PROJECT 2 ABSTRACT

EPA Grant #: RD83479701 **EPA Project Officer:** Mel Peffers/Sherri Hunt

Title: Cardiometabolic, Autonomic, and Airway Toxicity of Acute Exposures to $PM_{2.5}$ from Multipollutant Atmospheres in the Great Lakes Region

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Institution: Michigan State University, East Lansing, MI

Project Period: 12/1/2010 – 11/30/2015 **Project Costs:** $1,535,935

RFA: Clean Air Research Centers **Research Category:** Air Quality

Description: ***Objectives/Hypothesis:*** Our objectives in Project 2 arise out of GLACIER's overarching hypothesis that the major air pollutants, fine particulate matter ($PM_{2.5}$) and ozone (O_3), are 1) capable of eliciting multiple important adverse cardiometabolic health effects that are dependent on 2) the local multipollutant milieu, 3) an individual's pre-existing cardiovascular (CV) and metabolic condition (susceptibility factors), and 4) the interactive toxicity of $PM_{2.5}$ and O_3 co-exposure. Goals of Project 2 are to determine the cardiovascular (CV), autonomic nervous system (ANS), and airway toxicity in rats acutely exposed to concentrated ambient $PM_{2.5}$ (CAP) from distinct multipollutant atmospheres commonly found in the Great Lakes Region of the United States.

Approach: Our studies are extensions of our previous findings that CAP-induced alterations in heart rate variability are dependent on specific $PM_{2.5}$ emission sources in distinct locations in the Great Lakes Region. We will use a mobile air research facility (AirCARE 1) that is fully equipped with inhalation toxicology and atmospheric monitoring labs to conduct toxicology studies of rats exposed to CAP derived from real-world $PM_{2.5}$ in three distinct locations dominated by industrial/urban, transported/regional, or near-roadway/residential emission sources. Blood pressure, heart rate, heart rate variability and direct measurements of autonomic nerve activity will be continuously monitored during CAP and/or O_3 exposures in lean or obese rats with and without diet-induced facets of the cardiometabolic syndrome (CMS; hypertension, insulin resistance, endothelial dysfunction), respectively. Acute functional responses will be measured by radiotelemetry and will be correlated with specific PM constituents and their emission sources determined for the same highly resolved 30-minute timeframes, thereby making associations of exposure and health effects especially robust. Studies will feature novel real-time sympathetic nerve recordings during $PM_{2.5}$ and/or O_3 inhalation exposure. In addition, our project will highlight the unique integrative capabilities of our research team to link specific health cardiovascular effects in a sensitive obese population with PM content by a combined technological expertise that is unavailable elsewhere. Our GLACIER project will extend and complement the research of lean and obese human subjects (Project 1), conducted at the same exposure sites, by making invasive and prolonged measurements that could not be practically or ethically done in humans (e.g., repeated CAP exposures, continuous recordings of CV and autonomic nerve function, and microscopic examination of multiple organs for exposure-related pathology). Our acute animal studies will also overlap and integrate scientifically with the animal toxicology study of long-term air pollutant exposure in Project 3, where similar endpoints will be compared.

Expected Results: Our research has the potential to identify potentially harmful effects of exposures to specific $PM_{2.5}$ components, emission sources, and O_3 to cardiovascular function. It will also provide mechanistic evidence for the dysregulation of normal cardiovascular and metabolic pathways that leads to acute morbidity and mortality of obese individuals (susceptible population) exposed to $PM_{2.5}$ and/or O_3.

Supplemental Keywords: inhalation toxicology, acute multipollutant exposure, obesity, rats