Prior studies found lower levels of 5-methylcytosine (5-mC) and 5-hydroxymethylcytosine (5-hmC) in human cancers and this global hypomethylation is strongly implicated in skin cancer development. As a class I human carcinogen linked to skin lesions and cancer risk, arsenic (As) exposure is associated with changes in global 5-mC levels but its influence on 5-hmC has not been well studied.

To investigate the link between As and 5-hmC, a recent study conducted by Niedzwiecki, et al. evaluated associations of As in drinking water, urine, and blood with global %5-mC and %5-hmC in two studies of Bangladeshi adults: (i) leukocyte DNA in the Nutritional Influences on Arsenic Toxicity study (n=196; 49% male, 19-66 years); and (ii) peripheral blood mononuclear cell DNA in the Folate and Oxidative Stress study (375; 49% male, 30-63 year). Global %5-mC and %5-hmC were analyzed using LC-MS/MS. The study showed that As induces sex-specific changes in 5-hmC. No overall association was found between As and global %5-mC or %5-hmC. However, associations of As exposure with global %5-hmC were positive in males and negative in female using sex-specific analyses. In addition, plasma total homocysteine (tHcys), an indicator of B-vitamin deficiency, modified the association between As and global %5-hmC. These results suggest that As induces sex-specific changes in 5-hmC. Further research should explore whether alterations in 5-hmC levels is a mechanism underlying these sex-specific effects of As on skin lesion and cancer outcomes.

On Saturday, October 24th, 2015, the Columbia NIEHS Center hosted 42 seventh to tenth grade students and 36 parents from the tri-state area and beyond for an all day workshop titled, “The Environment and Public Health.” The day began with a brief overview of the various graduate programs and departments offered by the Columbia Mailman School of Public Health, as well as an introduction to the NIEHS Center, given by Center Director, Regina Santella. The intro was followed by a remarkable keynote presentation given by Joe Graziano, Director of the Superfund Research Program, titled, “Poison in the Well: Exposures, Consequences and Remediation of Arsenic in Drinking Water in Bangladesh.” This presentation resulted in many fascinating questions from parents and students.

The CTY participants were then divided into four groups with each group rotating through four different 45-minute workshops, two lab-based, and two classroom-based. The workshop topics included: “Climate Change and Health”, “Environmental Health and Justice 101”, “Allergens and Asthma” (Lab); and “Environmental Toxins and the Brain” (Lab). The workshops were led by four doctoral students, Alex Heaney, Ashlinn Quinn, Daniel Carrion, and Richard Remigio all in the Climate and Health Program, Ogonnaya Dotson-Newman and David Chang from WE ACT, Associate Research Scientists Kirstie Stansfield and Sara Guariglia, and Center Member Matt Perzanowski and lab tech Adnan Divjan. Participants learned how to work together to design a research study focused on climate change and allergies/asthma; had the opportunity to discuss ways that they can contribute
and use science to create change and improve their communities; learned how laboratory researchers determine allergy in people and measure allergenic proteins in the environment; and viewed actual rat brains and learned about various laboratory techniques for studying the effects of neurotoxins on the brain. The students were very engaged and asked extremely intelligent questions.

The day culminated with an EHS graduate student panel where the students discussed their educational journeys, from high school to undergraduate college, and finally how they ended up at Columbia pursuing various aspects of environmental health sciences and public health. A big thank you goes to Tiffany Sanchez, Julia Casciotti, Meghan Kiernan and Daniel Carrion for sharing their stories. All in all, the CTY event was a huge success. THANK YOU to everyone who helped in the planning of the program or participated in the event.

(Photos courtesy of COEC intern, Stanley Zou)
**Recent Center Member Research**

**PRENATAL EXPOSURE TO COMMON FLAME RETARDANTS MAY CONTRIBUTE TO ATTENTION PROBLEMS IN CHILDREN**

Even though polybrominated diphenyl ethers (PBDEs) were phased out in 2004, they remain ubiquitous in the environment. PBDEs were used extensively as flame retardant chemicals in consumer products including textiles, plastics, wiring, and furniture containing polyurethane foam. Since PBDEs are not chemically bound to these materials, they migrate into the environment over time. Humans are commonly exposed to PBDEs through accidental ingestion of house dust or by eating food that is contaminated with PBDEs. A recent study, conducted by researchers at the Columbia Center for Children’s Environmental Heath, showed the effects of prenatal exposure to PBDEs on children’s development, during both the preschool and school age periods.

The study followed 210 mother-child pairs, a subset of the Center’s World Trade Center study, from birth through early childhood. This cohort consists of white, black and Chinese women who were pregnant on Sept. 11, 2001 and delivered at one of three downtown NYC hospitals. Cord blood samples collected at delivery were analyzed for PBDE plasma levels to assess prenatal exposure to the chemicals. Maternal-child pairs were followed through age 7 years. Beginning at age 3, researchers assessed child behavior using *The Child Behavior Checklist*, a standardized maternal-report instrument, repeating the test annually through age 7. Investigators controlled for factors that have been previously associated with PBDE exposure levels or neurodevelopment in other studies including child age at testing, ethnicity, mother’s IQ, child’s sex, maternal age, marital status, prenatal exposure to environmental tobacco smoke, and maternal demoralization.

The results published in the journal, *Neurotoxicology and Teratology*, showed that at ages 3, 4, and 7 years, children with the highest exposure to certain PBDEs had approximately twice the number of maternally–reported attention problems compared to the other children in the study. The results support previous peer-reviewed epidemiological studies reporting associations between prenatal PBDE exposure and symptoms of inattentiveness, hyperactivity, and impulsivity among children.

Researchers in the Center are reaching out to the cycling community to get a better understanding on how much air pollution New York City cyclists are exposed to, and how this exposure affects cardiovascular health. While urban biking has many benefits, city cyclists may be exposed to high concentrations of air pollution because of the increasing breath rate and volume. With an ultimate goal of equipping urban planners with tools for developing healthy biking infrastructure, the study takes advantage of miniaturized electronics to measure or estimate both air pollution levels and the volumetric respiration rate each minute. Multiplying the pollution concentration by the volumetric respiration rate provides an estimate of the inhaled dose of air pollution a person is breathing in each minute.

Three monitors are being used as the NYC cyclists are riding through the city. One, developed by RTI International as part of the NIEHS Gene-Environment Initiative, measures minute-by-minute concentrations of PM2.5 together with estimates of the volumetric respiration rate based on an accelerometer. The other two are included in the combined sensor package, estimating the volumetric respiration rate. All three methods will be compared to lab-based measurement of oxygen consumption and volumetric respiration rates. In addition, the cyclists wear a special shirt that monitors heart rate and other parameters and an automatic blood pressure cuff. Each biker will wear the equipment for five 24-hour periods, each of which will include morning and potentially evening bike commutes.

A major challenge in designing personal exposure monitoring tools is to make the tool easy to use, reliable under real-world conditions, and burdenless for users to carry, according to the lead researchers, Darby Jack and Steve Chillrud. The unvarnished feedback from participants will be of great value to the development of the monitoring equipment.

This project began as NIEHS Center pilot funding to Drs. Jack and Chillrud in the spring of 2014, and resulted in an R21 grant R21ES024734 from the NIEHS in 2015 to expand the study.
**Gloria Su**, PhD, Associate Professor, Departments of Otolaryngology/Head & Neck Surgery and Pathology; “The impact of arsenic exposure on the progression of chronic pancreatitis to pancreatic cancer”; Award: $35K

**Abstract:** Pancreatic cancer, although relatively rare, is the fourth leading cause of cancer death in the USA because of its low 5-year survival rate. Besides, there is no cost-effective method to screen the general population for it and early detection, which is imperative for patient survival, is still not feasible. Smoking and chronic pancreatitis (CP) are two major risk factors for pancreatic cancer. However, the actual components or molecular events that link smoking and CP are still not understood.

One possible culprit for smoking-induced carcinogenesis that may augment the increased risks associated with CP may be arsenic. Arsenic is found in cigarettes and has recently been shown to associate with pancreatic cancer in epidemiologic studies. Elevated arsenic, measured in toenail samples, was reported to be associated with increased risk for pancreatic ductal adenocarcinoma (PDA). Exposure to arsenic-contaminated drinking water from wells was linked to increased risk for PDA. In a prospective study reported in 2013, arsenic exposure was prospectively associated with increased mortality for cancers of the lung, prostate, and pancreas. But arsenic has not been proven to cause pancreatic cancer.

This study aims to be the first to provide tangible evidence to establish a causal relationship between arsenic exposure and pancreatic cancer (Aims 1 & 2) and to provide a molecular predictor for CP progression to pancreatic cancer (Aim 2). In Aim 1, the study will use 3-D cultures of acinar cells isolated from two novel mouse models for CP and PDA to test if arsenic exposure will impact the acinar to ductal metaplasia step (ADM) in vitro. In Aim 2, the study will perform a pilot in vivo study on the CP model to investigate if arsenic exposure will exacerbate the CP phenotype and push disease progression from CP to pancreatic cancer. They will also identify a unique biomarker profile (exosomal proteins) that is specifically associated with this disease progression (from CP to pancreatic cancer) facilitated by arsenic exposure. The establishment of the causal relationship will not only significantly raise awareness of the risk associated with arsenic exposure, but more importantly, the completion of the research will promote new monitoring programs with novel biomarkers for high-risk patients.
Richard J. Levy, MD, FAAP, Professor of Anesthesiology and Pediatrics; “Carbon Monoxide Pollution and Fmr1 Gene Mutation: Exploring a Gene-Environmental Cause of Autism”; Award: $35K

Abstract: Autism spectrum disorder (ASD) affects one in 68 children and is the fastest growing developmental disability in the US. The most promising hypothesis regarding the cause of autism suggests a gene-environment interaction. Recent studies indicate that exposure to traffic-related air pollution during gestation or early postnatal development is associated with increased risk of ASD. There is a major gap in our knowledge because it is unknown how air pollution interacts with specific genetic defects to result in the autistic phenotype. Fragile X syndrome (FXS), due to a mutation that results in transcriptional silencing of the Fmr1 gene, is the leading known genetic cause of autism. Fmr1 mutant mice have been developed to model human FXS, making Fmr1 ideal for the study of the gene-environment interaction. Carbon monoxide (CO) is a major component of motor vehicle-related pollution and a known neurotoxin. We have shown that CO impairs natural apoptosis in the developing wild-type murine brain, resulting in excess number of neurons, larger brains, memory and learning deficits, and relative social avoidance. In preliminary work, we also identified a defect in the mitochondrial pathway of apoptosis in the postnatal forebrain of male Fmr1 mutant mice. Therefore, this proposal will focus on the Fmr1 gene-CO interaction using a mouse model of FXS. Our specific hypothesis is that CO exposure during Fmr1 mutant brain development compounds and exacerbates defects in neuronal apoptosis and physiologic neuron elimination resulting in a well-defined autistic phenotype. The experiments are aimed at identifying the mechanism of CO-mediated inhibition of neuronal apoptosis in the Fmr1 knockout mouse forebrain and defining the behavioral phenotype of Fmr1 mutant mice exposed to postnatal CO. Success of the proposal will establish compounded defects in programmed cell death as a neurodevelopmental consequence of this specific gene-environment interaction and a contributor to the autism phenotype. Because this critical process is essential for normal brain development, we anticipate that data generated from this proposal will identify novel targets for therapeutic intervention.
**Congratulations to Our 2015 Pilot Awardees!**

**Darby Jack**, PhD, Assistant Professor of EHS, **Steve Chillrud**, PhD, Lamont Research Professor, and **Pat Kinney**, ScD, Professor of EHS; “Improving data quality from low cost sensors”; Award: $35K

**Abstract:** Low cost sensors hold great promise in public health research, but their utility is currently limited by data quality problems. This is particularly true in the domain of air pollution epidemiology, where sensor networks will revolutionize exposure assessment if reliability can be achieved. We seek to pilot a new approach to addressing data quality problems arising in networks of low cost sensors. We propose to partner with Multitude, a software startup that has built a system that aggregates sensor data and pushes it through a series of correction algorithms. These algorithms draw both on prior knowledge about the physical properties of the sensors, and on coincidental and intentional collocation sensors in the field. We will use data from the current Columbia University air pollution and biking study and from regulatory monitors to validate this approach.

**Liza A. Pon**, PhD, Professor of Pathology and Cell Biology; “Mechanisms for Repair of Pesticide-Induced Damage to Mitochondria”; Award: $10K

**Abstract:** Paraquat, the most widely used herbicide globally, is also an environmental and occupational toxin. Paraquat exposure results in damage to the lungs, kidneys, heart and liver, and in serve cases, respiratory failure and death. Emerging evidence indicates that there are links between long-term paraquat exposure and Parkinson’s Disease. We will use yeast as a model system to study the repair mechanisms that promote resistance to chronic, low-level exposure to paraquat. The proposed studies will extend our understanding of the consequences of paraquat exposure and reveal approaches to reduce the negative impact of this widely used environmental and occupational toxin.
Recent Center Member Awards And Honors

DIANE RE, an Assistant Professor in EHS, received a 2015-16 Calderone Junior Faculty Award to fund studies to demonstrate potential similarities between two debilitating and currently untreatable conditions, organophosphate-induced delayed neuropathy (OPIDN) and amyotrophic lateral sclerosis (ALS).

JEFF SHAMAN was named as one of the four Mailman Tow Scholars in recognition of outstanding and innovative research and thought leadership. This 3-year award of $25K annually is from the Tow Foundation to support mentoring and training in leadership and development.

FREDERICA PERERA was awarded the second annual Jean and Leslie Douglas Pearl Award by the Cornell Douglas Foundation for her pioneering work in the field of molecular epidemiology. Dr. Perera also received the 2015 Environmental Advocate Award of New York on November 10th for groundbreaking research on the impact of prenatal and early childhood exposure to pollutants on the health and development of children in NYC, Poland, and China.

MARY BETH TERRY and RACHEL MILLER are leading a new NIH-funded Breast Cancer and Environmental Research Program (BCERP). The Mailman School and CUMC is one of six new research centers that will focus on prevention among minority and socially disadvantaged women.

ALFREDO MORABIA was named as new editor-in-chief of the American Journal of Public Health, effective June 2015.

GREG FREYER received the Mailman School Teaching Excellence Award in May 2015.
**Spring Seminar Schedule to Date**

**January 28:** Craig Steinmaus, MD, MPH, Associate Adjunct Professor of Epidemiology, UC Berkeley, CA; Title: “The toxicity of arsenic in water: what we’ve learned from the deserts of Chile”; 722 W. 168th Street, EHS Conference Room 1101, 12:00-1:00pm. Host: Manuela Orjuela-Grimm

**February 25:** Dana Dolinoy, PhD, Associate Professor, Environmental Health Sciences and Nutritional Sciences, University of Michigan, Ann Arbor, MI; Title: “Perinatal Environmental Exposures: Effects on Metabolic Homeostasis and the Epigenome”; 722 W. 168th Street, EHS Conference Room 1101, 12:00-1:00pm. Hosts: Pam Factor-Litvak and Regina Santella

**March 11:** Yang Liu, PhD, Associate Professor in Environmental Health, Emory University Rollins SPH, Atlanta, GA; Title: “Evaluating population health impacts of climate change with downscaled model simulation results”; 722 W. 168th Street, EHS Conference Room 1101, 12:00-1:00pm. Host: Pat Kinney

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**Change in Date:**

Spring Center Meeting

**Thursday, March 31st**

722 W. 168th Street, 10th floor, Hess Commons

12:00-1:45PM

Lunch will be served!

Students and postdocs are welcome to attend.

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**Save the Date:**

Annual Center Retreat/External Advisory Meeting

**Friday, June 3rd**

Faculty House

9:00AM-4:00PM

All interested faculty, students, postdocs, lab managers, etc. are welcome to attend.