題名:Rapid Activation of Stat3 and ERK1/2 by Nicotine Modulates Cell Proliferation in Human Bladder Cancer Cells

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摘要:Cigarette smoke is a major risk factor for bladder cancer. The main component in cigarette smoke, nicotine, can be detected in the urine of smokers. Nicotine has been implicated as a cocarcinogen that promotes lung cancer development through prosurvival pathways. Although the mechanisms of nicotineinduced cell proliferation have been well studied in lung epithelial cells, the molecular mechanism of its action in bladder epithelial cells is still unclear. The aims of this study were to investigate whether there is nicotine-induced bladder epithelial cell proliferation and to identify the signaling transduction pathway regulated by nicotine. We found that nicotine simultaneously activates Stat3 and extracellular signal regulated kinase 1/2 (ERK1/2) in T24 cells. Stat3 activation via nicotinic acetylcholine receptor (nAChR)/protein kinase C signaling pathway was closely linked to Stat3 induction and nuclear factor-kB DNA binding activity, which is associated with Cyclin D1 expression and

cell proliferation. ERK1/2 activation through nAChR and badrenoceptors
plays a dual role in cell proliferation; it phosphorylates
Stat3 at Ser727 and regulates cell proliferation.We conclude
that through nAChR and b-adrenoceptors, nicotine activates
ERK1/2 and Stat3 signaling pathways, leading to Cyclin D1
expression and cell proliferation. This is the first study to investigate
signaling effects of nicotine in bladder cells. The current
findings suggest that people exposed to nicotine could be at risk for
potential deleterious effects, including bladder cancer development.