Chronic Electronic Cigarette Use Elicits Changes in Biomarkers Related to Pulmonary Pathogenesis

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Electronic cigarettes (e-cigs) primarily originated as smoking cessation devices aimed at modifying the risk of developing pulmonary diseases associated with combustible tobacco use. However, more frequently never-smokers are adopting e-cig use de novo, and the relative safety of chronic exposure to e-cig vapor remains unclear in terms of lung pathogenesis. Thus, this study aims to evaluate gene/protein biomarkers, which are associated with cigarette-induced chronic obstructive pulmonary disease (COPD) and/or idiopathic pulmonary fibrosis (IPF), in animals chronically exposed to nicotine containing e-cig vapor. C57BL/6J mice (n=15/group) were randomly assigned to one of three 8-month exposure groups: e-cig vapor (commercially available, 18 mg/mL nicotine), UK 3R4F reference cigarette smoke, or filtered air as a control. Lung tissues and paraffin embedded slides were used to evaluate gene and/or protein expressions of COPD and IPF biomarkers from the CYP450 metabolism (CYP2A5, CYP3A11), oxidative stress (superoxide dismutase 1 (SOD1)), epithelial–mesenchymal transition (E-cadherin, vimentin), and survival/apoptotic pathways (p-AKT, B-cell lymphoma extra-large (BCL-XL), p53, p21, and chromosome region maintenance 1 (CRM1)). Results from the cigarette group were consistent with previously published studies. Expressions of E-cadherin and CRM1 were significantly decreased in the e-cig group as compared to the control group (E-Cadherin: 151% of control; $p<0.05$). Nuclear sub-cellular localization of p53, evaluated by immunohistochemistry staining, in bronchiolar tissues was higher in the e-cig group (25.3±0.9%) as compared to controls (12.1±0.6 %) ($p<0.01$). Moreover, there were few significant differences observed between the e-cig and cigarette groups. As these related molecular changes are involved in the pathogenesis of cigarette-induced COPD and IPF, the possibility exists that e-cigs can produce a similar outcome, although further investigation is warranted.