American Heart Association Tobacco Regulation and Addiction Center (A-TRAC)
Cardiovascular Toxicity of Tobacco Products (Project 1)
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Abstract:

To set standards for tobacco products to protect health, it is important to understand the cardiovascular effects of tobacco products and to identify biomarkers of CVD risk that can be associated with tobacco exposure. This project involves rigorous and quality-controlled toxicological evaluation of the cardiovascular effects of cigarette smoke and smokeless tobacco. Its main goal is to identify the biomarkers of cardiovascular injury that most sensitively and robustly reflect exposure to tobacco products. Exposure will be done in a barrier facility designed for controlled exposures.
Specific aims include:
1. To examine tobacco-induced endothelial injury: In adult mice exposed to varying intensities of tobacco smoke and smokeless tobacco, urinary metabolites of exposure-derived aldehydes will be identified to determine how they relate to the extent and duration of exposure as well as to changes in the biomarkers of endothelial injury and how the relationship between the biomarkers of injury and biomarkers of exposure is affected by gender and the time and duration of exposure. The experiments will identify specific indices of endothelial function and damage that reflect endothelial injury and thrombosis and how these biomarkers of injury are related to the biomarkers of exposure.
2. To delineate the contribution of harmful and potentially harmful (HPHC) constituents, such as aldehydes, to endothelial injury induced by tobacco exposure. To identify which constituents of tobacco and tobacco smoke contribute to endothelial damage, changes in the biomarkers of endothelial injury in mice exposed to individual constituents of exposure - nicotine, acrolein and crotonaldehyde will be examined, and determine how removal of these constituents affects endothelial injury due to tobacco smoke and whether increases in the extent of exposure to these aldehydes and related reactive chemicals increases the extent of endothelial injury. Successful completion of this project will lead to the development of a validated animal model to establish standard toxicity changes and the discovery of novel biomarkers of cardiovascular injury that can be associated with measures of tobacco exposure.