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CLEAN **AIR** RESEARCH PROGRAM

RESEARCH DETERMINES THE TOXIC MECHANISMS OF PARTICULATE MATTER AT THE CELLULAR AND MOLECULAR LEVELS

Issue:

Exposure to airborne particle pollutants, known as particulate matter (PM), has been linked with health hazards, including heart disease, diminished lung function, and lung cancer. While these adverse health connections have been proven through extensive scientific research, the underlying mechanisms for these effects have been harder to identify.

PM is a complex and varying mixture that can include thousands of organic and inorganic compounds, derived from both anthropogenic (human-made) and natural sources. Epidemiological evidence suggests that, rather than causing specific diseases, PM exposure is linked to exacerbations of and increased predisposition to a wide range of common adverse cardiovascular and pulmonary effects in humans. As a further complication, there appears to be great variability in the human effects of PM exposure from person to person—variations that are not well understood presently. In addition, much uncertainty remains regarding the specific toxic agents in PM and their toxicological effects on humans.

Currently, there is not enough data to provide a full assessment of the risks to human health that PM exposure entails, especially given the wide range of individual responses to these airborne pollutants. Understanding the toxicity of PM at the cellular and molecular level is essential for the U.S. Environmental Protection Agency to better protect exposed populations.

Scientific Objective:

EPA's Clean Air Research Program in the Office of Research and Development (ORD) is working in close partnership with EPA's regulatory programs and other organizations outside the Agency to identify, characterize, and model the cellular and molecular events that lead to adverse reactions to airborne pollutant exposure. This research effort seeks to answer relevant scientific questions about the nature of ambient particulate matter and its toxicity in humans.

These questions include, but are not limited to:

- What are the earliest molecular events that define lung cellular responses to PM exposure?
- What are the physical and chemical properties of PM that are associated with adverse reactions?
- Is it possible to develop predictive mathematical models of the activation of cellular responses to PM inhalation?

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The answers to these questions are being pursued through research studies using advanced cellular, biochemical and molecular biology approaches. Ultimately, these efforts will provide the basis for the generation of reliable models for predicting the effects of airborne particulate pollution across the widely varied ranges of PM and the populations that it affects.

Application and Impact:
Filling the knowledge gaps surrounding the adverse effects of airborne contaminants at the cellular and molecular levels will enable EPA to develop and implement regulatory measures to mitigate the adverse effects of PM exposure on human health with greater accuracy and efficiency.

Specifically, EPA expects this research effort to achieve the following:

- Elucidate critical cellular and molecular events that underlie adverse cellular responses to PM exposure
- Identify critical physicochemical properties of PM types that are responsible for adverse health effects
- Aid in the translation of laboratory data in cells and laboratory animals to the human situation
- Develop a predictive computational model of the intracellular pathways that lead to adverse cellular responses to PM inhalation. These models can be used for risk assessment in support of protective regulatory strategies

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