Siemens Competition
Math : Science : Technology
National Finalist

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Project Title: *Effects of the Environmental Pollutant Acrolein on Renal Fibrosis*

Acrolein decreased Nuclear Factor-Erythroid derived protein 2 (NF-E2) protein expression in human-renal-tubular (HK-11) cells, induced HK-11 cell apoptosis and increased expression of pro-fibrotic Connective Tissue Growth Factor (CTGF) protein. Over-expression of NF-E2 ameliorated acrolein effects in HK-11 cells. Interestingly, NF-E2 was released in acrolein-treated HK-11 cell supernatants (Acr-sups). Danger associated molecular patterns (DAMPs) are proteins released by dying renal cells that play a role in activating and recruiting inflammatory cells and exacerbating renal injury. Renal fibrosis is associated with DAMP-mediated inflammation. Therefore, we hypothesized that secreted extracellular NF-E2 acts as a DAMP and promotes neutrophil activation, recruitment, survival and promotes renal fibrosis. Neutrophils were exposed to control and Acr-sups and cell lysates were immunoblotted with appropriate antisera.

Acr-sups stimulated pro-survival ERK phosphorylation (pERK) and promoted neutrophil survival by inhibiting cleavage and activation of pro-apoptotic protein, caspase-3. Acr-sups also stimulated neutrophil actin polymerization and chemotaxis. To determine if NF-E2 mediates these effects, Acr-sups were subjected to anti-NF-E2 immunoprecipitation. Depletion of NF-E2 from these supernatants inhibited pERK, stimulated pro-apoptotic pP38MAPK and enhanced caspase-3 cleavage. Recombinant NF-E2 stimulated neutrophil pERK, actin polymerization, chemotaxis and survival. Anti-NF-E2 antibody therapy may serve as a therapeutic option to reduce inflammation and ameliorate acrolein-induced renal toxicity.