Tobacco specific carcinogen enhances colon cancer cell migration through α7-nicotinic acetylcholine receptor

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摘要

Abstract

Objective: To study the mechanism of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-enhanced migration of colon cancer cells. Background Data: Long-term cigarette smoking increases the risk of colorectal cancer mortality. Tobacco-specific carcinogen, NNK, was reported to increase DNA synthesis of colon cancer cells. Since metastasis is the major cause of cancer death, the influence of NNK on the migration of colon cancer cells remains to be determined. Methods: Receptor for NNK in colon cancer cells was identified by polymerase chain reaction (PCR) and real-time PCR. The influence of NNK on migration of colon cancer cells was evaluated by transwell and wound-healing assay. Receptor-mediated migration was studied by both inhibitor and small interfering RNA. Results: α7 nicotinic acetylcholine receptor, α7-nAChR, was identified in 2 colon cancer cell lines, HT29 and DLD-1. NNK enhanced HT29 cell migration in both transwell and wound-healing assays. NNK also enhanced DLD-1 cell migration in dose dependent manner. We used inhibitor and siRNA to demonstrate that α7-nAChR mediated NNK-enhanced colon cancer cell migration and downregulation of E-cadherin were involved in NNK-enhanced migration of colon cancer cells. Furthermore, Snail and ZEB1, 2 major transcription repressors of E-cadherin in colon cancers, were induced by NNK treatment. Conclusions: Tobacco specific carcinogen, NNK, enhanced colon cancer metastasis through α7-nAChR and E—cadherin—one of the hallmarks of epithelial mesenchymal transition—and its transcription repressors. Therefore, smoking should be avoided in the patients with colorectal cance