LIST OF CEHS STANDARD PILOT PROJECT AWARDS 2013-2014
(Each award is for $25,000)

PPP AWARD 2013-01

Project Title: Genotoxicity of epoxides from photochemical oxidation of biogenic volatile organic compounds contributing to SOA.

Principal Investigator: Zhenfa Zhang, Ph.D., Research Assistant Professor, **D**epartment of Environmental Science and Engineering

Abstract
Atmospheric photochemical oxidation of volatile organic compounds (VOC) forms gas phase products that are often more toxic than the parent compound. We recently demonstrated that oxidation of isoprene yields epoxydiol (IEPOX) isomers under low-NO_x conditions and methacrylic acid epoxide (MAE) under high NO_x conditions. Preliminary work shows that oxidation of 2-methyl-3-butene-2-ol (MBO) by ozone leads to two isomeric epoxides. These epoxides have not been previously identified in air; epoxides in general are genotoxic via alkylation of DNA. The hypothesis of this study is that health effects linked to SOA and VOC exposure may be attributable to genotoxicity induced by gas phase epoxides formed from photo-oxidation of BVOCs. To test the hypothesis, we propose the following specific aims: 1). *Examine the capacity of IEPOX isomers, MAE and MBO epoxides to cause DNA damage in the DT40 DNA damage response assay and the Ames assay.* In preliminary DT40 analysis *REV1*$^{-/-}$ and *PCNA*$^{K164R/K164R}$ cells are much more sensitive to IEPOX-2 and MAE than to MNU. *2) Characterize DNA adducts formed from deoxynucleosides or DNA exposed to authentic epoxides*.

PPP AWARD 2013-02

Project Title: Formaldehyde-mediated bone barrow toxicity in FancD2 knock-out mice induced by methanol treatment.

Principal Investigator: Scott Bultman, Ph.D., Assistant Professor of Genetics

Abstract
Formaldehyde has been classified by the IARC as a known human carcinogen that causes nasopharyngeal cancer and leukemia. However, the limited evidence for inhaled formaldehyde causing hematolymphopoietic cancers and the biological implausibility of the hypothesis that inhaled formaldehyde causes leukemia has raised many questions. While inhaled formaldehyde does not reach the bone marrow cells, methanol treatment (*p.o.*) significantly elevates the amount of formaldehyde DNA adducts in bone marrow cells in rats through metabolic activation in bone marrow. In this proposal, we will address whether Fanconi anemia group D2 (*Fancd2*) mutant mice are more susceptible to bone marrow cell toxicity and genotoxicity caused by methanol-derived formaldehyde than wild-type mice. The significance of this project is not only to demonstrate potential bone marrow toxicity caused by methanol-derived formaldehyde, but also to understand the formaldehyde-derived DNA adduct levels sufficient to initiate bone marrow toxicity in *Fancd2*$^{-/-}$ mice, which appear to be the most sensitive animal model of formaldehyde-mediated toxicity. These results will also be used as positive controls for future grant proposals to understand the potential for inhaled formaldehyde causing bone marrow toxicity.

PPP AWARD 2013-03

Project Title: Circadian oscillation of XPA expression in human hair follicles and PBMCs.
Principal Investigator: Shobhan Gaddameedhi, Ph.D., Post-doctoral Fellow, Department of Biochemistry & Biophysics, School of Medicine.

Abstract

Skin cancer is the most common form of cancer in the United States. Recently, we found that the rate of Nucleotide Excision Repair (NER) due to XPA protein oscillates with a circadian rhythm in mouse skin with a minimum in the morning and a maximum in the evening. As a consequence, mice exposed to UV radiation (UVR) in early morning display an earlier onset and increased squamous cell carcinoma than mice exposed to UVR in the evening. The goal of this proposal is to compare the human XPA expression as a function of time of day by analyzing human hair follicles and PBMCs and to translate the basic science findings to potential health ramifications. If XPA oscillates in humans as a time of day, it is likely that the mutagenicity and carcinogenicity of sunlight and tanning beds may be strongly affected by the time of day of light exposure and it might be advisable for humans, to the extent possible, to restrict their occupational, therapeutic, recreational and cosmetic UVR exposure to a given time of day.

PPP AWARD 2013-04

Project Title: Pathways for human uptake of emerging chemicals of concern in land-applied sewage sludge
Principal Investigator: Steve Wing, Associate Professor of Epidemiology.

Abstract

Annually, an estimated 4 million dry tons of U.S. sewage sludge are disposed of by application to land. Sludges, especially those from waste water treatment plants with household and industrial inputs, also contain complex mixtures of chemical contaminants. Although human exposures to these compounds are likely as many are persistent and bioaccumulative in the environment and wildlife, little is known about pathways of human exposure. Our objective is to identify important routes of exposure to sludge contaminants, specifically perfluorinated compounds (PFCs) and polybrominated diphenyl ethers (PBDEs), and identify the population of individuals exposed. We will assess multiple pathways of exposure to sludge contaminants, including airborne dispersion of contaminants, local fish consumption and drinking water contamination. Combining these data with previously assessed pathways, we will use probabilistic models to assess the contribution of each pathway to human internal contaminant dose. This research will provide the first comprehensive assessment of human exposure pathways to land-applied sludge contaminants and will be used to inform an assessment of the impacts of sludge contaminant mixtures on human health.