Atmospheric/Ambient Pollutant Dynamic Pathways into the Human Blood and Breast Epithelium Compartments: Biomarkers of Oxidative Stress to Model Cancer Risk

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Air pollution includes a range of human-initiated chemical emissions including gaseous combustion products, volatile chemicals, aerosols (particulate), and their atmospheric reaction products. Particulate matter (PM) is of special concern to lung and cardiovascular health. PM known as fine particles, less than 2.5 microns in diameter, can be inhaled deeply into the human lung. Once inhaled, fine particles can be absorbed into the bloodstream or may remain embedded indefinitely in the lung epithelial lining. Epidemiologic studies suggest an association between exposure to urban particulate air pollution (particulates < 10 μm [PM10]) and pulmonary and cardiovascular morbidity and mortality. Few data, however, exist to evaluate the influence of PM on other human body compartments, such as the breast, and risk for induction of breast cancer. Breast cancer is the second leading cause of death for American women, after lung cancer and environmental factors theoretically account for about 50% of its incidence. PM is associated with greater incidence of female related reproductive organ diseases suggesting an endocrine-disrupting, estrogenic agent. Other pathology theorized includes an inflammation mechanism related to the mutagenic influence of PM either mediated in the lung tissue or direct effects from PM that escapes into the blood compartment and travels to distal sites or that enters through the gastric route. Theoretically, chronic oxidative stress, such as that precipitated systemically by exposure to PM, may overwhelm the breast microenvironment, and instigate cell hyperplasia and risk for breast cancer. Proteomics of non-invasive obtained nipple aspirate has provided a window into the breast microenvironment that allows an analysis of cell responses to environmental cancer triggers. The study aim is to translate pollutant migration flow data from the NASA/DC-8 airborne research laboratory at our University and ground level pollution data from Mexico City (MIRAGE-MEX mission) to the human health issue of breast cancer. The hypothesis is that markers of breast cancer risk (proteomics, oxidative stress, epigenetic changes) will vary significantly between women exposed to chronic and minimal PM10 and related atmospheric pollutants, after controls. Forecasts from meteorological and chemical models, satellite observations, surface networks, and pollutant releases will inform selection of low/high exposure sites in Mexico to collect and analyze breast cancer risk markers of chronic and acute particulate exposure, oxidative stress, and carcinogenic protein in nipple aspirate. Subject recruitment will be from areas under constant exposure (chronic exposed group) to â€œpollution trainâ€ù plumes globally and areas minimally exposed (control group). This pilot study will examine breast aspirate from chronic and low level PM exposed women using a case-control method to account for extraneous variables. Subjects will be recruited by exposure site and study criteria. A health environment history, serum sample, and breast aspirate will be obtained. Proteomic, oxidative stress, and epigenetic changes analyses

will be conducted. Epidemiologic data outcomes suffer from a 30-year lag between environmental exposures and disease outcomes. This study will expedite greater awareness and appreciation of the critical nature of the link between atmospheric and ambient environment, risk for breast cancer, and the health of our nation.