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Project Title: Exosomes in Aging and Operative Hypothermic Circulatory Arrest.

Abstract

Background

Tobacco smoking is a major risk factor for cardiovascular and lung disease. Inhalation of aerosols formed by electronic nicotine delivery systems (ENDS) such as E-cigarettes (E-cigs) may expose the user to harms beyond those of nicotine alone. Data on the cardiovascular risks of E-cigs and vaping devices remain inconclusive. However, exposure to E-cigs induces the release of multiple substances, including exosomes and metabolites, into the bloodstream. There is limited information on the role of these exosomes and metabolites on cellular homeostasis. Mitochondria are highly sensitive to cigarette smoke, however E-cig aerosol induced changes in mitochondrial function are not well studied. We investigated the effects of E-cig plasma mediators on metabolism and function in human vascular

endothelial (EA.hy 926) and lung epithelial cells (A549).

Hypothesis

Plasma from E-cig users will induce alterations in the metabolism and mitochondrial function of endothelial and lung epithelial cells.

Methods

A longitudinal cohort study was conducted on subjects who exclusively used E-cigarettes (n=21) and 10 non-smoking, non-vaping subjects. We included active E-cig use without known lung disease and with normal lung function, between the ages of 18-30 years. E-cig use was confirmed with in-person interviews and plasma cotinine levels. Active E-cig use was defined as use of ≥0.5-1 mL e-liquid/day or 3.5-7 mL/week for >6 months. Plasma was isolated and stored at -70°C until exosomes were profiled. The effects of E-cig plasma (1%, 1h conditioning) mediators were assessed *in vitro* on endothelial cells (8x104/well) and epithelial cells (5x104/well) using the Seahorse XF Cell Mito Stress Test.

Results

Results were standardized for cell number and FCCP concentrations for both EA.hy 926 and A549 cells. Maximal mitochondrial respiration and spare capacity were decreased in human vascular endothelial cells and epithelial cells treated with E-cig plasma relative to plasma from non-smoker/non-vapers. Basal respiration and ATP-linked respiration was not different after treatment with plasma from E-cig users versus non-smoker/non-vapers in either cell type.

Conclusions

To our knowledge, our results are the first to suggest that factors in the plasma of E-cig users lead to reduction in maximal metabolic rates of human endothelial and lung cells *in vitro*. These results have important implications regarding the effects of E-cig use on cellular metabolism and mitochondrial function and eventual public health recommendations. We are currently investigating the underlying mechanisms of action of E-cig plasma components on mitochondrial biology.