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Project Number: 5K25ES020355-05 Former Number: 5K25ES020355-03

Title: THE INFLUENCES OF AIR POLLUTION MIXTURES ON BIOMARKERS OF AIRWAY OXIDATIVE STRESS

Contact PI / Project Leader: GREENWALD, ROBY

Awardee Organization: GEORGIA STATE UNIVERSITY

Abstract Text:

The immediate career goals of the candidate, Dr. Roby Greenwald, are to examine the **respiratory** response to inhaled **Oxidants**, specifically, the influence of air pollution mixtures on markers of airway inflammation and oxidative stress. The training portion of this application will be critically important to achieve these goals. Training activities will be conducted under the **Mentorship** of Dr. Lou Ann Brown of the Emory University Department of Pediatrics, a recognized authority on airway biochemistry, and the co-mentorships of Dr. Dana Boyd, a renowned analytical chemist in the Department of Environmental Health, and Dr. Jeremy Sarnat, an environmental scientist with expertise in air pollution exposure assessment. Dr. Greenwald's training will include enrollment in the Master of Science in Clinical **research** program for study of advanced epidemiological and biostatistical methods as well as the responsible conduct of **research**. Dr. Greenwald will also enroll in physiology and biochemistry courses examining the molecular and cellular mechanics of the **respiratory** response to inhaled toxicants and physiology courses pertaining to the **respiratory** and **Cardiovascular** systems. Dr. Greenwald will receive **laboratory training** in the analysis of exhaled antioxidants and **Redox** biomarkers (with Dr. Brown), training in biomarker discovery and development using high sensitivity **Chromatography** and **Mass Spectrometry** instrumentation (with Dr. Barr), and guidance in air pollution exposure assessment (Dr. Sarnat). Finally, the training portion will be supported by epidemiology consultant Dr. Mitchel Klein and physical activity analysis consultant Dr. Janet Fulton. The training facilitated by this award will make the candidate well-positioned to achieve his long-term career goal of establishing an independent **research** team that will achieve breakthroughs in understanding the mechanisms of air pollution health effects and ameliorating this public health risk. The candidate's institutional environment is highly supportive of proposed activities. Dr. Greenwald's department has 9 faculty members with a primary **research** focus on air pollution and public health, and is well-funded in this area, including a recently awarded five-year grant from the U.S. Environmental Protection Agency for the establishment of the Emory/Georgia Tech Clean Air **research** Center. The Department of Environmental Health has recently moved into a large new office and **laboratory facility** and has recently established state-of-the-art analytical chemistry facilities under the direction of the co-mentor, Dr. Barr. The mentor's facilities in the Department of Pediatrics are no less impressive and include high-sensitivity instrumentation for analysis of biological samples and a supportive **research** staff. The **research** portion of this proposal will examine the public health risks resulting from exposure to air pollution mixtures. These risks have been repeatedly recognized by epidemiological investigations. Although understanding of the precise mechanisms of **action** is incomplete, it is apparent that an elevated state of oxidative stress in the airways plays an important and possibly causal role in observed health effects. Similarly, the specific components of air pollution responsible for oxidant injury have not been completely identified, although there is likely a synergy between combustion-source particulate matter with the gas-phase oxidant ozone. Furthermore, the increased air pollution dose associated with outdoor physical activity is of substantial public health significance. Physical activity is a critical **tool** to fight the rising rate of obesity in children and adults; however, where and when this activity occurs must be carefully considered to avoid increasing the public health burden of air pollution and to maximize the positive effects of physical activity. The proposed study will address these knowledge gaps by measuring environmental exposure to air pollution mixtures and resulting acute health outcomes and biomarkers in adolescents. The first **research** objective is to characterize the concentration and composition of ambient air pollutants at 2 high schools in Atlanta during time periods when students are engaged in physical activities. Since the selected schools are in different local environments with one in a dense urban area and the other in a wooded, semi-rural setting, students at these sites have different levels of particle exposure. The candidate will conduct air quality sampling during seasons of both high and low ozone and will also conduct sampling during indoor physical activities as a reference. The second objective is to examine the relationship between air pollution exposures and acute **respiratory** response in active adolescents. The **Investigators** will use non-invasive approaches to assess acute changes in **lung function** and airway oxidative stress. Before and after athletic practice sessions, they will conduct **Pulmonary function tests**, measure exhaled **Nitric Oxide**, and collect samples of exhaled breath condensate for analysis of markers of oxidative stress and lipid peroxidation. Since the elevated ventilation rate associated with physical activity leads to increased **Inhalation** of ambient **Oxidants**, the investigators will **Monitor** activity intensity using a wearable device that contains a motion-sensing **Accelerometer** and **heart rate monitor**. The third objective is to examine the temporal development of airway oxidative stress following exposure to urban air pollution. They will recruit participants from soccer teams that conduct morning practices and perform 5 hours of follow-up monitoring each day. We will collect breath condensate samples at hourly time-points and analyze them for markers of oxidative processes, including several not previously assessed in the context of air pollution exposure. In addition, we will actively engage in a process of biomarker discovery and evaluation.

Public Health Relevance Statement:

This proposed study will address the significant public health issue of increased air pollution exposure resulting from outdoor physical activity during periods of poor air quality. It will examine the role of intense physical activity on the relationship between air pollution and measured health outcomes, and it will provide information useful to assessing the balance between the benefits of outdoor exercise and the risks of air pollution exposure. The biomarker analysis portions of this study will also provide insight into the steps leading to the development of airway oxidative stress and the influence of various mixtures of air pollution **Oxidants**.

Project Terms:

Accelerometer; Acute; Address; Adolescent; Adult; African American; Air; Air Pollutants; Air Pollution; airway inflammation; ambient air pollution; Analytical Chemistry; Antioxidants; Area; Athletic; authority; Award; Biochemical Process; Biochemistry; Biological; Biological Markers; biomarker development; biomarker discovery; biomarker evaluation; Biostatistical Methods; **Breathing**; **Cardiovascular** system; career; Child; **Chromatography**; Clinical **research**; Coupled; Data; Development; Devices; Dose; Dose-Rate; Enrollment; Environment; Environmental air flow; Environmental Exposure; Environmental Health; Epidemiologic Methods; Epidemiology; Equilibrium; Exercise; **Exhalation**; experience; Exposure to; Faculty; Female; fighting; follow-up; Funding; Gases; Glutathione Disulfide; Goals; Grant; Health; **heart rate monitor**; high school; Hour; Injury; insight; instrumentation; Investigation; Knowledge; **laboratory experience**; **laboratory facility**; Lead; Lipid Peroxidation; male; Malondialdehyde; **Mass Spectrum** Analysis; Master of Science; Measures; member; **Mentors**; **Mentorship**; Molecular; **Monitor**; Motion; **Nitric Oxide**; obesity in children; Outcome; **Oxidants**; **Oxidation-Reduction**; Oxidative Stress; Ozone; Participant; particle exposure; Particulate; Particulate Matter; pediatric department; Phase; Physical activity; Physical Education; Physiology; Play; pollutant; Pollution; Positioning Attribute; Process; programs; prospective; Public Health; **Pulmonary function tests**; Recruitment Activity; Reduced Glutathione; **research**; **research** Personnel; **respiratory**; **respiratory** Mechanics; **respiratory** physiology; **respiratory** System; response; responsible **research** conduct; Risk; Role; Rural; Sampling; Schedule; Schools; Scientist; Seasons; Site; Soccer; Source; specific biomarkers; student athlete; Students; Time; **tool**; **toxicant**; Training; Training Activity; United States Environmental Protection Agency; Universities; urban area; Youth

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