Effects of the Environmental Pollutant Acrylic Aldehyde on Renal Fibrosis

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Cigarette smoke promotes renal fibrosis but the direct effects of acrolein (acrylic aldehyde), a constituent of cigarette smoke on renal fibrosis had not been determined. Heat shock protein 27 (Hsp27) is known to regulate renal fibrosis. Nuclear Factor Erythroid derived protein-2 (NF-E2) is a novel Hsp27-binding protein. Therefore, the purpose of my study was to determine the effects of acrolein exposure on renal fibrosis by examining NF-E2 expression, pro-fibrotic Connective Tissue Growth Factor (CTGF) expression, and induction of apoptosis in acrolein treated renal epithelial (HK-11) cells. I hypothesized that acrolein will induce renal fibrosis by altering CTGF expression and HK-11 cell apoptosis in a NF-E2 dependent manner. HK-11 cells were exposed to varying concentrations of acrolein (10 microM, 25 microM, 50 microM) for 24 hours and cell lysates were immunoblotted with anti-CTGF, anti-NF-E2, and anti-cleaved caspase-3 antisera. Exposure of HK-11 cells to acrolein significantly induced CTGF expression in a dose dependent manner with a concurrent decrease in NF-E2 expression. Increased NF-E2 expression was detected in acrolein treated HK-11 supernatants. The role of extracellular NF-E2 currently has not been determined. Acrolein also induced caspase-3 cleavage, and Hoechst staining demonstrated nuclear condensation indicative of apoptosis. Increasing acrolein concentration decreased HK-11 cell viability as documented by MTT reduction. Over-expression of NF-E2 inhibited CTGF expression and prevented HK-11 apoptosis by inhibiting caspase-3 cleavage. Thus, my studies identified NF-E2 as novel regulator of acrolein-induced CTGF expression and HK-11 apoptosis. Therefore, inducers of NF- E2 expression may serve a therapeutic role in treating renal fibrosis.

Awards Won:

Second Award of $2,000