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"Fibrotic and inflammatory markers in the hearts of mice exposed to chronic nicotine inhalation"

Cardiovascular disease (CVD), the leading cause of premature death globally, is frequently associated with tobacco use. Tobacco use accounts for as much as 30% of all CVD deaths in some countries. While the use of traditional cigarettes is declining, the use of electronic cigarettes, including vapes or vape pens containing nicotine, is increasing in most countries. This is concerning as the use of electronic cigarettes has also been associated with increased risk of heart failure. Nicotine found in electronic cigarettes has been shown to cause myocardial remodeling and fibrosis via continual stimulation of the sympathetic nervous system, leading to elevated heart rate and blood pressure in animal models. Further, recurrent vaping exposure causes inflammation in myocardial cells, contributing to cardiac fibrosis and increasing the risk of future CVD.

7-week-old male C57BL/6J mice were exposed to either room air or nicotine vapor for one week before transverse aortic constriction surgery (TAC). After surgery, TAC and sham mice were exposed to nicotine vapor or room air for 12 hours a day for 9 weeks. Cotinine levels measured in sham mice (572±93 ng/mL) were not significantly different than those measured in TAC mice (617±102 ng/mL). Air-sham and nicotine-sham mice did not have significantly different ejection fractions (EF). It was determined that chronic nicotine inhalation reduced the adaptive cardiac remodeling process in response to pressure overload induced by TAC.

Left ventricle (LV) samples from air-sham and nicotine-sham mice were assessed using qPCR to identify molecular targets of a fibrotic and inflammatory marker. We hypothesize that both the inflammatory and fibrotic markers will be upregulated in LV samples taken from the chronic nicotine exposed sham mice. qPCR has been completed analyzing gene markers TRAF3IP2 and LARP6 in LV samples. LARP6 is an RNA binding protein that binds a 5' stem-loop structure in mRNA, a binding that is central to type I collagen expression in fibrosis. The average LARP6 level, normalized using 18S, in air mice (n=8) was 0.72±.42 and in nicotine mice (n=7) was 0.44±.17 ($p=0.11$; ns). TRAF3IP2 is the gene responsible for encoding ACT1, a ligase adaptor protein that recruits other factors resulting in upregulated pro-inflammatory cytokines and chemokines. TRAF3IP2 levels in air mice (n=9) and nicotine mice (n=8) were 1.13±.50 and 0.81±.23, respectively. Additional inflammatory and profibrotic markers will be assessed to further establish the changes caused by chronic nicotine inhalation.