5241
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Semi-Synthetic Glycosaminoglycan Ethers Decrease Receptors for Advanced Glycation End-Products and Increase AXL Receptor in the Lung from Secondhand Smoke Treated Mice

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Tobacco exposure is one of the top three global health risks leading to the development of chronic obstructive pulmonary disease (COPD). Although there is extensive research into the effects of cigarette smoke, the effect of secondhand smoke (SHS) in the lung remains limited. SHS induces Receptors for advanced glycation end-products (RAGE) and an inflammatory response that leads to the development of COPD characteristics. Semi-synthetic glycosaminoglycan ethers (SAGEs) are sulfated polysaccharides derived from hyaluronic acid (HA) that inhibit RAGE signaling. The growth arrest-specific 6 (Gas6) protein is known to induce dynamic cellular responses and is correlated with cell function. Gas6 binds to the AXL tyrosine kinase receptor and AXL-mediated signaling is implicated in proliferation and migratory mechanisms in several tissues. This project's purpose was to study the correlation between RAGE. AXL, and Gas6 during SHS exposure in the lung. C57/Bl6 mice were exposed to SHS alone or SHS + SAGEs for 4 weeks and compared to control animals exposed to room air (RA). At the time of necropsy lungs were extracted, frozen for mRNA studies or embedded for immunohistological analysis. Compared to controls we observed: 1) increased RAGE mRNA expression in SHS-exposed lungs which was decreased by SAGEs; 2) no difference in Gas6 or AXL expression in SHS lungs and expression was significantly increased with SAGEs; 3) increased RAGE protein expression in SHS lungs that was decreased by SAGEs; and 4) decreased AXL protein in SHS animals and increased AXL protein in animals treated with SAGEs. Our results suggest that there is a direct correlation between RAGE and AXL during SHS exposure. These studies provide insight into tobacco-mediated effects in the lung and clarify possible avenues for alleviating complications that could arise during SHS exposure such as those observed during COPD.

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