecular basis of breast cancer. He has recently published one review paper in 2016 and another is original research in human pathology 2018.

Abdhraa@yahoo.com

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