Role of the XPC Gene Expression in the Prevention of Oxidative and DNA Damage to Lung Squamous Carcinoma Cells

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Background and Hypothesis: Xeroderma pigmentosum group C (XPC) is a DNA repair protein involved in the detection and repair of DNA damage caused by oxidative lesions through global genomic repair. Carcinogens, chemotherapeutics, and UV-lesions require repair of DNA by XPC. Exposure to one environmental toxin, cigarette smoke (CS), leads to cancer development and can worsen outcomes of those with cancer, however, the precise mechanisms and why susceptibility varies individually remains poorly understood. This study examines the role of XPC in cell survival in human lung squamous cancer cells (H520), and hypothesizes that XPC protects against DNA damage and cell death after exposure to cigarette smoke extracts (CSE).

Methods: Lentiviral vector transduction for XPC knock-down (XPC^{KD}) was completed in H520 cells. Transfection efficiency was measured by green fluorescence protein to determine multiplicity of infection (MOI); puromycin resistance was measured by CCK. XPC was targeted at two sites (Mission shRNA 118 and 119, Sigma), and gene knock-down efficiency determined by qRT-PCR. Survival of unmodified and H520-XPC^{KD} cells to CSE exposure was determined by CCK and clonogenic survival assays.

Results: Lentiviral knock-down decreased XPC gene expression by 68-78% in H520-XPC^{KD} as measured by RT-qPCR, with protein knock-down confirmed by Western blot. There was increased susceptibility of H520-XPC^{KD} to CSE with decreased cell survival in XPC^{KD} compared to non-transduced H520 cells.

Conclusion: XPC protects H520 cells against cell death due to exposure to cigarette smoke. Future studies will be performed to confirm the degree of protection and to determine the mechanism of XPC protective effect. These findings could be important for the discussion of risk factors with patients to understand the risks of smoking in patients with lung cancer and help physicians determine patient specific susceptibility.