Improved Models to Inform Tobacco Product Regulation
Quantification and Biomarkers of Short-Term Pulmonary Effects of Tobacco Smoke Exposure:
Infection-Related Acute Lung Injury (Project 4)
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Abstract:

The health consequences of smoking are primarily perceived to be cancer, cardiovascular disease, and chronic pulmonary disease, but acute pulmonary consequences of exposure to cigarette smoke are likely to be as or more important. However, there has been little research on smoking and acute lung injury a common cause of acute respiratory failure in critically ill patients. Cigarette smoking and secondhand smoke exposure are associated with a nearly threefold increase in the odds of developing acute lung injury after severe blunt trauma, but the effects of cigarette smoke exposure on susceptibility to infection-associated, the most common type of acute lung injury, are unknown. This project will increase our understanding of the adverse health consequences of tobacco use by quantifying the increased susceptibility to infection-related acute lung injury We hypothesize that cigarette smoke exposure before infection primes patients to develop acute respiratory failure from acute lung injury. We will leverage the infrastructure of our ongoing prospective cohort of critically ill patients with severe infection and our experience with animal models of acute lung injury and cigarette smoke exposure to: 1) quantify the strength, dose-response curve, and time course of the association between cigarette smoke exposure, as measured by validated biomarkers, and the development of acute lung injury in patients admitted to the hospital with severe infection; 2) test the effects of cigarette smoke exposure and varying nicotine content on the development of infection-related acute lung injury in mouse models, with a focus on identifying plasma biomarkers of tobacco-related lung epithelial or endothelial injury that can then be tested in critically ill patients; and 3) validate the association between biomarkers of tobacco-related lung epithelial and endothelial injury and the development of acute lung injury in critically ill human subjects with severe infection. The results of this project will inform more accurate models of the economic and public health effects of cigarette smoke exposure. This project will also identify biomarkers of tobacco-related lung injury that can be used in future studies of toxicity and take the critical first steps towards determining which constituents of tobacco smoke promote lung injury, including studies of the roles of nicotine and acrolein in tobacco smoke toxicity, with important regulatory implications.