Smoking and Drinking Activates NF-κB /IL-6 Axis to Promote Inflammation During Cervical Carcinogenesis

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ABSTRACT

BACKGROUND: High-risk strains of HPV are known to cause cervical cancer. Multiple clinical studies have emphasized that smoking and drinking are critical risk factors for cervical cancer and its high-grade precursors. In this study, we investigated the molecular mechanisms involved in the interplay of smoking and/or drinking with HPV infectivity and defined a systematic therapeutic approach for their attenuation in cervical cancer.

METHODS: The impact of benzo[a]pyrene (B[a]P) and/or ethanol (EtOH) exposure on cervical cancer cells was assessed by measuring changes in cell proliferation, clonogenicity, biophysical properties, cell migration, and invasion. Expression of HPV16 E6/E7, NF-κB, cytokines, cell cycle, and inflammation mediators was determined using qRT-PCR, immunoblotting, ELISA, luciferase reporter assay and confocal microscopy.

RESULTS: The exposure of cervical cancer cells to B[a]P and/or EtOH altered the expression of HPV16 E6/E7 oncogenes and EMT markers; it also enhanced cellular clonogenicity, migration, and invasion. In addition, B[a]P and/or EtOH exposure promoted inflammation pathways through TNF-α and NF-κB signaling, leading to IL-6 upregulation and activation of VEGFA. These molecular effects caused by B[a]P and/or EtOH exposure were effectively attenuated by Cur/PLGA-Cur.

CONCLUSIONS: These data suggest a molecular link between smoking, drinking, and HPV infectivity in cervical carcinogenesis. However, these events were determined to be attenuated by treatment with Cur/PLGA-Cur treatment, implying its role in cervical cancer prevention/treatment.

Keywords: Cervical cancer, HPV16 E6/E7; Cigarette smoking and drinking; Benzo[a]pyrene; Human immunodeficiency virus; NF-κB