Center Executive Summary –Columbia University Superfund Research Program -P42ES10349

A. Center Highlights: Below we provide four highlights of our research accomplishments in the past year.

Highlight Project 1: Health Effects of Arsenic Longitudinal Study (HEALS)
PI: Habibul Ahsan

Highlight Title: Association Between Inorganic Arsenic Exposure and Cardiovascular Disease

Background:
Epidemiologic studies have documented associations between arsenic exposure from drinking water and cardiovascular disease (CVD), and heart disease in particular. However, the underlying mechanism by which arsenic may lead to CVD is unclear. Once ingested, InAs is methylated to monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA). Mechanistic studies have shown that MMA^{III} is more toxic than InAs or any of the pentavalent metabolites. The relative distribution of total MMA and DMA in urine reflects arsenic methylation capacity. Research is needed to consider susceptibility biomarkers for arsenic exposure and their joint effect with arsenic exposure on subclinical and clinical endpoints of CVD.

Advances:
This highlight involves three manuscripts regarding the association between inorganic arsenic exposure and cardiovascular disease (CVD). We first reported an association between baseline water arsenic concentrations and prolonged heart-rate corrected QT (QTc), a susceptibility factor for ventricular arrhythmia and sudden cardiac death. The association was stronger in women than in men (1); this adds to the long list of sex specific consequences of arsenic exposure. We subsequently evaluated the relationship between arsenic exposure, arsenic methylation capacity and the risk for CVD, involving 369 incident fatal and non-fatal cases of CVD including 211 cases of heart disease and 148 cases of stroke (2). In this study, we found that increased arsenic methylation capacity was associated with a relatively reduced risk for arsenic-induced heart disease, but not stroke (2), in both men and women. At any given level of water arsenic, individuals with incomplete arsenic methylation capacity, indicated by higher MMA% or lower DMA%, experienced a greater risk than their counterparts. Finally, we described a relationship between water (and urinary) arsenic concentrations and carotid intima-media thickness (cIMT), an ultrasound measure of early atherosclerosis and a valid surrogate marker for clinical endpoints, in men and women. Once again, arsenic methylation capacity significantly influenced risk, with those more capable of synthesizing DMA at lower risk, and those with higher monomethylarsenic (MMA) at higher risk.

Significance:
The U.S. EPA is in the midst of re-evaluating the toxicity of arsenic with regard to cancer and non-cancer outcomes in its IRIS database. The National Research Council (NRC), in response to a request by Congress, convened a committee of experts to provide guidance to EPA prior to its effort to update the IRIS database. The 15 member NRC committee, which included by Drs. Ahsan and Graziano (as Chair), issued a report on November 7th, 2013, entitled “Critical Aspects of EPA’s IRIS Assessment of Inorganic Arsenic (4).” *The report is notable in that for the first time, a non-cancer outcome, namely CVD, has been placed in the top-tier of concern*, in part because of the body of evidence that arisen from the HEALS study, which has been heavily supported by the Trace Elements Core Lab. EPA is currently working to revise the IRIS database for inorganic arsenic, and will present its draft version to the NRC committee for its review sometime toward the end of 2014.

For More Information Contact:
Yu Chen
Habibul Ahsan
Joseph Graziano

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1. *__Chen Y__, Wu F, __Parvez F__, Ahmed A, Eunus M, McClintock TR, Patwary TI, __Islam T__, Ghosal AK, Islam S, Hasan R, __Levy D__, __Sarwar G__, __Slavkovich V__, __van Geen A__, __Graziano JH__, __Ahsan H__. Arsenic exposure from drinking water and QT-interval prolongation: results from the Health Effects of Arsenic Longitudinal Study. Environ Health Perspect 2013;121:427-32. 432e1-7. doi: 10.1289/ehp.1205197. PMCID: PMC3620737

2. *__Chen Y__, Wu F, Liu M, __Parvez F__, __Slavkovich V__, Eunus M, Ahmed A, __Argos M__, __Islam T__, Rakibuz-Zaman M, Hasan R, Sarwar G, __Levy D__, __Graziano J__, __Ahsan H__. A prospective study of arsenic exposure, arsenic methylation capacity, and risk of cardiovascular disease in Bangladesh. Environ Health Perspect 2013;121:832-8. PMCID: PMC3701993

3. *__Chen Y__, Wu F, __Graziano JH__, __Parvez F__, Liu M, Paul RR, Shaheen I, Sarwar G, Ahmed A, __Islam T__, __Slavkovich V__, Rundek T, Demmer RT, Desvarieux M, __Ahsan H__. Arsenic exposure from drinking water, arsenic methylation capacity, and carotid intima-media thickness in Bangladesh. Am J Epidemiol 2013;178:372-81. PMCID: PMC3727341

4. National Research Council: Critical Aspects of EPA's IRIS Assessment of Inorganic Arsenic. http://dels.nas.edu/report/critical-aspects-iris/18594

Highlight Project 3: Impact of Nutrition on Arsenic-Induced Epigenetic Dysregulation
PI: Mary Gamble

Highlight Title: Batch Effects and Pathway Analysis: Two Potential Perils in Studies Involving DNA Methylation Array Analysis using Arsenic Exposure as a Paradigm **(**Kristin N. Harper, Brandilyn A. Peters, and Mary V. Gamble)

Background: DNA methylation microarrays have become an increasingly popular means of studying the potential influence of environmental exposures on epigenetic outcomes, although the methods used to analyze array data are still being developed and existing methods are not always widely disseminated among microarray users. Using the paradigm of exposure to arsenic-contaminated drinking water, we investigated two problems likely to confront DNA methylation microarray users: (i) batch effects and (ii) the use of widely available pathway analysis software created for gene expression to analyze DNA methylation results. First, peripheral blood mononuclear cell DNA samples taken from individuals exposed to low and high levels of water arsenic were plated (Run) twice on Illumina's Infinium 450 K Human Methylation Array, once in order of exposure and once via randomization. In both cases, we used ComBat software to attempt to correct for batch effects. Second, we conducted 100 *in silico* simulations. Within each simulation, 100 randomly selected CpG sites were drawn from the 450K array and subjected to pathway analysis using Ingenuity's IPA software.

Advances: First, we found that the majority of CpG sites differentially methylated according to arsenic exposure that were identified in Run One were due to batch effects. After adjustment for batch, 24,184 differentially methylated sites were identified in Run One; however, only 25 of these were also identified in Run Two. In total, 187 CpG sites differentially methylated according to arsenic exposure were identified in the properly randomized Run Two. We have already verified differential methylation at 12 of these sites using NextGen sequencing and are in the process of analyzing data for additional sites. The issue of batch effects is particularly problematic in studies investigating the effects of environmental exposures on DNA methylation, for often the magnitude of the effect is expected to be relatively small.

Second, we found that the IPA pathway analysis software reported many highly significant associations between our *in silico* data, i.e. randomly drawn CpGs from the 450 K array, and various diseases and biological functions. This is because CpGs associated with genes involved in diseases and biological functions

of scientific interest are over-represented on the 450K array. They are therefore more likely to be selected at random than CpGs associated with “less interesting” genes or CpGs in repetitive elements, and to appear as false positives in a list of differentially methylated CpG sites.

These analyses illustrate the pitfalls of not properly controlling for chip-specific batch effects as well as using pathway analysis software created for gene expression arrays to analyze DNA methylation array data.

Significance: We present evidence that (i) chip-specific effects can erroneously simulate plausible differential methylation results and (ii) popular pathway analysis software developed for expression arrays can yield spurious results when used in tandem with DNA methylation microarrays. Our findings are broadly applicable to projects using DNA methylation microarrays and/or pathway analysis software, and they are important in light of the popularity of these methods in environmental health research.

For further information, please contact:
Mary V. Gamble
Kristin N. Harper

Reference:
Harper KN, Peters B, Gamble MV. Batch effects and pathway analysis: Two potential perils in cancer studies involving DNA methylation array analysis. Cancer Epidemiol Biomarkers Prev 2013;22(6):1052-60. PMCID: PMC3687782.

Highlight- Project 5: Application of Enhanced Mitigation Methods for Groundwater Arsenic at US Superfund Sites
PI: Steve Chillrud

Highlight Title: Arsenic *In-Situ* Immobilization by Magnetite Formation within Contaminated Aquifer Sediments

Background:
Magnetite, or ferrous-ferric, iron is stable in a wide range of conditions including Fe-reducing environments where As is typically mobilized and bioavailable. It can scavenge both As(III) and As(V) from solutions through surface adsorption and it is also capable of trapping As(V) into the crystal structure. Therefore, magnetite may represent a long-term host-mineral in which to immobilize groundwater As. However magnetite is difficult to make in situ in acidic to circum-neutral conditions found in most contaminated aquifers. Previous laboratory microcosm experiments of ours (Sun *et al.*, In preparation), which used oxidized aquifer sediments and groundwater from the Vineland Chemical Company Superfund site, suggested that magnetite formation could be achieved by the oxidation of ferrous Fe (added as ferrous sulfate) by nitrate. Those Fe(II)-nitrate microcosms yielded magnetite and ferrihydrite in in solid phase, efficiently removed As from solution, and maintained low dissolved As concentrations for more than 5 weeks under reduction. Other microcosms did not achieve low dissolved As concentrations, including those stimulating sulfide precipitation.

Advances:
To better develop this magnetite-based strategy, we need to understand how best to produce magnetite and sequester As under field conditions of continuous and dynamic flow, and also how to achieve these with different site geochemical and mineralogical characteristics. Based on this, we did a multi-stage column study (column = flow-through setting), loaded with reduced aquifer sediments from the Dover Landfill Superfund site. We stimulated the formation of magnetite which sequestered As from solution, tested its ability of maintaining As retention under reducing conditions, and evaluated its potential to immobilize additional As flowing into the system. Evolution of both water and sediment properties was monitored over time. The columns were pre-equilibrated with continuous oxygen-free artificial groundwater containing lactate and arsenite As(III), during which highly elevated aqueous As level in column effluents was observed. Then nitrate and ferrous Fe were added to the same influent groundwater, which yielded considerable magnetite and some other iron minerals

and resulted in very low As in the effluent. These amended columns were able to maintain low aqueous As concentrations when influent groundwater with high lactate concentration (and no As) were introduced to further encourage reduction. Even under long term addition of arsenite- and lactate-containing groundwater, aqueous As level in effluents remained low for many pore volumes. The data suggest that the adsorption capacity and stability of As(III) greatly increased in amended sediments.

Significance:
One remediating approach for As-contaminated aquifers involves stimulating Fe mineral transformations that decrease aqueous As concentrations through sorption or precipitation. But these immobilization strategies are often ineffective, in part because Fe host minerals are often mobilized under redox changes. Our data demonstrates that magnetite, produced via simultaneous addition of ferrous Fe and nitrate, is a promising target mineral for long-term As remediation. This year's work helped refine this *in situ* immobilization strategy where our ultimate goal is field-deployable procedures.

For More Information Contact:
Benjamin Bostick, Steven Chillrud, Brian Mailloux, Martin Stute

References:
Sun, J., S.N. Chillrud, B.J. Mailloux, M. Stute, B.C. Bostick. Magnetite Formation under Acidic Conditions in Arsenic Contaminated Aquifer Sediments. *Environ. Sci. Technol*., In preparation.

Highlight- Project 6: *Defining the Sustainable Uses of Low-Arsenic Aquifers in Bangladesh*
PI: Alexander van Geen

Highlight Title: Comparison of two blanket surveys of arsenic in tubewells conducted 12 years apart in a 25 km^2 area of Bangladesh.

Background:
A decade of field research by the Columbia SRP in Araihazar and other groups elsewhere has shown that switching to a low-arsenic well lowers human exposure more sustainably than any form of groundwater treatment in rural Bangladesh. In order for this happen, however, a household must know the status of its well and that of neighboring wells. In order to demonstrate the feasibility of testing wells using a field-kit and providing the necessary quality control at a significant scale, Columbia SRP scientists and their collaborators in Bangladesh decided to test all wells within the administrative unit of Araihazar upazilla where participants in Project #1's "Health Effects of Arsenic Longitudinal Study" (HEALS) reside.

Advances:
Field-kit testing of a total of 49,790 wells across Araihazar upazilla by a team of 10 village-health workers started in March 2012 and was completed in September 2013. The new test results were compared within a subset of 61 contiguous villages that were sampled a first time in 2000-01 at the launch of HEALS. The two surveys indicate that the total number of tubewells within the area almost doubled from 5,560 to 10,879 over 12 years. The evolution of the distribution of well ages between the two surveys is consistent with a simple model that combines an annual increase of 42 wells/year in the rate of installations within the 61 villages starting in 1980 and a 7%/year rate of abandonment of wells as a function of well age. The new installations and rapid turnover help explain why, despite blanket testing campaigns conducted under the Columbia SRP in 2000-01 and by the government's Bangladesh Arsenic Mitigation and Water Supply Program (BAMWSP) in 2003, only half the households claimed to know the status of their well 2012-13. Disturbingly, the proportion of safe and unsafe wells in Araihazar did not shift markedly over a decade.

Significance:
Whereas the turnover rate of tubewells in South or Southeast Asia was suspected to be high, it has to our knowledge never been quantified by comparing the distribution of well ages from repeated blanket surveys of

the same area. The findings from Araihazar confirm that one-time surveys are insufficient to lower the exposure of the rural population of Bangladesh and that testing needs to be available to villagers on a permanent basis. One possibility would be for entrepreneurs to provide this service for a fee. With separate funding from the UK's International Growth Center, this approach was recently explored by offering tests across of range of prices in 26 villages of the Indian state of Bihar, which is affected by arsenic in a way similar to Bangladesh (van Geen and Singh, 2013). Building on these results, two testers were trained and provided with a field kit and handheld GPS in Araihazar in June 2013. Their baseline salary of $50/month is supplemented by collecting $0.40/test from households. As of December 2013, a total of 800 newly installed wells were tested through this mechanism, suggesting that a semi-commercial testing service is viable and could be expanded throughout the country.

For More Information Contact:
Alexander van Geen

References:

vanGeen A, EB Ahmed, L Pitcher, JL Mey, H Ahsan, JH Graziano, KM Ahmed. Comparison of two blanket surveys of arsenic in tubewells conducted 12 years apart in a 25 km2 area of Bangladesh. Science of the Total Environment, accepted December 2013. NIHMSID: NIHMS557871

vanGeen, A, and CK Singh. Piloting a novel delivery mechanism of a critical public health service in India: arsenic testing of tube well water in the field for a fee.IGC Policy Note 13/0238, 2013.(http://www.theigc.org/sites/default/files/13_0238_POLICYNOTE_V4_LR.pdf).

B. Personnel Updates: There have been no changes in the key personnel listed in the Notice of Grant Award.

C. SRP Trainee Highlights:

Megan Hall, Dr. Gamble's former post-doctoral research fellow (currently an Assistant Professor) worked on statistical analyses and manuscript preparations for Dr. Gambles SRP Project. Her work has been selected for oral presentation at the 2014 SRP/NIEHS Arsenic Workshop entitled, "Health effects and mitigation of arsenic: current research efforts and future directions". Dr. Hall has also been invited to speak at the 2014 FASEB Summer Research Conference on Folate and One Carbon Metabolism in August 2014. Dr. Hall is in the R00 phase of a K99/R00 award from NIEHS to study nutritional influences, particularly of choline and betaine, on arsenic methylation. Finally, Megan Hall was an invited speaker at the 2013 Annual SRP Meeting in Baton Roughe, LA. The title of her talk was, "Urinary creatinine: implications of its use as a urine dilution adjustment factor in epidemiologic studies of Metal Exposure."

Kristin Harper, Dr. Gamble's post-doctoral research fellow is working on analyses of differentially methylated CpGs by arsenic exposure using Illumina's new 450K array (see Highlight and 2013 publication) and this data is currently being validated by NextGen sequencing. Dr. Harper presented her work at our P30 Center's Epigenetics Working Group on Nov. 22, 2013 (described above and manuscript in preparation).

Caitlin Howe is a PhD student in Dr. Gamble's laboratory. She has been working on analyses related to our SRP Project in which we are analyzing associations between arsenic exposure and histone modifications as well as on s-adenosylhomocysteine and s-adenosylmethionine and both histone and arsenic methylation (manuscript in revision). Caitlin successfully passed her qualifying exams in December 2013.

Yongfeng Jia is a PhD candidate at China University of Geosciences supported by the China Scholarship Council to carry out SRP-related at LDEO from September 2013 through December 2014.

Fiona Kinniburgh graduated from Columbia College with a bachelor's in Sustainable Development in June 2013 and carried her honors thesis research at LDEO.

Peter Knappett, PhD is a hydrogeologist and became a post-doctoral investigator at LDEO in 2012. Starting in August 2013, he joined the faculty of Texas A&M University as an assistant professor and continues to collaborate with Columbia SRP PIs.

Ivan Mihajlov, a PhD candidate in Earth & Environmental Sciences co-advised by the PI, successfully defended his PhD in November 2013.

Md. Rajib Mozumder, a geology graduate from the University of Dhaka, entered the PhD program in Earth & Environmental Sciences in September 2012 and continues to be advised by the Dr. van Geen.

Megan Niedzwiecki, Dr. Gamble's PhD student, successfully defended her thesis in December 2013. The title of her thesis was, "Mechanisms of Arsenic Toxicity in Humans: Interplay of Arsenic, Glutathione, and DNA Methylation in Bangladeshi Adults." She worked on laboratory and data analyses for the folate and oxidative stress (FOX) study from Aim 3 of Project 4 of Dr. Gamble's previous SRP Project. She studied the effects of redox status on methylation of arsenic and DNA which was one focus of her thesis. Her work was selected for a poster presentation at the 2013 SRP Meeting in Baton Rouge, LA. She has recently accepted a post-doctoral position at the Mount Sinai School of Medicine where she will be working with Dr. Robert Wright.

Brandilyn Peters, Dr. Gamble's PhD student is also working on analyses of differentially methylated CpGs by arsenic exposure and was, along with Kristin (above), instrumental in generating preliminary data for our new SRP Project 3. She also analyzed all of the homocysteine data for aim 2. Brandi is also working on a project related to the potential renal toxicity of arsenic exposure in Bangladesh (manuscript in preparation). Brandi presented her work as a poster at the 2013 Annual SRP Meeting in Baton Rouge, LA entitled, "Arsenic metabolism and renal function in an arsenic-exposed population in Bangladesh." She also presented a poster at the Pacific Basin Consortium for Environment and Health in Hawaii in September 2013.

Meridel Phillips is Master's student in the Department Earth and Environmental Engineering conducting SRP research at LDEO.

Tiffany Sanchez is a third year PhD student in the Department of Environmental Health Sciences who is working with Dr. Graziano on Project #2. Specifically, she is analyzing data regarding the relationship between arsenic exposure a pulmonary function in adolescents in Bangladesh, and is examining the hypothesis that arsenic exposure is associated with lung inflammation, as measured by the pH of exhaled breath condensate and the concentration of 8-isoprostane in the condensate.

Jing Sun, a fourth year PhD student in Department of Earth and Environmental Sciences who is working on Project 4 and 5 under the direction of Drs. Bostick and Chillrud, won the best student poster award (Title of Poster: Arsenic *In-Situ* Immobilization by Magnetite Formation within Contaminated Aquifer Sediments) within the Environmental Sciences division of the Annual SRP Meeting in New Orleans in October 2013. She also gave a platform presentation at the 23nd V.M. Goldschmidt 2013 conference entitled "Formation of Magnetite within Aquifer Sediments and Its Effects on Arsenic Mobility."

D. Publication/Patent Consolidated List

2013 Publications:

***Argos M**, **Parvez F**, Rahman M, Rakibuz-Zaman M, Ahmed A, Hore SK, **Islam T**, **Chen Y**, **Pierce BL**, **Slavkovich V**, **Olopade C**, Yunus M, Baron JA, **Graziano JH**, **Ahsan H**. A prospective cohort study of urinary total arsenic concentration and skin lesion status in relation to malignant and non-malignant lung disease mortality in bangladeshi adults. Epidemiology 2014; In press.098/09 PMCID: in process

Argos M, Melkonian S, **Parvez F**, Rakibuz-Zaman M, Ahmed A, **Chen Y**, **Ahsan H**. A population-based prospective study of energy-providing nutrients in relation to all-cause cancer mortality and cancers of digestive organs mortality. Int J Cancer 2013;133:2422-8. PMCID: in process

Argos M, Rahman M, **Parvez F**, Dignam J, **Islam T**, Quasem I, K Hore S, T Haider A, Hossain Z, I Patwary T, Rakibuz-Zaman M, **Sarwar G**, La Porte P, Harjes J, Anton K, Kibriya MG, Jasmine F, Khan R, Kamal M, Shea CR, Yunus M, Baron JA, **Ahsan H**. Baseline comorbidities in a skin cancer prevention trial in Bangladesh. Eur J Clin Invest. 2013 Jun;43(6):579-88. doi: 10.1111/eci.12085. Epub 2013 Apr 17. NIHMSID: NIHMS457153

*Balasubramanya S, **Pfaff A**, Bennear L, Tarozzi A, **Ahmed KM**, Schoenfeld A, **van Geen A**, Evolution of households' responses to the groundwater arsenic crisis in Bangladesh: information on environmental health risks can have increasing behavioral impact over time. Environ Develop Econ 2013;pp.1-17. doi:10.1017/S1355770X13000 NIHMSID: NIHMS558341

Brocato J and **Costa M**. Basic mechanisms of DNA methylation and the unique landscape of the DNA methylome in metal-induced carcinogenesis. Crit Rev Toxicol 2013;43(6):493-514. PMCID: PMC3871623

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***Chen Y**, Wu F, Liu M, **Parvez F**, **Slavkovich V**, Eunus M, Ahmed A, **Argos M**, **Islam T**, Rakibuz-Zaman M, Hasan R, Sarwar G, **Levy D**, **Graziano J**, **Ahsan H**. A prospective study of arsenic exposure, arsenic methylation capacity, and risk of cardiovascular disease in Bangladesh. Environ Health Perspect 2013;121:832-8. PMCID: PMC3701993

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Feighery F, **Mailloux BJ**, Ferguson AS, **Ahmed KM**, **van Geen A**, Culligan PJ. Transport of *E. coli* in aquifer sediments of Bangladesh: Implications for widespread microbial contamination of groundwater. Water Resources Res DOI: 10.1002/wrcr.20289, 2013. NIHMSID: NIHMS558342

*George CM, **Gamble M**, **Slavkovich V**, **Levy D**, Ahmed A, **Ahsan H**, **Graziano J**. A cross-sectional study of the impact of blood selenium on blood and urinary arsenic concentrations in Bangladesh. Environ Health 2013;12:52. doi:10.1186/1476-069X-12-52. PMCID: PMC3724573

***Hall MN**, **Niedzwiecki MM**, **Liu X**, **Harper KN**, Alam S, **Slavkovich V**, **Ilievski V**, **Levy D**, Siddique AB, **Parvez F**, Mey JL, **van Geen A**, **Graziano JH** and **Gamble MV**. Chronic arsenic exposure and blood glutathione and glutathione disulfide concentrations in Bangladeshi adults. Environ Health Persp 2013;121(9):1068-74. PMCID: PMC3764071

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Water Res 2014;63:120–30. http://dx.doi.org/10.1016/j.advwatres.2013.11.005, 2013. NIHMSID: NIHMS558343

Lee JE, McLerran DF, Rolland B, **Chen Y**, Grant EJ, Vedanthan R, Inoue M, Tsugane S, Gao YT, Tsuji I, Kakizaki M, **Ahsan H**, Ahn YO, Pan WH, Ozasa K, Yoo KY, Sasazuki S, Yang G, Watanabe T, Sugawara Y, **Parvez F**, Kim DH, Chuang SY, Ohishi W, Park SK, Feng Z, Thornquist M, Boffetta P, Zheng W, Kang D, Potter J, Sinha R. Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies. Am J Clin Nutr 2013;98:1032-41. PMCID: PMC3778858

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***Mailloux BJ**, Trembath-Reichert E, Cheung J, Watson M, **Stute M**, Freyer GA, Ferguson AS, **Ahmed KM**, **Alam MJ**, Buchholz BA, Thomas J, Layton AC, **Zheng Y**, **Bostick BC**, **van Geen A**. Advection of surface-derived organic carbon fuels microbial reduction in Bangladesh groundwater, PNAS 110: 5331-5, 2013. PMCID: PMC3619377

*Melkonian S, **Argos M**, **Hall MN**, **Chen Y**, **Parvez F**, **Pierce B**, Cao H, Aschebrook-Kilfoy B, Ahmed A, **Islam T**, **Slavkovich V**, **Gamble M**, Haris PI, **Graziano JH**, **Ahsan H**. Urinary and Dietary Analysis of 18,470 Bangladeshis Reveal a Correlation of Rice Consumption with Arsenic Exposure and Toxicity. PLoS ONE 2013;8(11):e80691. doi:10.1371/journal.pone.0080691 PMCID: PMC3829854

***Niedzwiecki M**, **Hall MN**, **Liu X**, Oka J, **Harper K**, **Slavkovich V**, **Ilievski V**, **Levy D**, **van Geen A**, Mey J, **Alam S**, **Siddique A**, **Parvez F**, **Graziano JH**, **Gamble MV**. Blood glutathione redox status and global methylation of peripheral blood mononuclear cell DNA in Bangladeshi adults. Epigenetics 2013;8(7):730-8. PMCID: PMC3781192

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van Geen A, **Bostick BC**, Pham TK, Vi ML, Nguyen-Ngoc M, Phu DM, Pham HV, **Radloff K**, **Aziz Z**, Mey JL, Stahl MO, **Harvey CF**, Oates P, Weinman B, Stengel C, Frei F, Kipfer R, Berg M. Retardation of arsenic transport through a Pleistocene aquifer. Nature 2013;501:204-7. doi:10.1038/nature12444. PMCID: PMC3772538

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Yinon L, **Chen Y**, **Parvez F**, Bangalore S, **Islam T**, Ahmed A, Rakibuz-Zaman M, Hasan R, **Sarwar G**, **Ahsan H**. A prospective study of variability in systolic blood pressure and mortality in a rural Bangladeshi population cohort. Prev Med 2013;57:807-12. PMCID: in process

*-denotes publications that resulted from collaborations between project and core activities.

2013 Patents:

vanGeen, A., B. C. Bostick, C. Manning. 2011. A Peltier freeze shoe sampler to recover aquifer sediment and groundwater. US Provisional Patent Application Serial Nos. 13/210.834 and 61/374,193.Filed August 16, 2011.

Progress Reports of Individual Projects and Core Operations

Project 1: A Cohort Study of Health Effects of Arsenic Exposure in Bangladesh
PI: Habibul Ahsan

A. Specific Aims

There are no deviations in the specific aims from those that have already been reported.

B. Studies and Results

This prospective cohort study recruited 11,746 men and women in Araihazar, Bangladesh, during 2000-2002 to investigate the health effects of arsenic exposure, with an initial focus on skin lesions and skin cancers. Between 2006 and 2011, the cohort was expanded to 30,033 individuals. Expansion participants were enrolled into the cohort through in-person interviews and had blood and urine samples collected in the same manner as the original cohort. The design of this multidisciplinary project and cohort description has been published (Ahsan et al., 2005). We have numerous publications utilizing the baseline cross-sectional data on arsenic exposure and adverse health effects, including prevalent skin lesion cases, as well as longitudinal analyses of mortality, incident skin lesions, diabetes, cardiovascular disease, and respiratory disease with the prospective data.

In-person interviews and clinical examinations of the cohort participants are conducted every 2 years. The twelve-year follow-up visit of the original cohort and six-year follow-up visit of the expansion cohort is currently being planned and will be underway soon. To date, we have completed laboratory measurement of urinary total arsenic concentration in all baseline, two-year follow-up, and four-year follow-up samples from the original HEALS cohort and all baseline and two-year follow-up samples of the expansion cohort.

In the last 12 months, analysis of data collected by the HEALS study has contributed to a wide variety of health-related fields, including cardiovascular disease, pulmonary health, and cancer. Three papers by Chen et al. in 2013 established that cardiovascular disease and its precursors were found to be associated with higher levels of arsenic exposure, and a lower ability to excrete arsenic from the body. Results from Parvez et al. (2013) suggested that even low-levels of arsenic exposure may impair lung function. Melkonian et al. (2013) established that steamed rice consumption is associated with higher levels of urinary arsenic, as well as higher levels of the skin lesions that often precede other arsenic-related morbidity and mortality. Analysis of the HEALS study data also provided evidence that the levels of selenium in a person's blood may help reduce the

levels of arsenic (George et al., 2013). In a recently accepted publication, Argos et al. (2014) showed that arsenic exposure is associated with increased non-malignant lung disease mortality and arsenical skin lesion status is associated with increased lung cancer mortality. The cohort data was also utilized in several secondary analyses, leading to several notable publications. Analysis by Wu et al. (2013) reported an association between tobacco smoking and mortality for the first time in a Bangladeshi population. An analysis by Argos et al. (2013) found an association between high protein diet and cancer mortality. Variability in blood pressure was linked with the risk of death for the first time in a population-based cohort (Yinon et al., 2013). Quality of life and mental health were lower in HEALS participants with high levels of arsenic exposure (Syed et al, 2012). Several other manuscripts in preparation and under review will be reporting results of a number of additional analyses from the HEALS data.

The objectives of our current analyses and follow-up interviews are to specifically examine the aims stated in the renewal of this project and have not been modified since the last progress report. Several other manuscripts are being drafted for publication, including investigations into the effect of arsenic exposure on DNA methylation and gene expression, the genetic determinants of body mass index, interactions between genetic and nutritional determinants of body mass index, and descriptions of medication use in this population.

In addition to the above-mentioned components, resources from this prospective cohort study have also yielded many other ancillary studies and publications including three additional R01 grants from NIH to investigate the genetic and nutritional aspects as well as chemoprevention of arsenic health effects.

C. Significance

The association between individual-level arsenic exposure and dermatological, pulmonary, and cardiovascular health outcomes has not been well established in the scientific literature, particularly at low-to-moderate exposure levels. Our overall goal is to prospectively evaluate the effects of various measures of arsenic exposure and metabolism on: i) incidence of skin lesions and skin cancer, ii) incidence and mortality from chronic lung disorders and mortality from lung cancers, iii) incidence and mortality from cardiovascular disease (CVD), and iv) a number of biological and preclinical markers potentially involved in skin and lung disorders/cancers and CVD. The information derived from this study will have direct public health impact on arsenic-exposed populations and can be readily incorporated in future prevention and mitigation measures for reducing arsenic-induced health effects in this population.

Additionally, this study has collected up to 14 years of longitudinal clinical information on a population-based cohort in a lower-income country, and on a South Asian population. This study can validate or refute associations that have been observed in other populations between exposure and morbidity.

D. Plans

We will continue to actively follow-up participants biennially as well as through our chronic disease surveillance mechanism between follow-up visits for the successful achievement of the aims of this project.

E. Publications

Argos M, Parvez F, Rahman M, Rakibuz-Zaman M, Ahmed A, Hore SK, Islam T, Chen Y, Pierce BL, Slavkovich V, Olopade C, Yunus M, Baron JA, Graziano JH, Ahsan H. A Prospective Cohort Study of Urinary Total Arsenic Concentration and Skin Lesion Status in relation to Malignant and Non-malignant Lung Disease Mortality in Bangladeshi Adults. Epidemiology 2014; In press.

Yinon L, Chen Y, Parvez F, Bangalore S, Islam T, et al. A prospective study of variability in systolic blood pressure and mortality in a rural Bangladeshi population cohort. Prev Med 2013;57:807-12.

Wu F, Chen Y, Parvez F, Segers S, Argos M, et al. A prospective study of tobacco smoking and mortality in Bangladesh. PLoS One 2013;8: e58516.

Parvez F, Chen Y, Yunus M, Olopade C, Segers S, et al. Arsenic exposure and impaired lung function. Findings from a large population-based prospective cohort study. Am J Respir Crit Care Med 2013;188:813-9.

Melkonian S, Argos M, Hall MN, Chen Y, Parvez F, et al. Urinary and dietary analysis of 18,470 bangladeshis reveal a correlation of rice consumption with arsenic exposure and toxicity. PLoS One 2013;8: e80691.

Lin Y, Fu R, Grant E, Chen Y, Lee JE, et al. Association of body mass index and risk of death from pancreatic cancer in Asians: findings from the Asia Cohort Consortium. Eur J Cancer Prev 2013;22:244-50.
Lee JE, McLerran DF, Rolland B, Chen Y, Grant EJ, et al. Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies. Am J Clin Nutr 2013;98:1032-41.
George CM, Gamble M, Slavkovich V, Levy D, Ahmed A, et al. A cross-sectional study of the impact of blood selenium on blood and urinary arsenic concentrations in Bangladesh. Environ Health 2013;12:52.
Chen Y, Wu F, Parvez F, Ahmed A, Eunus M, et al. (2013) Arsenic exposure from drinking water and QT-interval prolongation: results from the Health Effects of Arsenic Longitudinal Study. Environ Health Perspect 2013;121:427-32. , 432e421-427.
Chen Y, Wu F, Liu M, Parvez F, Slavkovich V, et al. A prospective study of arsenic exposure, arsenic methylation capacity, and risk of cardiovascular disease in Bangladesh. Environ Health Perspect 2013;121: 832-8.
Chen Y, Wu F, Graziano JH, Parvez F, Liu M, et al. Arsenic exposure from drinking water, arsenic methylation capacity, and carotid intima-media thickness in Bangladesh. Am J Epidemiol 2013;178:372-81.
Argos M, Melkonian S, Parvez F, Rakibuz-Zaman M, Ahmed A, et al. A population-based prospective study of energy-providing nutrients in relation to all-cause cancer mortality and cancers of digestive organs mortality. Int J Cancer 2013;133:2422-28.
Syed EH, Poudel KC, Sakisaka K, Yasuoka J, Ahsan H, et al. Quality of life and mental health status of arsenic-affected patients in a Bangladeshi population. J Health Popul Nutr 2012;30:262-9.
Scannell M. (2013) Cross-sectionally study of the predictors of medication use, hypertension prevalence, and hypertension treatment in Bangladeshi Adults. poster session of the Society for Epidemiologic Research, Boston

F. Project Generated Resources

The research supported by this grant has been used in collaboration with the Asia Cohort Consortium, and as part of a pooled analysis on the effect of meat intake on mortality. This project has generated genome-wide DNA data of 5,499 participants using the Illumina INfinium HumanCytoSNP-12 v.2.1 chip. 1,825 of the individuals with DNA data also had gene expression data from the Illumina HumanHT-12-v4 chip.

Student Involvement

Molly Scannell Bryan Is a PhD student in Habibul Ahsan's lab at the University of Chicago. She has worked with the genetic and medication data generated by the HEALS study in work that is currently being published, and was presented at the 2013 SER meeting.

Project 2: *Consequences of Arsenic and Manganese Exposure on Children*
PI: Joseph Graziano

A. Specific Aims: The specific aims of this project have not changed.

B. Studies and Results:

This project builds upon our discovery that exposure to arsenic (As) and manganese (Mn) in drinking water has adverse effects on intelligence in children. The research under project 2 now focuses on the consequences of As and Mn exposure on respiratory and neuropsychological functions in 780 adolescents in Bangladesh:

We successfully launched this new study in 2012, and recruitment has continued to go well during 2013. To date a total of 355 participants have been enrolled. Each study participant visits our field clinic twice, one week apart. At the first visit we perform standard pulmonary function tests by spirometry, and also collect exhaled breath condensate (over a ten minute period) for the measurement of pH and 8-isoprostane levels. Low pH and elevated 8-isoprostane are indicators of pulmonary inflammation. At the second visit, we assess child IQ and also administer seven subtests of the CANTAB, a computerized assessment of brain/neuropsychological functioning.

Basically, this study first asks whether the As-induced respiratory disease observed in adults also manifests itself in adolescents, and what are possible physiologic mechanisms? Second, to what extent do associations between WAs and both lung function and brain function reflect the effects of exposure in utero and in infancy, periods of dramatic development for these systems? Third, are WAs and WMn associated with specific domains of cognitive function in addition to overall intelligence?

This study draws on an existing sample of 780 adolescents (15-17 years old) whose mothers are participants in the HEALS Study (Project #1). Based on mothers' well As, measured five times from 2000 until the present, we were able to define four groups of adolescents with varying levels and patterns of exposure to As. Defined on the basis of WAs levels, four groups include adolescents with exposures that are: Group 1) consistently low (mean WAs = 3 ppb); Group 2) consistently moderate (mean WAs = 26 ppb); Group 3) consistently high (mean WAs = 146 ppb); and Group 4) high from conception through roughly age one (mean WAs = 201 ppb) but much lower thereafter (mean WAs =13 ppb). Within each group, there is wide variation in WMn concentrations. Three specific aims target As exposure and pulmonary function (FEV1 and FVC) as well as biomarkers of lung dysfunction in exhaled breath condensate.

Three additional aims expand our earlier work on As, Mn and neuropsychologic outcomes by considering components of Executive Function (planning, sustained attention, working memory) that have been mapped to brain regions thought to be affected by exposure to these elements. Components of Executive Function will be measured with the Cambridge Neuropsychological Test Automated Battery (CANTAB), a computerized and well validated set of tests; intelligence will also be assessed. We will examine adolescents, an understudied age group, because certain components of Executive Function and lung development do not mature until this age; studies with younger children would miss these health effects.

In September, 2013, a problem arose when the hard drive of the computer used to conduct the CANTAB assessments failed. The computer was brought back to New York for an assessment of whether data could be retrieved. Fortunately, an outside company was able to successfully retrieve all study data. At the same time we purchased another instrument which has now been delivered to Bangladesh so that this aspect of the study can continue to be pursued.

C. Significance:

Collectively, the work conducted in this project has contributed to the growing body of knowledge concerning the adverse health effects of both As and Mn on children's health. We believe that knowledge of these adverse health effects on children will increase the rate at which families will alter their behavior – both in the United States and abroad – to test their wells and pursue remediation when necessary.

D. Plans:

In the coming year we expect to nearly complete the recruitment and assessment of the target study population of 780 teenagers..

E. Publications:

Since this new study is still in the recruitment stage, there have been no publications yet.

F. Project Generated Resources

None yet

Student Involvement:

One doctoral student is currently involved in this project. **Tiffany Sanchez**, a minority PhD student, will ultimately derive her PhD dissertation from the pulmonary aims of this project.

PI Initiated Research Translation

Dr. Joseph Graziano chaired the National Research Council (NRC) committee to evaluate critical scientific issues to assess effects from oral exposure to inorganic arsenic. The committee also includes CU SRP Principal Investigator Habibul Ahsan as well as SRP grantees Margaret Karagas, Rebecca Fry, and Robert Wright. The committee conducted public workshops to gather a variety of perspectives from key stakeholders and the public. During the past year, Dr. Graziano guided this NRC Committee to the successful completion of its report. On November 7, 2013, Dr. Graziano presented the NRC report to EPA providing recommendations on how to address these issues in EPA's Integrated Risk Information System (IRIS) assessment of inorganic arsenic. During the ensuing several days he presented briefings to three Congressional House Committees and two Senate Committees. After the IRIS assessment is revised by EPA, Dr. Graziano's NRC committee will then review the EPA document to determine whether dose-response relationships between inorganic arsenic and cancer and non-cancer effects are appropriately estimated and characterized. A final report will be published when the project is completed at the end of 2015.

Dr. Graziano organized and chaired a session devoted to arsenic at the September, 2013, Pacific Basin Consortium on Environmental Health. A small supplement to our SRP was devoted to travel expenses for six speakers, including Drs. CJ Chen (National Taiwan University); Rebecca Fry (University of North Carolina); Craig Steinmaus (University of California, Berkeley); Habibul Ahsan (University of Chicago); Aaron Barchowsky (University of Pittsburgh); and Mary Gamble (Columbia University).

Project 3: Impact of nutrition on arsenic-induced epigenetic dysregulation
PI: Mary Gamble

A. Specific Aims

There are no deviations in the specific aims from those that have already been reported other than that we have decided to analyze an additional selection of histone modifications.

B. Studies and Results

An emerging body of evidence suggests that As exposure leads to epigenetic dysregulation. We have previously demonstrated that chronic As exposure is associated with increased global DNA methylation. We hypothesize that the mechanism underlying this relates to As-induced alterations in post-translational histone modifications (PTHM). This work involves a cross-disciplinary collaboration with Max Costa at NYU that will take advantage of samples collected from our folate trial (FACT) to carry out a set of aims related to nutrition/environment/epigenetic interactions. We plan to characterize the influence of As exposure on histone modifications, relate changes in histone modifications to changes in DNA methylation, and characterize the impact of folic acid supplementation on these marks. Finally, using the Infinium Human Methylation450 array, we have identified a set of genes that are differentially methylated by As exposure and plan to determine gene-specific histone modifications at these loci. Collectively, these aims will begin to elucidate the molecular events that underlie the effects of As and folate on DNA methylation.

We have made significant progress on aims 1a to 1d that have been published (Chervona et al, 2012) and aim 3 (manuscript in preparation). In this preliminary study of N=40 FACT study participants, we have found that total urinary As (uAs) was positively correlated with H3K9me2 ($r = 0.36$, $P = 0.02$) and inversely with H3K9ac ($r = -0.47$, $P = 0.002$). The associations between As and other PTHMs differed in a gender dependent manner. Follow-up work has evaluated gender specific effects of arsenic exposure on gene expression; this work is still in progress.

C. Significance:

These findings contribute to the growing body of evidence linking As exposure to epigenetic dysregulation, which may play a role in the pathogenesis of As toxicity. Improving our scientific knowledge in the field of As-

induced epigenetic dysregulation has tremendous implications for both preventive- and treatment-based approaches to reducing the burden of As-induced diseases. First, methyl donor status is readily amenable to manipulation by nutritional interventions. While it is generally accepted that folate influences DNA methylation, it is not known if this effect is direct, or if it is mediated by an upstream effect on histone modifications which may be more dynamic than changes in DNA methylation. Thus, folate and other modifiers of the methyl donor pool may represent simple, low cost, low-risk interventions for prevention of As-induced disease. Furthermore, gaining mechanistic insights of As-induced epigenetic dysregulation may lead to additional therapeutic approaches for As toxicity, as multiple components of the epigenetic machinery are targets for existing and emerging drug development. Currently, there are no proven effective interventions -- preventive or therapeutic -- that specifically target intermediates in the underlying pathways that may be common to As-induced disease. Such interventions are critically needed.

D. Plans:

In the next funding cycle, we plan to continue to analyze PTHMs in a much larger number of study participants from samples collected at multiple time points from our folic acid supplementation trial and to analyze plasma folate, B12, SAM, SAH and homocysteine levels in these same participants. We are also studying changes in gene expression in peripheral blood mononuclear cells from a subset of the FACT study participants as a function of As exposure. Gene expression is being assessed using Affymetrix gene chips and RT PCR. We will also study the persistence of gene expression following removal of As exposure using cell culture systems. If gene expression alterations persist after removal of the As we will study epigenetic histone marks in the promoter of genes using CHIP.

Finally, we have also initiated joint lab meetings between the Costa lab at NYU and the Gamble lab at Columbia University to further foster our continued collaboration. The first such joint lab meeting was on December 20th, the second was on June 19th, 2013. Another meeting will be scheduled for the Spring 2014.

E. Publications from the current funding cycle:

Harper, KN, Peters, B, **Gamble, MV** (2013) Batch effects and pathway analysis: Two potential perils in cancer studies involving DNA methylation array analysis. Cancer Epidemiol Biomarkers Prev 22(6):1052-60. PMCID: PMC3687782.

Hall MN, Niedzwiecki MM, Liu X, Harper KN, Alam S, Slavkovich V, Ilievski V, Levy D, Siddique AB, Parvez F, Mey JL, van Geen A, Graziano JH and **Gamble MV**. (2013) Chronic arsenic exposure and blood glutathione and glutathione disulfide concentrations in Bangladeshi adults. Environ Health Persp 121(9):1068-74. PMCID: PMC3764071

Niedzwiecki M, Hall MN, Liu X, Oka J, Harper K, Slavkovich V, Ilievski V, Levy D, van Geen A, Mey J, Alam S, Siddique A, Parvez F, Graziano JH, and **Gamble MV**. (2013) Blood glutathione redox status and global methylation of peripheral blood mononuclear cell DNA in Bangladeshi adults. Epigenetics 8(7):730-8. PMCID: PMC3781192

Niedzwiecki MM, Hall MN, Liu X, Oka J, Harper K, Slavkovich V, Ilievski V, Levy D, van Geen A, Mey J, Alam S, Siddique AB, Parvez F, Graziano JH, and **Gamble MV**. (2013) A Dose-response study of arsenic exposure and global methylation of peripheral blood mononuclear cell DNA in Bangladeshi adults. Environ Health Persp 121(11-12):1306-1312. PMCIID: PMC3855504

Melkonian S, Argos M, Hall MN, Chen Y, Parvez F, Pierce B, Cao H, Aschebrook-Kilfoy B, Ahmed A, Islam T, Slavkovich V, Haris P, **Gamble MV**, Graziano J, Ahsan H. (2013) Urinary and Dietary Analysis of 18,470 Bangladeshis Reveal a Correlation of Rice Consumption with Arsenic Exposure and Toxicity. PLoS ONE 8(11):e80691. doi:10.1371/journal.pone.0080691 PMCID: PMC3829854

Brocato J and Costa M. Basic mechanisms of DNA methylation and the unique landscape of the DNA methylome in metal-induced carcinogenesis. Crit Rev Toxicol 43(6):493-514. PMC3871623

Harper K, Khan K, Hall M, Liu X, Graziano JH and **Gamble MV**. Arsenic exposure is not associated with urinary 8oxodG or risk for arsenic-induced skin lesions in Bangladesh J Occup Environ Med (accepted with minor revisions).

Niedzwiecki MM, Hall MN, Liu X, Slavkovich V, Ilievski V, Levy D, Alam S, Siddique AB, Parvez F, Graziano JH, and **Gamble MV**. Interactions of plasma glutathione redox and folate deficiency on arsenic methylation capacity in Bangladeshi adults. Am J Clin Nutr (submitted).

Howe CG, Niedzwiecki MM, Hall MN, Liu X, Ilievski V, Slavkovich V, Alam S, Siddique AB, Graziano JH, **Gamble MV**. Folate and cobalamin modify associations between s-adenosylmethionine and methylated arsenic metabolites in arsenic-exposed Bangladeshi adults. J Nutr (in revisions).

Peters BA, Hall MN, Liu X, Neugut YD, Pilsner JR, Levy D, Ilievski V, Slavkovich V, Islam T, Factor-Litvak P, Graziano JH, **Gamble MV**. Creatine, arsenic metabolism and renal function in an arsenic-exposed population in Bangladesh (manuscript in preparation).

Hall MN, Liu X, Alam S, Slavkovich V, Ilievski V, Levy D, Siddique A, Parvez, F, Caudill M, Graziano JH and **Gamble MV**. Choline, betaine, and arsenic methylation in Bangladeshi adults (manuscript in preparation).

Harper KN, Liu X, Hall MN, Niedzwiecki M, Oka J, Ilievski V, Slavkovich V, Levy D, Siddique A, Graziano JH and **Gamble MV**. Low dose arsenic exposure is associated with sex-specific telomere length alterations in an arsenic-exposed population in Bangladesh (manuscript in preparation).

Chervona Y, Munoz A, Hall M, Kluz T, **Gamble MV**, Costa M. Arsenic-contaminated drinking water deregulates human gene expression patterns in a gender-specific manner in Bangladeshi adults. (manuscript in preparation).

Oral/Poster Presentations in 2013

December 9, 2013. Invited speaker at Child Health Research Seminar Series at the Icahn School of Medicine at Mount Sinai. "Influence of folate nutritional status on the methylation and toxicity of arsenic."

April 4, 2103. Invited speaker at the National Research Council. "Interplay between one-carbon metabolism, arsenic metabolism and epigenetics."

September 24 to 27, 2013. Invited speaker at the Pacific Basin Consortium on Environment and Health in Hawaii. "Nutritional Influences on the Metabolism and Toxicity of Arsenic." Dr. Gamble's student, Brandilyn Peters, also presented a poster at this conference.

October 30 to November 1, 2013. Served as a Member of the University of AZ SRP Program's External Advisory Board.

October 15 to 18, 2013. Attended the SRP's 25th Annual Meeting in Raleigh, NC. Dr. Gamble's lab was represented by poster presentations by two PhD students. Brandilyn Peters' poster was entitled, "Creatinine, arsenic metabolism, and renal function in an arsenic-exposed population in Bangladesh" and Caitlin Howe's poster was entitled, "Associations between s-adenosylmethionine, s-adenosylhomocysteine and arsenic methylation." In addition, Dr. Gamble's former post-doc gave an oral presentation entitled, "Urinary creatinine: implications of its use as a urine dilution adjustment factor in epidemiologic studies of Metal Exposure."

F. Project Generated Resources:

This project has generated genome wide DNA methylation data using the 450K Human Methylation Array from Illumina. The first manuscript utilizing this data is published (Harper et al, see above) and another is

forthcoming. In accordance with our data sharing plan, once the findings (included in the second manuscript) have been published, we will make it publicly available.

Student Involvement in Project 4 (Gamble, PI)

Yana Chervona was a PhD student in Max Costa's lab at NYU. She ran all of the laboratory assays of histone modifications for our pilot study for aims 1a to 1d and aim 2b. This work has been published (see Chervona et al CEBP 2012). Yana successfully defended her thesis on August 2nd, 2013.

Megan Niedzwiecki, Dr. Gamble's PhD student worked on laboratory and data analyses for the folate and oxidative stress (FOX) study from Aim 3 of Project 4 of Dr. Gamble's previous SRP Project. She studied the effects of redox status on methylation of arsenic and DNA which were a major focus of her thesis. Her work was selected for a poster presentation at the 2013 SRP Meeting in Baton Rouge, LA.

Kristin Harper, Dr. Gamble's post-doctoral research fellow is working on analyses of differentially methylated CpGs by arsenic exposure using Illumina's new 450K array (see Highlight and 2013 publication) and this data is currently being validated by NextGen sequencing. Dr. Harper presented her work at our P30 Center's Epigenetics Working Group on Nov. 22, 2013 (described above and manuscript in preparation).

Brandilyn Peters, Dr. Gamble's PhD student is also working on analyses of differentially methylated CpGs by arsenic exposure and was, along with Kristin (above). She also analyzed all of the homocysteine data for aim 2. Brandi presented her work as a poster at the 2013 Annual SRP Meeting in Baton Rouge, LA. She also presented a poster at the Pacific Basin Consortium for Environment and Health in Hawaii in September 2013.

Caitlin Howe is a PhD student in Dr. Gamble's laboratory. She has been working on analyses related to aim 2 of our previous SRP Project in which we are analyzing associations between arsenic exposure and histone modifications as well as on s-adenosylhomocysteine and s-adenosylmethionine and both histone and arsenic methylation. She is currently working on analyzing additional histone modifications for all aims of the current SRP Project 3.

PI Initiated Research Translation

In December of 2013, Dr. Gamble was an invited speaker at Child Health Research Seminar Series at the Icahn School of Medicine at Mount Sinai. Title: "Influence of folate nutritional status on the methylation and toxicity of arsenic."

In April of 2103, Dr. Gamble was invited to speak at the National Research Council. The title of her talk was, "Interplay between one-carbon metabolism, arsenic metabolism and epigenetics."

In September of 2013, Dr Gamble was invited to speak at the Pacific Basin Consortium on Environment and Health in Hawaii. Title: "Nutritional Influences on the Metabolism and Toxicity of Arsenic." Dr. Gamble's student, Brandilyn Peters, also presented a poster at this conference.

In October of 2013, Dr. Gamble served for the third year as a Member of the University of AZ SRP Program's External Advisory Board.

Also in October of 2013, Dr. Gamble attended the Annual SRP meeting in Baton Rouge, LA. Her lab was represented by poster presentations by two PhD students. Brandilyn Peters' poster was entitled, "Creatinine, arsenic metabolism, and renal function in an arsenic-exposed population in Bangladesh" and Caitlin Howe's poster was entitled, "Associations between s-adenosylmethionine, s-adenosylhomocysteine and arsenic methylation." In addition, Dr. Gamble's former post-doc gave an oral presentation entitled, "Urinary creatinine: implications of its use as a urine dilution adjustment factor in epidemiologic studies of Metal Exposure."

Project 4: Arsenic, Iron, Sulfur and Organic Carbon Speciation

PI: Benjamín Bostick
Co-Investigators: Brian J. Mailloux, Steve Chillrud, Lex van Geen

A. Specific Aims

The specific aims of Project 4 address the role of mineralogy and organic matter source and properties on the expression of dissimilatory iron and sulfur reduction, and how such properties affect arsenic solid solution partitioning in a wide array of environments. These processes are intimately linked to the location of groundwater arsenic contamination and thus the location and extent of human and environmental risk, yet we do not understand these processes. Our overall goal is to understand the fundamental connection between sediment properties, biogeochemical processes, and arsenic fate and transport. We make use of samples from field environments at both existing Superfund sites (in collaboration with Project 5) and Bangladesh (in collaboration with Project 6).

B. Studies and Results

This project examined both the connection between (a) sediment mineralogy and (b) organic matter source on biogeochemical processes in arsenic-contaminated aquifers. (a)Many (but not all)iron minerals retain arsenic strongly, minimizing its solubility and thus limiting its transport, and bioavailability/toxicity. Despite their importance, it is quite difficult to accurately quantify these phases, or to study their properties.

Role of Ferrihydrite in Regulating the Fate of Arsenic. Ferrhyrite and other reactive Fe(III) oxides are not only much more reactive as scavengers of aqueous arsenic, but their reduction is rapid and linked to the release of adsorbed As into solution under reducing conditions. In 2013, we collected additional samples from a variety of field environments, and determined their mineralogy using three methods of characterizing Fe mineralogy. In all, we analyzed the Fe and As speciation in more than 100 new core and sediment samples during the year. First, we used existing and well developed methods of linear combination analysis to determine the fractional composition of iron minerals in this diverse set of samples. These results suggested that ferrihydrite was an important mineral component in many, but not all, samples. The second and third methods of quantifying mineralogy were developed to more conclusively establish the presence of ferrihydrite and other trace mineral components. Second, we developed a standard addition method to quantify ferrihydrite, goethite, and magnetite in these sediments. Standard addition methods are useful because they allow matrix matching, which minimizes bias in quantitation resulting from the presence of other components or an unpredictable background. The method also minimizes errors by depending on a regression of many measurements to determine the mineral concentration in a single sample. This application of standard addition is the first of its kind for XAS data, and was able to improve the detection limits for ferrihydrite and other minerals to a few hundreds of ppm. Third, we used statistical methods including principal components analysis (PCA) and cluster analysis. These methods are advantageous in that they do not require a complete understanding of mineral components for accurate quantitation. These methods were able to determine oxidation state, and to define a signature of Fe mineralogy that is attributed to the source location (provenance) and potentially the age of sediments that does not change in response to sediment reduction .Remediation strategies based on inducing magnetite formation are currently being developed in collaboration with Project 5 to enhance *in situ* magnetite formation as a method of immobilization-based remediation strategies. These remediation strategies depend on magnetite formation, which also was able to be measured using these methods.

Molecular-Scale Studies within Complex Environments. To properly assess the long term risks of arsenic contamination at contaminated sites and in groundwater, we need to be able to predict arsenic adsorption and transport properties. To this end, we continued to develop our methodologies for measuring the adsorption and transport properties of arsenic under field conditions. We built upon our previous efforts examining iron mineralogy and As desorption at synchrotrons to examine the advection of As from high-As aquifers to low-As

aquifers in model systems. These methods were able to determine the rate of adsorption, and to document the kinetic control of these adsorption processes for the first time at a scale smaller than the grain scale. We interpret these data to indicate that As adsorption often is incomplete due to poor access to adsorption sites. The transport parameters (partition coefficient and retardation) also could be estimated from these experiments, and are in good agreement with larger scale batch measurements, and partition coefficients measured in the field.

This data is relevant to project 5 and 6. First, it shows that groundwater plumes at Superfund sites containing As may not be effectively attenuated, and As is susceptible to off-site migration, and provides a mechanism for this. In doing so, it suggests that enhancing As retention should target the kinetic limitations to adsorption, or the solution composition that inhibits adsorption. In reference to groundwater contamination in Bangladesh (Project 6), these data indicate that sediments containing Fe oxides provide some measure of protection from advection of high-As groundwater, and that this protection is important at preserving groundwater quality in aquifers currently used for drinking.

Mineral Reactivity in Model Systems. Often, it is beneficial to use model systems to fully understand the mechanisms of environmental processes. In 2013, we used model systems containing both real sediments collected from superfund sites to study the conditions affecting iron mineralogy, and the potential of in situ remediation methods for the remediation of groundwater As contamination. Arsenic contamination represents a significant and potentially problematic contaminant in that remedial efforts often can facilitate the release of natural levels of As in sediments into unsafe levels in groundwater. Under oxidizing conditions, we determined that the concomitant addition of ferrous iron and nitrate stimulated autotrophs and chemical Fe(II) oxidation, and thereby produced magnetite that was an effective trap for groundwater arsenic. Moreover, columns studies in which magnetite was produced were able to retain arsenic for as much as 100 pore volumes following the in situ magnetite synthesis. These data suggest that magnetite synthesis in contaminated environments could be an effective means of groundwater remediation in that they would remove existing As, and then remove advected arsenic for many years to come (at least 20 based on groundwater flows for the Dover and Vineland sites studied in our work).

Reactive Organic Matter in Reducing Sediments. The microbes that reduce reactive iron phases like ferrihydrite require a reactive organic matter source. In 2013, we collected DNA from a new series of arsenic-contaminated aquifers in Bangladesh to ascertain the source of organic matter that drives this reduction. These samples are still being processed, but the data should help elucidate the relative role of infiltration rates and groundwater age on carbon substrate utilization. We have shown in other field studies, including one published in Nature in Sept., 2013, that such processes can be important in perturbed groundwater systems, and that they are a part of the contamination of previously low-As aquifers. The samples that are have been selected for radiocarbon DNA analysis also have been studied for detailed mineralogy and using genomic approaches to determine the microorganisms that are present in these environments, and to allow us to directly relate the activity of Fe reduction and other biogeochemical processes with sediment properties such as mineralogy, and aquifer properties like dissolved As and Fe concentrations.

C. Significance

The chemical parameters that describe arsenic transport are needed to understand the distribution of arsenic in the environment, and to predict how this spatial distribution will evolve over time. The physic-chemical parameters derived from these studies, and the underlying importance of specific mineral phase concentrations on these parameters, should be useful both characterize contamination, and to develop effective remediation strategies for arsenic. In these studies, we have found that reactive phases such as ferrihydrite affect arsenic fate. Since these phases are found in limited concentrations in many natural systems, there is a limited capacity of natural aquifer sediments to retard arsenic. The reduction of these phases can release arsenic into solution, but can in some cases form magnetite, which can immobilize arsenic. Much of our future plans revolve around understanding how enhance magnetite formation to improve remediation technologies, and how to improve the binding efficiency of As to sediments by tuning mineralogy as part of a comprehensive remediation plan.

D. Plans

In collaboration with Project 5. We have data that suggest that oxidative pathways are most effective to produce magnetite in contaminated sediments and are highly effective at remediating arsenic, and in the last year have made considerable progress in identifying how best to synthesize magnetite in situ. We completed a series of column experiments designed to optimize magnetite formation through the oxidation of ferrous iron by nitrate, and now need to think about how best to scale these column studies to field systems with complex flow paths and heterogeneous contamination. These field systems need to be able to monitor and quantify the spatial and temporal evolution of these mineral transformations. In collaboration with Lee Slater and Demitris Ntarlagiannis (Rutgers-Newark), we are developing biogeophysical methods of doing so, first in columns, which eventually will be extended to field trials of various remediation technologies. In the coming year, we hope to develop calibrations for these methods so that we can interpret the signals that result in columns, and eventually in the field. We also will continue other column and batch studies with both model systems and Superfund site sediments, to determine how geochemical processes occur. We have begun to work at the Dover Municipal Landfill Superfund site, and we will begin to characterize both the arsenic and iron speciation in those sediments, and the potential remediation of that site using both the oxalate- and magnetite-based remediation strategies. In the coming year, we hope to start to develop a quantitative reactive transport model of the Dover site that could be used to predict site hydrology and groundwater geochemistry under a proposed remediation strategy, and use this model in the coming years to design an effective means of reactant delivery and pumping. We hope that these remediation options can be used at this site as part of its long term management strategy.

In collaboration with Project 6.In project 6, we have begun the critical process of understanding the distribution of iron minerals and reactive organic matter sources within the site B and F areas, where we are trying to characterize how surface water and be advected to depth either through or laterally to contaminate intermediate and deep aquifers often tapped as alternative water supplies, and to understand the mineralogy of sediments in deep, low-arsenic aquifers. We also will examine the source of reactive organic carbon in deep aquifers that are low in arsenic but that appear to contain bomb tritium (and thus young groundwater that implies there is effective advection from the surface). These sites could be particularly vulnerable to arsenic contamination in the future as a consequence of anthropogenic forcing (i.e., extensive groundwater pumping).

E. Publications, Patents, Other supported by Project 5

Van Geen, A., B.C. Bostick, Pham T.K. Trang, Vi Mai Lan, Nguyen-Ngoc Mai, Phu Dao Manh, Pham Hung Viet, K. Radloff, Z. Aziz, J. L. Mey, M.O. Stahl, C.F. Harvey, P. Oates, B. Weinman, C. Stengel, F. Frei, R. Kipfer & M. Berg. 2013. Retardation of arsenic transport through a Pleistocene aquifer. Nature 501, 204–207 (12 September 2013) doi:10.1038/nature12444.

B. J. Mailloux, E. Trembath-Reichert, J. Cheung, M. Watson, M. Stute, G. A. Freyer, A. Ferguson, K. M. Ahmed, Md, J. Alam, B. A. Buchholz, J. Thomas, A. Layton, Y. Zheng, B. C. Bostick, A. van Geen. 2013. Advection of Surface-Derived Organic Carbon Fuels Microbial Reduction in Bangladesh Groundwater. Proc. Nat. Acad. Sci. USA 110 (14), 5331-5335.

Nielsen, L. N. and B. C. Bostick.2013. Integrating Variable Aquifer Geochemistry and Sediment Properties into Models of Contaminant Retention. Appl. Geochem. Submitted.

Sun, J., S. N. Chillrud, B. J. Mailloux, M. Stute, B. C. Bostick. 2013. Magnetite Formation and Arsenic Retention Under Cyclical Redox Transformations. Environ. Sci. Technol. Submitted.

Kraal, P, B. C. Bostick, C. P. Slomp, G.-J. Reichart. 2013. Spectroscopic approaches to quantify phosphorus forms of variable crystallinity in marine sediments. Soil Sci. Soc. Am. J., In Revision.

Bostick, B.C. 2013. Human-Induced Change in Natural Arsenic Contamination in Asian Groundwaters. Zhejiang University-Columbia University Joint Conference on Sustainability. Hangzhou, China, 26 Sept., 2013.

Bostick, B.C. 2013. Human-Induced Change in Groundwater Quality in low-As Aquifers in Asia. Chian University of Geosciences. Bejing, China, 22 Sept., 2013.

Bostick, B.C. Modern Careers in Environmental Sciences. SIPA Career Development Workshop. 31 July, 2013.

Bostick, B.C. Preliminary Results Characterizing Soils and Aerosols Associated with Ferroalloy Production. Tracing Sources and Identifying Soil Resuspension. My Sinai School of Medicine, New York NY. 28 June, 2013.

Sun, J. S. Chillrud, B. Mailloux, and .C. Bostick. Arsenic In-Situ Immobilization by Magnetite Formation within Contaminated Aquifer Sediments. Superfund Research Program Annual Meeting, Baton Rouge LA, Oct. 15-17, 2013.

Van Geen, A., B.C. Bostick, Pham T.K. Trang, Vi Mai Lan, Nguyen-Ngoc Mai, Phu Dao Manh, Pham Hung Viet, K. Radloff, Z. Aziz, J. L. Mey, M.O. Stahl, C.F. Harvey, P. Oates, B. Weinman, C. Stengel, F. Frei, R. Kipfer & M. Berg. 2013. Human impacts on arsenic-impacted aquifers in SE Asia. Superfund Research Program Annual Meeting, Baton Rouge LA, Oct. 15-17, 2013..

Bostick, B.C. and J. Sun. 2013.Polyoxometalates and Their Effect on Tungsten Speciation and Transport. V. M. Goldschmidt Conference, Firenze, Italy. June, 2013.

Mihajlov, I., M. Stute, I. Choudhury, K.M. Ahmed, A. van Geen and B.C. Bostick. 2013. Kinetics of arsenic sorption on aquifer sediment from Bangladesh imaged by XRF microprobe in flowing columns. V. M. Goldschmidt Conference, Firenze, Italy. June, 2013.

Sun, J. S. Chillrud, B. Mailloux, and B.C. Bostick. 2103. Formation of Magnetite within Aquifer Sediments and Its Effects on Arsenic Mobility. V. M. Goldschmidt Conference, Firenze, Italy. June, 2013.

Students and Post-docs whose research is supported completely or in part by Project 5:

Jing Sun, 3rd yr PhD student, Earth and Environmental Sciences, Columbia University. Advised by PI.
Ivan Mihajlov, 5th year PhD student, Earth and Environmental Sciences, Columbia University
Louis Smith (undergraduate, Columbia University). _Role: to examine iron mineralogy in contaminated sediments and study how those transformations affect arsenic retention in batch system.
Rajib Mozumder, 1st year PhD student, Earth and Environmental Sciences, Columbia University
Khue Nguyen, postgraduate student, Environmental Sciences, Barnard College, Role: molecular methods for radiocarbon analysis of DNA.
Rachel Silvern, undergraduate, Barnard College, Role: radiocarbon analysis of DNA of Bangladeshi sediments, mineralogical analysis by X-ray absorption spectroscopy.
Carol Kim, undergraduate, Barnard College, Role: radiocarbon analysis of DNA of Bangladeshi sediments.
Ezazul Haque; undergraduate, CUNY-York. Role: to examine groundwater quality in the Queens NY aquifer system.

PI Initiated Research Translation

To determine how to minimize arsenic exposure in contaminated areas, it is necessary to identify low-arsenic groundwater sources, and other potential problems with those groundwater sources. PI Bostick is actively doing this through a World Bank supported project in Cambodia, where a significant population is exposed to high-As groundwater. This alternatives analysis suggests that centralized water treatment may in fact be much more cost-effective than previously recognized. PI Bostick is also working with consultants and EPA officials in Region 2 to identify areas where natural arsenic is being released at landfill sites that have been classified as Superfund sites, and where in situ magnetite formation may be particularly effective to contain the extent and spread of this groundwater contamination.

In working with EPA region 2, PI Bostick worked with the responsible parties including Mike Webster and others at the Dover site to convey the results of our study, and to get input from them about their research needs and regarding the best way to make our research relevant to site remediation.

PI Bostick also worked with NIEHS and EPA staff, as well as officials from the City of New York to examine the relative effects of revising soil lead standards on urban areas heavily affected by legacy contamination. These areas are extensive in New York City, and are likely to become ever more extensive if soil contaminant

thresholds decrease to 150 mg/kg through continued monitoring. Bostick proposed developing a screening method that is capable of differentiating between lower level Pb contamination such as that found in brownfields to prioritize remedial action.

The analytical techniques that are used in this project represent cutting-edge technologies that are uniquely possible at synchrotron. PI Bostick is a leader in using these technologies, and has been appointed by the Stanford Synchrotron Radiation laboratory (SSRL) at Stanford University as a representative to the National User Facility Organization (NUFO), which working closely with the Association of American Universities (AAU) and government relation experts to develop plans and compile material for outreach purposes. This position spans the sciences and engineering. During 2013, Bostick made one trip to Washington DC to present sycnhrtron research to the congressional delegations of New York.

PI Bostick also attended a series of community meetings regarding environmental health. In the first, US Representative Nita Lowey, who represents the Lamont Doherty Earth Observatory constituency and who is head of the House Committee on Science, was presenting on the role of NIEHS and on environmental health, and Bostick served with PI Chillrud (Project 5) and Graziano (Proj. 2) and others. In another panel, PI Bostick presented on the impacts of climate change on environmental and human health to a public meeting in Orange, NJ.

PI Bostick initiated a project in collaboration with the State of New York Department of Environmental Quality (with Paul John, and student Ezazul Haque). In this project, we are collecting water samples from former municipal wells in Queens NY that could be used in the coming years for drinking water. These wells have unknown levels of contaminants, and are reduced groundwaters that could contain arsenic. The data from these studies should be used to make recommendations about water treatment prior to use, or to preclude the use of specific water sources.

Project 5: Application of enhanced mitigation methods for groundwater arsenic at US Superfund sites

PI: Steven Chillrud
Co-Investigators: Benjamin Bostick, Brian J. Mailloux, Martin Stute

A. Specific Aims

Our overall goal has not changed and is to investigate enhanced remediation options for groundwater contaminated with arsenic; specifically on two separate approaches including oxalic acid injections to improve the efficiency of pump-and-treat at removing arsenic and the potential of immobilization of arsenic onto the target mineral magnetite. We have been heavily investigating the applicability of the two methods for the Dover site where the local managers have been enthusiastic about the work we plan on doing there.

B. Studies and Results

In 2013, we have primarily focused on laboratory experiments on contaminated aquifer sediments from the Dover Municipal Landfill Site sample and data analyses, and manuscript preparations, and a series of meetings with the geophysicists from Rutgers University-Newark and Dover Site Managers to plan future activities. The vast majority of our efforts this year were spent on column experiments in collaboration with the geophysicists from Rutgers-University Newark on forming an iron oxide mixture including magnetite within sediments in columns and then testing its ability to adsorb As and keep low As concentrations in solution.

Magnetite, unlike many other iron minerals, is stable across typical groundwater redox zones found at arsenic-contaminated Superfund sites. Accordingly, magnetite is a potentially attractive mineral in which to immobilize arsenic in the solid phase in many contaminated environments. We have been investigating the concept of amendment injections to promote the *in situ* production of porous reaction barrier zones of magnetite as a long-term arsenic sink. Over the past year, we have focused on a series of columns which was

designed to initially promote *in situ* magnetite formation, to evaluate the extent to which mineral formation maintains decreased aqueous arsenic levels under changing geochemical conditions, and then to determine if it can sequester additional arsenic after formation. In this study, aquifer sediments from the Dover Landfill Superfund site, where the As contamination is associated with the leachate plume by reduction, were mixed and packed into columns. These columns were treated with artificial groundwater and various combinations of reacting chemicals under continuous flow (flow rate = 2 pore volumes (PV) per day). All the columns were conducted at circumneutral pH, similar to site conditions but much lower than is normally considered ideal for magnetite formation. Column effluent composition was closely monitored, and after different experiment stages columns were sacrificed to analyze the sediment iron mineralogy and arsenic speciation. The columns were pre-equilibrated with oxygen-free groundwater containing arsenite and lactate (40 PV), during which arsenic release from sediment phase to water phase was observed (peak arsenic concentration in effluents > 250ug/L). Nitrate and ferrous iron were then added to the column influents (35 PV), which produced magnetite and some other iron minerals and quickly decreased aqueous arsenic level. Under further elevated lactate level which promoted bioreduction, little arsenic was released from the columns (45 PV). Even during long term addition of arsenite- and lactate-containing groundwater, which was the same with the pre-equilibration influent, arsenic level in effluents remained below 10ug/L for almost 80 PV. And groundwater arsenic behaved differently in sand control columns due to distinct mineralogical characteristics and corresponding sulfide accumulation. Overall, a simple extrapolation directly the column data suggest that, if we could implement this magnetite-based strategy at the field scale, the mineral assemblage formed by such a single injection could immobilize almost all the arsenic from a contaminated groundwater plume similar to the one at Dover Landfill for at least 10 years. Much more work needs to be done before this extrapolation can be tested.

This series of columns were performed using a column setup designed by the Rutgers-Newark group, in which geophysical parameters (spectral induced polarization (SIP)) can be measured simultaneously. The Rutgers-Newark column setup was greatly complementary to the traditional geochemical approaches in that it offers a potential method to quantitatively transfer SIP signatures into real-time information about the amount and location of magnetite (and iron sulfides) precipitation in columns. We are in the process of analyzing the SIP signals with our collaborators at Rutgers-Newark (see Core D write up).

C. Significance

With the exception of lead, more National Priority Sites have arsenic as an issue than any other contaminant of concern. Yet, there are very limited remediation strategies for groundwater systems contaminated with dissolved As that are efficient and time effective. As such more methods are needed. Our work focuses on developing two enhanced remediation strategies which could potentially save time and money at Superfund sites contaminated with arsenic.

D. Plans

Over the next year, in collaboration with Project 4 and Cores C and D, we will continue working on our aims. Firstly, we will seek parallel ways to analyze/prove magnetite formation in the solid phase(such as magnetic susceptibility, magnetic separation, synchrotron X-ray microprobe and SEM/TEM). And, we will use coupled geochemical and transport modeling (simulations) to identify the processes critical for As sequestration in sediments, and try to predict the evolution of the magnetite based strategy under various site scenarios. Finally, together we will also carry out additional baseline field site characterization in preparation for *in situ* pilot experiments.

E. Publications, Patents, Other supported by Project 5

Sun, J., Arsenic *In-Situ* Immobilization by Magnetite Formation within Contaminated Aquifer Sediments. Columbia University Superfund Research Program Monthly Seminar/Webinar, Sept. 16, 2013.

Sun, J., S.N. Chillrud, B.J. Mailloux and B.C. Bostick. Arsenic *In-Situ* Immobilization by Magnetite Formation within Contaminated Aquifer Sediments. Poster at the 2013 Superfund Annual Meeting. Won Best Student Poster for the Environmental Science Section.

Sun, J., S.N. Chillrud, B.J. Mailloux and B.C. Bostick. Formation of Magnetite within Aquifer Sediments and Its Effects on Arsenic Mobility. Oral presentation at the 23rd V.M. Goldschmidt 2013 Conference.

Students and Post-docs who worked on Project 5:

Jing Sun, 4thyr PhD student, Earth and Environmental Sciences, Columbia University
Dr. Peter Knappett is a post-doctoral investigator with expertise in hydrogeology appointed in 2012.

PI and investigator Initiated Research Translation

Most of project 5 is focused on developing and understanding enhanced remediation approaches and if successful transfer them to Superfund sites. As such much of these projects efforts can be said to be directly related to technology transfer including our meetings and updates with Dover Landfill Site Managers. Additional efforts include being a conference call with EPA related to in situ methods for lead remediation and the implications of the lower blood lead standard (Steven Chillrud and Ben Bostick), the webinar Jing Sun gave on "Arsenic *In-Situ* Immobilization by Magnetite Formation within Contaminated Aquifer Sediments" (Sept 16. 2013), a meeting at LDEO with Steven Parisio from NYSDEC on PAHs and metals in Demolition and Construction Debris Landfills (June 4, 2013), and the discussion with Larry Reed, contractor to EPA, on how to improve interactions between EPA, NIEHS SRP scientists and ATSDR at Superfund Sites, (January 2014). Furthermore, Steve Chillrud and Beizhan Yan have granted one interview to Chinese TV station and met with Chinese researchers on several issues including a study they have of lead contaminated soils and children's elevated blood lead levels.

Project 6: *Defining the Sustainable Uses of Low-Arsenic Aquifers in Bangladesh*
PI: Alexander van Geen
Outside Collaborator: Kazi Matin Ahmed

A. Specific Aims

The aims of this applied environmental science project have not changed, and are (1) to lower the exposure to arsenic (As) in the cohort of >30,000 participants in the Health Effects of Arsenic Longitudinal Study (HEALS) in Araihazar and (2) to improve our understanding of the processes that threaten the quality of groundwater in low-As aquifers of Bangladesh.

B. Studies and Results

(1) Field-kit testing of a total of 49,790 wells across the entire administrative unit of Araihazar upazilla where HEALS participants reside started in March 2012 and was completed in September 2013. The new test results were compared within a subset of 61 contiguous villages that were sampled a first time in 2000-01 at the launch of HEALS (van Geen et al., 2013). The two surveys indicate that the total number of tubewells within the area almost doubled from 5,560 to 10,879 over 12 years. The evolution of the distribution of well ages between the two surveys is consistent with a simple model that combines an annual increase of 42 wells/year in the rate of installations within the 61 villages starting in 1980 and a 7%/year rate of abandonment of wells as a function of well age. The new installations and rapid turnover help explain why, despite blanket testing campaigns conducted under the Columbia SRP in 2000-01 and by the government's Bangladesh Arsenic Mitigation and Water Supply Program (BAMWSP) in 2003, only half the households claimed to know the status of their well 2012-13. Colored placards were posted on each pumphead in 2012-2013 on the basis of the kit results relative to the WHO guideline for As and the Bangladesh standard for As in drinking water: blue for As <10 ug/L, green >10-50 ug/L, and red: >50 ug/L. According to quality-control samples collected from 502 tubewells for comparing the kit results with laboratory measurements, not a single well labeled blue in 2012-13 should have been labeled red and vice-versa. Field-kit testing in 2012-13 did not change the status of wells relative to the Bangladesh standard of 876 (87%) out of 1,007 wells with a placard based on laboratory

measurements in 2000-01 still attached to the pumphead. The high proportion of tubewells believed by households to be unsafe (66% out of 2,041) that were still used for drinking and cooking in 2012-13 underlines the need for more widespread testing to identify low-As wells as an alternative source of drinking water.

(2) Field measurements and modeling concerning to assess the vulnerability of low-arsenic aquifers that remain key for lowering exposure continues. Knappett et al. (in review) analyzed the draw-down cone from urban Dhaka pumping in Araihazar15 to 35 km east and explored the implications in terms of the vulnerability of deep community wells to contamination with As. Pressure transducers were placed in 17 community wells 130-240 m deep in Araihazar upazilla and in the adjacent Meghna River. Water levels varied by 3 m seasonally in both the deep aquifer and the river, with hydraulic gradients of $2\text{-}4x10^{-4}$ trending consistently westward towards Dhaka throughout the 13-month deployment. Steady-state modeling indicates that the deep aquifer could be recharged laterally from the river or downward from shallow aquifers. In either case, increased Dhaka pumping over time could therefore be accompanied by intrusion of shallow groundwater that is elevated in As or in dissolved organic carbon that promotes the release of As to groundwater. Enhanced movement of river water into aquifers caused by urban pumping may affect other aquifers across South and Southeast Asia. The recent study of the interface between a high- and a low-arsenic by van Geen et al. (2013) affected by municipal pumping for the city of Hanoi has shown, however, that contamination with arsenic is delayed by a factor of 20 relative to the movement of groundwater due to adsorption of arsenic onto aquifer sands.

C. Significance

Beyond the ethical motivation, lowering exposure will help define exposure estimates of the study population in Araihazar and, therefore, the dose-response relationships for various end-points studied under Projects 1, 2, and 3. Our work on the vulnerability of intermediate and deeper aquifers to contamination with As in South Asia is yielding an improved understanding of the impact of groundwater flow on transport of both reactive carbon and As transport and retardation that is applicable elsewhere, including US Superfund sites.

D. Plans

Response surveys will be conducted in a subset of Araihazar villages in order to quantify the extent of exposure reduction triggered by the recent testing. In addition, the local office of the Department of Public Health Engineering will be provided with a prioritized list of locations where deep community wells should be installed by the government. An analysis of the depth distribution of arsenic in Araihazar in relation to the local hydrogeology will be conducted. The monthly monitoring network of the most vulnerable low-arsenic aquifers has been extended.

E. Publications, Patents, Other under Project 6 in 2013

Knappett, PSK, BJ Mailloux, I Choudhury, M Khan, H Michael, S Barua, DR Mondal, M Steckler, H Akter, KM Ahmed, B Bostick, C Harvey, M Shamsudduha, I Mihajlov, R Mozumder, A. van Geen. Vulnerability of intermediate and deep low-arsenic aquifers to municipal pumping in Bangladesh. Submitted to Environmental Sciences and Technology, January 2014.

vanGeen A, KH Win, T Zaw, W Naing, JL Mey, B Mailloux. Confirmation of elevated arsenic levels in groundwater of Myanmar. Science of the Total Environment, accepted January 2014.NIHMSID #558340

vanGeen A, EB Ahmed, L Pitcher, JL Mey, H Ahsan, JH Graziano, KM Ahmed. Comparison of two blanket surveys of arsenic in tubewells conducted 12 years apart in a 25 km2 area of Bangladesh. Science of the Total Environment, accepted December 2013.NIHMSID #557871

Knappett, P.K., J. Du, P. Liu, V. Horvath, B. J. Mailloux, J. Feighery, A. van Geen, P. J. Culligan. Importance of reversible attachment in predicting *E. coli* transport in saturated aquifers from column experiments. Advances in Water Resources http://dx.doi.org/10.1016/j.advwatres.2013.11.005, 2013.NIHMSID # 558343

Balasubramanya S, A Pfaff, L Bennear, A Tarozzi, KM Ahmed, A Schoenfeld, A van Geen, Evolution of households' responses to the groundwater arsenic crisis in Bangladesh: information on environmental health risks can have increasing behavioral impact over time. In press, Environment & Development Economics, September 2013. NIHMSID # 558341

vanGeen, BC Bostick, PTK Trang, VM Lan, NN Mai, PD Man, PH Viet, K Radloff, Z Aziz, JL Mey, MO Stahl, CF Harvey, P Oates, B Weinman, C Stengel, F Frei, R Kipfer, M Berg. Retardation of arsenic transport through a Pleistocene aquifer. Nature 501: 204–207, 2013.PMCID: PMC3772538

Feighery F, BJ Mailloux, AS Ferguson, KM Ahmed, A van Geen, PJ Culligan, Transport of *E. coli* in aquifer sediments of Bangladesh: Implications for widespread microbial contamination of groundwater. Water Resources Research DOI: 10.1002/wrcr.20289, 2013.NIHMSID # 558342

Mailloux BJ, E Trembath-Reichert, J Cheung, M Watson, M Stute, GA Freyer, AS Ferguson, KM Ahmed, MJ Alam, BA Buchholz, J Thomas, AC Layton, Y Zheng, BC Bostick, A van Geen, Advection of surface-derived organic carbon fuels microbial reduction in Bangladesh groundwater, PNAS 110: 5331-5335, 2013. PMCID 3619377

Patents-

vanGeen, A., B. C. Bostick, C. Manning. 2011. A Peltier freeze shoe sampler to recover aquifer sediment and groundwater. US Provisional Patent Application Serial Nos. 13/210.834 and 61/374,193.Filed August 16, 2011.

Student and post-doc involvement under Project 6

Ivan Mihajlov, a PhD candidate in Earth & Environmental Sciences co-advised by the PI, successfully defended his PhD in November 2013.

Md. Rajib Mozumder, a geology graduate from the University of Dhaka, entered the PhD program in Earth & Environmental Sciences in September 2012 an continues to be advised by the PI.

Fiona Kinniburgh graduated from Columbia College with a bachelor's in Sustainable Development in June 2013 and carried her honors thesis research at LDEO.

Meridel Phillips is Master's student in the Department Earth and Environmental Engineering conducting SRP research at LDEO.

Yongfeng Jia is a PhD candidate at China University of Geosciences supported by the China Scholarship Council to carry out SRP-related at LDEO from September 2013 through December 2014.

Dr. Peter Knappett is a hydrogeologist and became a post-doctoral investigator at LDEO in 2012. Starting in August 2013, he joined the faculty of Texas A&M University as an assistant professor and continues to collaborate with Columbia SRP PIs.

PI initiated Research Translation under Project 6 in 2013

Dr. Lex van Geen, PI

a. January 22, 2013 Yangon, Myanmar : Invited presentation on arsenic mitigation at Symposium on Arsenic in Drinking Water, Myanmar, on the Yangon University campus.
b. July 24-27, 2013 Punjab, India: Launched testing campaign of 20,000 wells for arsenic in fluoride by collaborator C.K. Singh from TERI University supported under a new USAID PEER Science grant.
c. August 25-30, 2013 Florence, Italy: Goldschmidt Conference sponsored by the Geochemical Society and the European Association of Geochemistry. Convened session entitled "Impact of air, soil, and water geochemistry on human health".

Administrative Core
Director: Joseph Graziano
Associate Director: Alexander van Geen

Dr. Graziano, the Program Director, and Dr. van Geen, the Associate Director, have been working together to provide leadership to SRP investigators to achieve the goals of the Administrative Core, which include the facilitation of interaction and communication among investigators leading the Research Projects, Support Cores, RTC and CEC; to provide fiscal management and planning; to coordinate SRP activities including seminars, retreats, symposia, and preparation of the annual progress report; to coordinate the reviews of our SRP activities by the External Advisory Committee; and to supervise the utilization of the Research Support Core Laboratories. We communicate continuously with regard to the integration of our biomedical and non-biomedical research programs, and hold joint monthly meetings of all participating faculty to maximize the interactions across biomedical and non-biomedical projects. This communication is evidenced by the number of truly multi-disciplinary publications that have come from our program, involving close collaboration between biomedical, earth, and social scientists.

A meeting of our External Advisory Committee was held February 25, 2013. Our External Advisory Committee continues to provide valuable input to our program. The composition of the committee includes: a) Chien-Jen Chen, Committee Chair, and Chairman of the Graduate Institute of Taiwan; b) Andrew Gelman, Professor of Statistics at Columbia University; c) Zoltan Szabo, Research Hydrologist, USGS; d) Margaret Karagas, Chair, Section of Biostatistics and Epidemiology, Dartmouth University; e) X. Chris Le, Professor of Public Health Sciences, University of Alberta; f) Peggy O'Day, Associate Professor of Natural Sciences, University of California, Merced; and g) Robert Wright, Professor of Preventive Medicine and Pediatrics at the Mount Sinai School of Medicine. The next meeting of the EAB is scheduled for March 7, 2014.

All of our scientific team assembles monthly for a joint two hour meeting which rotates between the Health Sciences Campus and the Lamont-Doherty Earth Observatory Campus; the two campuses are separated by a 20 minute University bus ride. Our monthly meetings include two hours of seminars, typically one hour for biomedical and one for non-biomedical presentations. During the past year we have begun to offer our seminars as a webinar, one that is now attended by many outsiders from EPA, NIH and academia. The seminar series includes a mix of internal and external speakers and has evolved into a world class set of events.

Seminars that have occurred during 2013 include:

January 28
Dr. Koren Kathleen Mann Assistant Professor in Oncology from Lady Davis Institute for Medical Research and McGill University: **"Mechanisms of arsenic-enhanced atherosclerosis: what we've learned from mouse models"**

March 18
Dr. Arup K. SenGupta, P.C. Rossin Professor, Departments of Civil & Environmental Engineering and Chemical Engineering, Lehigh University: **"Mitigating Global Arsenic Crisis Through Innovations: Past Progress and Future Challenges"**

April 15
Dr. Miroslav Stýblo, Associate Professor at Department of Nutrition, Gillings School of Global Public Health, UNC-Chapel Hill: **"Diabetes Associated with Environmental Exposure to Arsenic: The Phenotype and Mechanisms"**

Dr. Alexander van Geen, Lamont Research Professor at Lamont-Doherty Earth Observatory of Columbia

University: **"Myanmar and Bangladesh: Cultures at odds, with a groundwater arsenic problem in common"**

May 20
Director Zhou Yun of the International Cooperation Center at the Chinese Research Academy of Environmental Sciences (CRAES): **"Groundwater Environmental Management and Challenges in China"**

Dr. Yan Zheng, Professor of Earth and Environmental Sciences at Queens College, CUNY, and Adjunct Senior Research Scientist at Lamont-Doherty Earth Observatory, Columbia University: **"MARCH: Maine Arsenic Reduction for Community Health"**

Dr. Joseph Graziano, Director of the CU SRP**: Overview of the Columbia Superfund Research Program**

Dr. Alexander van Geen, Deputy Director: **"The international drilling program and Columbia Global Center proposal on groundwater arsenic in Asia**

September 16
Dr. Ana Navas-Acien, Associate Professor from the Department of Environmental Health Sciences and Epidemiology at Johns Hopkins Bloomberg School of Public Health: **"Low-to-moderate arsenic exposure in the US: Health implications for American Indian communities"**

Ms. Jing Sun, Columbia SRP Graduate Student at Lamont-Doherty Earth Observatory of Columbia University: **"Arsenic In-Situ Immobilization by Magnetite Formation within Contaminated Aquifer Sediments"**

October 21
Dr. Dibyendu Sarkar Professor of Earth and Environmental Studies and Director of Environmental Management PhD Program at Montclair State University: **"Urban Sprawl and 'Green' Remediation of Residential Soils: A Case Study With Arsenic"**

November 18
Ms. Sara V. Flanagan, a scientist with the Columbia SRP Community Engagement Core (CEC): **"Overcoming barriers to environmental health protective behavior: Examples from private well testing and treatment for arsenic in Maine"**

December 16
Dr. Ershad Sumon, Project Manager of the Arsenic Testing Program, University of Dhaka and Mr. M. Rajib Mozumder, Columbia SRP Graduate Student with the Department of Earth and Environmental Sciences: **"Implications for mitigation of the recent field-kit testing of 50,000 wells for arsenic in Araihazar, Bangladesh"**

Dr. Tomás R. Guilarte, Leon Hess Professor & Chairman of the Department of Environmental Health Sciences at Columbia University's Mailman School of Public Health, Director of the NIEHS Training Grant and Deputy Director of the NIEHS Center for Environmental Health in Northern Manhattan: **"Neurological Consequences of Chronic Manganese Exposure: Behavioral, Neuroimaging and Neuropathological Findings"**

Core A: *Data Management Core*
PI: Diane Levy

1. Project 1:
    a. The customized data entry system in Bangladesh is currently being utilized to complete 2 phases of entry of follow up data for HEALS:
        i. Follow up 4 for 11,746 original participants
        ii. Follow up 2 for 8,267 new participants (ACE: Arsenic Cohort Expansion)

All data are automatically transferred to Columbia University SQL database located in NY.

b. An Access database was recently programmed and is now in production in Bangladesh to accommodate data entry for the approximately 10,000 newest HEALS participants (ACE-2) who had a baseline interview. Data are sent to New York on a scheduled basis, following secure protocols, and are synced with the Microsoft SQL database so that they are integrated into the greater project data.
c. All data from the Trace Metals Core laboratory, and all water analyses from Lamont-Doherty are received by the data management core and stored in the integrated arsenic database.

2. Project 2:
   a. Creation of database to capture questionnaires, scales and PFT for children in Bangladesh
   b. Procedures have been programmed to download data from the CANTAB equipment to interim data files. These files will be imported into our SQL database.
3. Project 3:
   a. Procedures were programmed to parse genotyping data (received from our collaborating university) for the Gene Environment Nutrient Interactions database; data were parsed and loaded into the arsenic database. Comprehensive datasets were distributed to the investigator as requested.
   b. Periodic uploads of laboratory data to Microsoft SQL server database have taken place and continue to occur.
   c. Data sets have been distributed to the PI and biostatistician for analyses
   d. Close collaboration occurs with students who work with the PI. Students are introduced by the data manager to the data structure that exists; they are oriented to the codebooks. This orientation helps them design and request appropriate datasets for analysis.
4. Security
   a. Note: all data capture and transfer are done according to security protocols established at Columbia University. Data are stored on secure servers; electronic transfers are done over encrypted connections; data are physically moved using encrypted peripheral devices.
5. Additional efforts:
   a. Biomass and HEALS
      i. Creation of comprehensive dataset (including all aspects of study data: questionnaire data from baseline and all follow ups; urine; water analyses; summarization of blood analyses) for follow up study on biomass exposure for women in HEALS study
   b. Choline-Betaine Pilot Study
      i. Programmed routines to parse lab data received from Columbia University and Cornell University laboratories; data stored in arsenic database and datasets created as requested by PI (Hall)
   c. Presented data management workshop for NIEHS and Superfund investigators, staff and students.
   d. Continued support for undergraduate and graduate students working with PIs on Arsenic related projects.
   e. Continued maintenance of secure database and web servers. Projects detailed above are direct beneficiaries of these services.
   f. Management of data flow continues using the Issue Tracking System and the Query Tracking Systems.
   g. Attending weekly project team meetings to provide data management consultation as projects move forward.

Data Management Core-Supported Publications:

Every publication involving participant data has relied on the Data Management Core for datasets used for analyses.

Core B: *Trace Metals Core Laboratory*
PI: Joseph Graziano
Laboratory Director: Vesna Slavkovich

A. Specific Aims:

The primary purpose of the Trace Metals Core Laboratory, which is jointly funded by SRP and our P30 Center, is to provide Center investigators with the capability to obtain analyses of biological samples for a broad array of metals. In addition, the facility provides method development for these analyses, standardization, and quality control. The Trace Metals Core provides analytical support to projects #1, #2 and #3. The Core Laboratories performance in several quality control programs has been outstanding during the past year.

In March, 2013, Dr. Graziano submitted a "Shared Instrumentation Grant" application to NIH for the purchase of a new ICP-MS which is needed to replace our aging ten year old instrument. The grant received a score of 21 and is pending a decision by Council in February, 2014.

B. Studies and Results:

Collectively, during the past five years, the lab has performed more than 140,000 measurements of metals in urine, blood, nail and other tissue samples, using either atomic absorption spectrophotometry or inductively coupled plasma mass spectrophotometry (ICP-MS), as needed. During the past year, this Core Lab conducted more than 20,000 "routine" analyses of biological samples, primarily from projects 1 and 2. A main focus of the Core's activities has been analytical support for As and creatinine measurements for the HEALS Cohort Study (Project #1), which is now in the midst of its fifth biannual follow-up visit. The Trace Metals Core has completed about the analysis of roughly 8,000 urine samples from the first follow-up of the first expansion of the cohort, and roughly 7,000 samples from the baseline of the second cohort expansion. In addition, we have analyzed 8,000 samples from our NCI R01-funded Bangladesh Vitamin E and Selenium Trial (BEST), of which Dr. Ahsan is the PI. In addition to urine samples from the BEST study we continue to measure blood As and Se for the study. Once again, this year a portion of ICP-MS running time was devoted to Dr. Gamble's NIEHS funded R01 study entitled "Folate and Creatine Supplementation as Therapeutic Approaches to Lowering Blood Arsenic" (FACT study), mainly measuring As and Se in blood samples from 600 subjects. Finally, the lab has also analyzed hundres of blood and urine samples from adolescents in Bangladesh who are enrolled in Project #2.

C. Significance:

The biomedical projects of this Superfund Research Program have made an enormous contribution to the overall knowledge concerning the health effects of – in particular – arsenic on human health and the factors that increase the risk of developing arsenic related disease outcomes. The Trace Metals Core Laboratory has given each of these biomedical projects the capacity to test their various hypotheses and to have biological samples analyzed with precision and quality control. A very practical use of these findings will be their utility in assisting the US EPA with their ongoing reassessment of the toxicity of inorganic arsenic in the IRIS database.

D. Plans:

We plan to continue to support the three biomedical projects with analyses of trace elements in biological samples.

E. Publications: Every publication listed for Projects 1, 2 and 3 has relied on the Trace Metal Core.

Students involved with this work:

Tiffany Sanchez, Dr. Graziano's PhD, student has worked preparing the field supplies and pilot studies for her thesis dissertation project (Project #2). In addition, several undergraduate students were employed or volunteered as lab personnel for the summer of 2013 and/or throughout the entire year. Yukari Sumizu, a Columbia College student, worked for part of the year and has now moved on to graduate school. In addition, Teodora Odzakovic, a New Jersy high school student, once again volunteered during the summer .

F. Project-Generated Resources: n/a

Core C: *Biogeochemistry Core Laboratory*
PI: Alexander van Geen
Co-Investigators: Steven Chillrud, Beizhan Yan

A. Specific Aims

The specific aims of this core have not changed. The Biogeochemical analytical core laboratory is housed at Lamont-Doherty Earth Observatory (LDEO) and provides analyses in support of projects 1, 2, 4, 5, 6 , the Community Engagement Core (CEC), and the Research Translation Core (RTC). Analyses have been carried out by high-resolution inductively coupled plasma mass spectrometry (HR ICP-MS), partly on a newly installed Thermo Element 2 instrument purchased with NSF funds, for up to 33 elements for water, soil, sediment, and sediment leachate. Other analyses carried out include dissolved organic carbon content, x-ray fluorescence (XRF) analyses of sediments, and diffuse spectral reflectance to estimate iron speciation. Finally, this core also analyses exhaled breath condensate for isoprostanes and urea by liquid chromatography mass spectrometry (LC-MS).

B. Studies and Results

In support of the Bangladesh related projects (1,2,3, 4, 6), over 4,200 groundwater and leachate samples were analyzed by HR-ICP-MS. In support of projects 4 and 5 efforts at Superfund sites, over 600 samples from incubation and column experiments were analyzed by HR-ICP-MS and 50 sediment samples were analyzed by XRF. In addition the 60 column effluent samples were analyzed for As speciation analyses on the HR-ICP-MS. In support of the RTC core, 56 analyses of the Newark Basin Core were carried out by X-ray fluorescence. The sedimentary organic carbon content of 100 samples of sand and mud sediments from Bangladesh and was also measured.

In support of project 2, Core C is responsible for providing analyses of 8-isoprostane, a biomarker of oxidative stress, and urea a marker of dilution, for exhaled breath condensate samples collected in Bangladesh. In the past year, efforts have been made in Dr. Yan's lab to deal with the reduction in sensitivity observed with the aging of the instrument installed in Yan's lab. The sensitivity of TSQ Quantum has decreased from 30 pg/mL to 200 pg/m. Although this decrease means that the instrument is not appropriate for measuring 8-isoprostane in EBC samples with low to moderate concentrations, it can still be used for method development and running high concentration samples. To deal with this issue Dr. Yan has started working on an instrument in a biomarker lab in Albert Einstein School of Medicine. Dr. Yan already has had many years of collaboration with the researchers in this lab and by working closely with them in the past one year, a new 8-isoprostane analysis method was established. The new method uses freeze-drying to concentrate samples rather than the enzyme sorbent method we have used. Acceptable analytical quality was obtained in the run of standards and lab-based quality control solutions of EBC. Five real samples were tested and results indicate a sensitivity approaching X pg/ml allowing the analyses of the samples from Bangladesh to proceed now. To be able to meet service requests from the Superfund project and members from the NIESH Center For Environmental Health Science in Northern Manhattan (PI Santella), Yan plans to apply the Shared Instrument Grant (S10) to upgrade the LC-MS/MS. The LOD (limit of detection) of the proposed instrument (API 6500 from ABI) is about 2 pg/ml, resulting in no need for pre-concentration for 8-isoprostane analysis; thus it will greatly

reduce the labor and cost of this analysis as well as explore more possible biomarker analyses with even less sample volume.

C. Significance

The significance of the analytical support provided under the Biogeochemistry Core extend beyond the aims of HEALS cohort study (Project 1). The children's health study (Project 2) also relies on the groundwater measurements of As and Mn to investigate neurodevelopmental issues. Mn exposure is a confounding factor for studies of children's mental health and there is no alternative to measuring Mn concentrations in groundwater because no biological sample, urine or blood, has been shown to reflect exposure. In addition, Core C supports Project 2 by making measurements of exhaled breath condensate to investigate respiratory issues and their relationship to As groundwater exposure. In order to understand the processes regulating As concentrations in groundwater, the accurate determination of additional groundwater constituents is essential. The multi-element capability based on high-resolution plasma mass spectrometry (HR ICP-MS) that was developed under a previous funding cycle of the Core has been and will continue to be applied also to a large numbers of groundwater samples and sediment leachates in support of the proposed studies of Superfund sites and in Bangladesh.

D. Plans

We will continue to support the analytical needs of the different projects and the Research Translation and Community Engagement Cores. Project 1 is expected to start shipping exhaled breath condensate samples for analysis and the other projects will continue to have analytical needs for water, soil, sediment, and sediment leachate.

E. Publications, Patents, Other supported by Core C

vanGeen A, KH Win, T Zaw, W Naing, JL Mey, B Mailloux. Confirmation of elevated arsenic levels in groundwater of Myanmar. Science of the Total Environment, accepted January 2014.

vanGeen A, EB Ahmed, L Pitcher, JL Mey, H Ahsan, JH Graziano, KM Ahmed. Comparison of two blanket surveys of arsenic in tubewells conducted 12 years apart in a 25 km2 area of Bangladesh. Science of the Total Environment, accepted December 2013.

Balasubramanya S, A Pfaff, L Bennear, A Tarozzi, KM Ahmed, A Schoenfeld, A van Geen, Evolution of households' responses to the groundwater arsenic crisis in Bangladesh: information on environmental health risks can have increasing behavioral impact over time. In press, Environment & Development Economics, September 2013.

vanGeen, BC Bostick, PTK Trang, VM Lan, NN Mai, PD Man, PH Viet, K Radloff, Z Aziz, JL Mey, MO Stahl, CF Harvey, P Oates, B Weinman, C Stengel, F Frei, R Kipfer, M Berg. Retardation of arsenic transport through a Pleistocene aquifer. Nature 501: 204–207, 2013.

Mailloux BJ, E Trembath-Reichert, J Cheung, M Watson, M Stute, GA Freyer, AS Ferguson, KM Ahmed, MJ Alam, BA Buchholz, J Thomas, AC Layton, Y Zheng, BC Bostick, A van Geen, Advection of surface-derived organic carbon fuels microbial reduction in Bangladesh groundwater, PNAS 110: 5331-5335, 2013.

Sun, J., Arsenic In-Situ Immobilization by Magnetite Formation within Contaminated Aquifer Sediments. Columbia University Superfund Research Program Monthly Seminar/Webinar, Sept. 16, 2013.

Sun, J., S.N. Chillrud, B.J. Mailloux and B.C. Bostick. Arsenic In-Situ Immobilization by Magnetite Formation within Contaminated Aquifer Sediments. Poster at the 2013 Superfund Annual Meeting. Won Best Student Poster for the Environmental Science Section.

Sun, J., S.N. Chillrud, B.J. Mailloux and B.C. Bostick. Formation of Magnetite within Aquifer Sediments and Its Effects on Arsenic Mobility. Oral presentation at the 23rd V.M. Goldschmidt 2013 Conference.

F. Project-Generated Resources- n/a

PI initiated research translation

Beizhan Yan- Co-I.

Core C:
Dr. Beizhan Yan, Co-I

a. May 20th, 2013, NY: Dr. Yan gave a lab tour to a delegation of six scientists from the Chinese Research Academy of Environmental Sciences discussed with them about current challenges for environmental protection in China.
b. August 6, 2013, NY: Together with Steve Chillrud, Yan attended an on-camera interview with Christine Schiffner, NY correspondent for Chinese Xinhua news to talk about crucial issue related to water and air pollution and sustainable development in China and made comments/suggestions on Chinese government's announcement of spending more than 3 trillion yuan to enhance water and air quality. The interview can be seen in the following websites: http://www.cncworld.tv/Lifestyles/v_show/35302_5.shtml(in English) and http://www.xhstv.com/show/Ljwlowtx4RibCAGg.html (in Chinese)
c. Oct. 19, 2013, Nanjing, China: Together with Steve Chillrud, Yan met with Prof. Huang Lei from Nanjing University to discuss her recent findings about exposure from lead-contaminated soils in a village in Nantong, China. This village has more than 10 metal wiring plants and elevated levels of Pb were found in soils and blood in children.

Core D: *Hydrogeology Support Laboratory*
PI: Peter Schlosser
Outside Collaborators: Dimitrios Ntarlagiannis, Lee Slater, Charles Harvey, Holly Michael

A. Specific Aims:

The overall goal of the Hydrogeology Support Core remains the same, to support our projects by providing information on the groundwater and surface water flow and transport regime at our field sites in Bangladesh and the US.

B. Studies and Results

In 2013, ^{3}H-^{3}He ages measured in 13 intermediate-depth monitoring wells of Araihazar, Bangladesh in order to constrain the vulnerability of low-As aquifers. The full suite of noble-gas concentrations were measured in a total of 38 wells, along with radiocarbon measurements for dissolved organic carbon (DOC) in 15 wells and for dissolved inorganic carbon (DIC) in 4 wells. Leak tests were carried out in half-dozen community wells by increasing the salinity uniformly within the well and profiling the well with a conductivity meter on the next day (Stahl et al., in review). Leaks were documented in two out of six wells, which may explain why arsenic levels were higher than expected from the local geology.

In May-June 2013, 3 new nests, comprising a total of 12 piezometers, were installed and logged to monitor water levels in the intermediate and deep aquifers and obtain detailed lithology. Cuttings retrieved at a total of 400 5-ft intervals and analyzed for diffuse spectral reflectance (color) and bulk composition (As, Fe, and Ca in particular) by X-ray fluorescence. The locations of two of the new monitoring nests were in geochemically sensitive areas east and west of the Meghna River where Dhaka pumping may be drawing river water into the

intermediate and deep aquifers as the Dhaka drawdown cone grows. Another monitoring well nest of 6 wells was installed half way between central Araihazar and central Dhaka (Site U) to better document the hydraulic connection between urban pumping and changes in the geochemistry of rural intermediate and deep aquifers. In addition a river piezometer was installed in the Shitoloka River near site U to monitor water levels. Further, a two new deep community wells east and west of the Meghna River were instrumented with pressure transducers to measure the potentiometric surface of the deep aquifer in strategic places which lacked those measurements before. All new well nests and newly instrumented community wells were surveyed with Fast Static GPS and instrumented with pressure transducers to measure continuous water levels for comparison with the approximately 60 pressure transducers already deployed across Araihazar in shallow, intermediate and deep monitoring and community wells. In November 2012, 15 deep community wells were logged with a downhole EM/Gamma logger to obtain higher confidence mapping of subsurface clay and silt layers than was previously available.

For studies of US Superfund aquifer material by monitoring the magnetite based immobilization of As we are testing the use of geophysical methods. Geophysical methods can offer continuous, real time monitoring, with high spatial and temporal resolution, while being non invasive. The method of choice for monitoring potential production of magnetite in situ is the spectral induced polarization (SIP) since it is known to be sensitive to microbial induced biogeochemical transformations, including new mineral phases forming and dissolving. The initial magnetite based experiment utilized columns modified for SIP measurements, based on previous research. For all columns, 4 monitoring electrodes were installed, allowing for SIP monitoring along each column. We collected SIP data, on all columns, for the duration of the experiment. Early results are encouraging since distinctive SIP responses are associated with the “active” columns where magnetite and other iron oxide formation was confirmed, while no response was recorded for the control columns which did not have magnetite formation. Based on the results of this first experiment we built new columns, better fitted for SIP measurements, and prepared a variety of well characterized porous media containing various amounts of added magnetite in an effort to quantify the SIP response in a simplified environment.

C. Significance

Detailed knowledge of groundwater flow is essential for understanding geochemical processes in the subsurface. Identification of recharge and discharge areas and mechanisms, as well as flow lines are essential for delineating trends in geochemical evolution, including changes in As concentrations, and to quantify reaction rates. Hydrogeology Core D will provide the tools and expertise for collection and analysis of a broad range of hydrogeological data in the US and in Bangladesh under Projects 4, 5, and 6 and the Research Translation Core.

D. Plans:

We will continue to support the laboratory, field and modeling needs of projects 5 and 6.

E. Publications, Patents, Other supported by Core D

Knappett, PSK, BJ Mailloux, I Choudhury, M Khan, H Michael, S Barua, DR Mondal, M Steckler, H Akter, KM Ahmed, B Bostick, C Harvey, M Shamsudduha, I Mihajlov, R Mozumder, A. van Geen. Vulnerability of intermediate and deep low-arsenic aquifers to municipal pumping in Bangladesh. Submitted to Environmental Sciences and Technology, January 2014.

Knappett, P.K., J. Du, P. Liu, V. Horvath, B. J. Mailloux, J. Feighery, A. van Geen, P. J. Culligan. Importance of reversible attachment in predicting *E. coli* transport in saturated aquifers from column experiments. Advances in Water Resources http://dx.doi.org/10.1016/j.advwatres.2013.11.005, 2013.

Stahl, MO, JB Ong, CF Harvey, CD Johnson, ABM Badruzzaman, MH Tarek, A. van Geen, JA Anderson, JW Lane. Well-casing leak detection: Applications of fluid replacement logging in arsenic-contaminated aquifers of Bangladesh. Revision submitted to Groundwater, September 2013.

Student and Post-doc involvement under Core D

Dr. Peter Knappett is a hydrogeologist and became a post-doctoral investigator at LDEO in 2012. Starting in August 2013, he joined the faculty of Texas A&M University as an assistant professor and continues to collaborate with Columbia SRP PIs.

Ashley Samuel, PhD student at Rutgers- Newark.

F. Project-Generated Resources- n/a

Core E: Community Engagement Core
PI: Yan Zheng

A. Specific Aims

To determine and reduce barriers for testing and treatment of well water arsenic, doubling the rates of both testing and treatment in the central Maine community area by year 5compared to baseline.

B. Studies and Results

During 2013 the Maine Arsenic Reduction for Community Health (MARCH) Citizen Advisory Committee was formed, bringing together residents of the CEC's project area in Central Maine that also represent local government, Maine CDC, education, USGS, and the well drilling and treatment companies. The first meeting was held in Readfield, Maine on May 9, 2013 and a second meeting is planned for Feb 7, 2014. The CEC and its MARCH partnership aims through direct engagement with community to enable vulnerable households including those with children, to regularly test their well water for arsenic and other water quality parameters, to have access to information of water quality test results and treatment options, and to take actions to mitigate arsenic in most effective and economic ways. MARCH will work with all its partners and members of the community towards eliminating the exposure to arsenic and other contaminants in domestic well water to improve community health.

The strategy to reduce barriers to testing and treatment is to develop community interventions based on improved understanding of key behavior influencing factors, implement them on a pilot basis and evaluate. Tools are being developed based on the results of a baseline community survey implemented early 2013 in the greater-Augusta area that was designed to uncover barriers to testing and treatment and was developed with input from Maine CDC and the Maine Geological Survey. A large portion of the survey instrument was designed to identify key behavioral factors using an integrated model of health and social psychology theories based on the RANAS (Risk, Attitude, Norm, Ability, Self-Regulation) blocks of factors that have to be favorable in order for a new behavior to take root. For example, the returned survey of 452 Maine well owners (Flanagan et al 2013a submitted) found knowledge that years of exposure increases arsenic-related health risks, attitude beliefs that regularly testing does not take too much time, norm beliefs that neighbors regularly test well water, and action knowledge of whom to contact to get well tested were all significant predictors of the behavior of having included arsenic on the most recent well test. Regular testing behavior in the project area is low and norm perceptions in the population are also low, yet descriptive norms were identified as a significant predictor of testing behavior and could be a potential target for intervention. Testing behaviors were also significantly associated with education, income, and length of time lived in home.

A similar survey was also implemented in early 2013 and responses were analyzed from 255 households in the area that participated in a Columbia SRP well-testing program between 2006-2010 and were found to have higher than recommended levels of arsenic. This follow-up survey was designed to determine barriers to treatment specifically among households that have already had their well water tested and know their arsenic

status. We found that although 41.5% of households installed some kind of water treatment system in response to the arsenic in their well water and another 26.3% switched to drinking bottled water or took some other action, the remaining 29.8% did not take any action to reduce their arsenic exposure (Flanagan et al 2013b submitted). The majority of households not taking action were at lower levels of arsenic exposure (10-50 µg/L) and their reasons were primarily lack of concern or the expense of treatment. Perceived vulnerability that the untreated water is not safe to drink, and instrumental beliefs that reducing drinking water arsenic would increase home value were the significant predictors of mitigation behavior. Income and education were both significantly associated with use of a treatment system, and negatively associated with drinking purchased bottled water, indicating a socio-economic influence on mitigation choices. The results from both of these surveys have been developed into manuscripts that have been submitted for publication to a special issue entitled “Arsenic in Groundwater of Northeast America” for *Science of the Total Environment*, guest edited by CEC PI Yan Zheng and Joseph Ayotte of USGS Regional Center in New Hampshire.

Follow-up survey participants that indicated they treat their well water in some ways but not necessarily for arsenic were contacted to volunteer for home visits from partner Maine Geological Survey in order to perform on-the-spot arsenic tests of both raw and treated waters using a test kit and to collect basic information about the treatment system in use. During the Summer/Fall 2013 99 households were visited. Tap water samples from 8 out of 76 households with arsenic treatment systems were not in compliance with the 10µg/L drinking water arsenic standard, indicating incorrect or inefficient treatment systems in use. There was strong agreement with reported use of treatment and observed use, though the variety of products available to and utilized by consumers may create confusion among households for reporting their use on surveys.

Our results indicate that different community interventions may be required at the different stages of arsenic mitigation behavior, first motivating households to test their water, then to treat their water, and finally to monitor and maintain treated water quality. The favoring and hindering factors are different for each stage of the arsenic mitigation behavior. Our interventions will rely on this new understanding.

C. Significance

Within the 17-town greater-Augusta project area it is estimated that at least 13,000 people are at risk of elevated arsenic in their drinking water, based on the rates of well water supply and arsenic testing results. Maine CDC estimates that the rate of well water testing for As was 42% in 2009. Among the estimated 17,600 households relying on private wells for drinking water in the project area, a doubling of the testing rate would result in about 7400 additional households, more than 18,000 people, knowing their well arsenic status, the first step to reducing exposure and lifetime risks for cancer and excess fatality.

D. Plans

Community interventions to promote arsenic testing and treatment will be developed based on the results of these household surveys and visits, to be implemented over the next 2-3 years in the greater-Augusta project area and then evaluated through an endline survey. Due to budget constraints, interventions will utilize direct-mailings to motivate well testing and treatment, with messages crafted based on the improved understanding of behaviors from analysis of household surveys. The innovative methods for behavior change developed through this project can be used for outreach to residents of other priority areas of Maine and beyond.

Already this survey methodology is being expanded into New Jersey, where the CEC in collaboration with RTC has been requested to assist the NJ Department of Environmental Protection to implement a similar household well testing and treatment survey in 2014, in the areas of Northern NJ affected by arsenic. The Department of Environmental Health in New Hampshire has also consulted CEC PI Zheng for findings reported above to guide their survey efforts targeting arsenic affected households in NH.

E. Publications, Patents, Other

Flanagan, S.V.; Marvinney, R.G.; & Zheng, Y. (2013, November) Well testing and treatment behaviors in Central Maine: Engaging the community for arsenic mitigation. Platform presentation at the SETAC North America 34th Annual Meeting, Nashville, TN

Flanagan, S.V. (2013, November) Overcoming barriers to environmental health protective behavior: Examples from private well testing and treatment for arsenic in Maine. Columbia University Superfund Research Program 2013-2014 Seminar Series, Palisades, NY

Flanagan, S.V., R.G. Marvinney, and Y. Zheng (2013a).Influences on domestic well water testing behavior in a Central Maine area with frequent groundwater arsenic occurrence. *Science of the Total Environment*, submitted.

Flanagan, S.V., R.G. Marvinney, C.W. Culbertson, and Y. Zheng (2013b). Dissemination of well water arsenic results to homeowners in Central Maine: Influences on mitigation behavior and continued risks for exposure. *Science of the Total Environment*, submitted.

F. Project-Generated Resources: n/a

Research Translation Core
Project co-PIs: Meredith Golden and Steven Chillrud
Co-Investigators: Joseph Graziano, Stuart Braman, Paul Olsen, James Ross, Tricia Chai-Onn, Sara Flanagan

A. Specific Aims:

Our specific aims have not changed and we have made progress on all of them in this last year. However, due to the significant cuts in budget we found it necessary to scale back efforts on some of the aims. For example, we did not have the resources to update the Superfund Footprint Mapper layers. Instead, we continued to present the Mapper at meetings, workshops, and via webinars to a broader range of potential users.

B. Studies and Results:

We present progress over the last year organized into categories of partnering with government agencies, communicating with NIEHS SRP staff and broad audiences, technology transfer, and assisting and/or recording investigator initiated research translation.

Partnering with government agencies: We have several on-going government partnerships related directly to research translation activities. In collaboration with the NJ DEP Office of Science and the NJ Geological Survey, three short videos for homeowners who may have arsenic in their drinking water were extensively edited based on reviewer comments and then presented at the RTC session of the annual SRP program in Baton Rouge in October 2013. Based on annual meeting comments a final editing round is underway now and will be completed by March. Discussions have been initiated with Judy Louis and Nick Procopio of the NJ DEP Office of Science and Steve Spayd of the NJ Geological Survey on incorporating links to the videos on the appropriate state agency websites. Once these links are in place we will proceed to work with county and township health and environmental officials to distribute links to the videos locally as well, prioritizing our efforts based on the % of private wells with arsenic exceeding state standards. The goal is to encourage well testing, to demystify the testing process, and help homeowners understand test results.

The Columbia SRP RTC and Community Engagement Core (CEC) are collaborating and in the planning stages to replicate in northern New Jersey the survey work already undertaken in Maine to begin to understand ongoing testing and treatment practices and key factors influencing testing and treatment behavior. The survey, to be undertaken in Q1 2014, will allow researchers to look at the impact of the demographic

differences between central Maine and northern New Jersey as well as strengthening our understanding of which approaches to encouraging testing and treatment are most likely to have an impact. This new effort was undertaken both by leveraging funds from the state and by temporarily postponing the ongoing work on the Newark Basin to next year. Both the distribution of the arsenic awareness and testing videos and the survey work in New Jersey dovetail with New Jersey state efforts in a multistate CDC-funded Private Well Initiative aimed in part at informing private well owners about potential health risks associated with drinking water from private wells and the need to test for possible contaminants.

As part of the ongoing follow-up to work with Dan Miller, County Hydrologist from the Rockland County Department of Health with Alden Wolfe, Chairman of the Rockland County legislature and with Harriet Cornell, Chair of the Rockland County Legislature Environment Committee on local water supply issues, and in response to discussions with Darcy Casteleiro of Assemblywoman Ellen Jaffe's office and Hayley Carlock of Scenic Hudson, Stuart Braman testified before the Public Service Commission in October and submitted two rounds of written comments in November and December.

CU RTC continues to actively participate in a variety of workshops and conferences with representatives from different government agencies. Dr. Braman attended the "Naturally occurring contaminants in groundwater used for drinking water supply in the northeastern United States" session at the Geological Society of America meeting In Bretton Woods, NH, March 2013. From July 29- August 1, Meredith Golden participated in the "2013 US EPA Community Involvement Training Conference" and preconference "Superfund Monday," organized by the U.S. Environmental Protection Agency (EPA) in Boston. She presented a live technology demonstration and a poster on the NPL Superfund Footprint: Site, Population, and Environmental Characteristics Mapping Tool. The Mapper was created for academic researchers, government regulators, and community stakeholders to help visualize critical data related to the area and inhabitants near Superfund sites in order to better assess the vulnerability of affected populations and to prioritize cleanups. Golden also participated remotely this January in the NASA Soil Moisture Active Passive (SMAP) Applications Focus Session on Health and Disease Exposure Workshop with scientists from the CDC and ATSDR. The CU RTC has been invited by the NIH Disaster Research Response project to be on its Environmental Health Networks group which is focusing on establishing a framework for the development and prioritization of the systems, tools, protocols, and subject matter expertise among NIEHS intramural/extramural researchers related to disaster response.

The CU SRP RTC assisted NIEHS in planning the Risk e Learning GIS series by identifying key topics and potential speakers. After consulting with contacts at EPA and ATSDR, our RTC contacted the U.S. Department of Energy (DOE) Oak Ridge Reservation (ORR) personnel and invited them to give a presentation on the geospatial capabilities of the Oak Ridge Environmental Information System (OREIS). This is the ORR database for storing and retrieving historical and environmental characterization data used for risk assessments to support source remediation decisions under watershed Interim Records of Decision (RODs). Co-presenting during this Risk e Learning session on December 6th, Meredith Golden and GIS specialist Tricia Chai-Onn reviewed the history, administration, and implementation of the Superfund program and demonstrated the CU SRP NPL Superfund Footprint Mapper. Over 170 participants joined the webinar. The announcement of the CU RTC presentation prompted EPA Region 2 STL Diana Cutt to suggest Columbia contact Betsy Smith, the Associate National Program Director for EPA's Sustainable and Healthy Communities Research Program (SHCRP). The SHCRP is very interested in mapping tools that are being used by communities, including tools external to EPA. Specific to the "Mapper", the SHCRP would like to explore if there's any possibility to link with their EnviroAtlas and/or C-FERST. Golden and Chai-Onn have been invited to present the Mapper as part of EPA's SHCRP's webinar series in February 2014.

Furthermore, several scientists from EPA Region 1 (W. Brandon, D. Luce, A. Gardner,), Region 2 (E. Keveney, B. Ofrane,), Region 3 (B. Pluta), Region 4 (L. Carr, J. Ruiz), Region 5 (l. Burkhard, C. Maurice), Region 7 (J. Bernard-Drakey, C. McLaughlin), Region 8 (K. Keteles), Region 9 (B. Arthur, A. Bain, M. Gill, B. Macler, Y. Martinez, A. Toy), and Region 10 (M. Gubitosa), EPA NEIC (C. Middleton), EPA ORD (M. Mills), EPA RTP (C. Croghan, B. Pickard), NIH (H. Chen, M. Gant, H. Henry, R. Moody, W. Suk), CDC/ATSDR (T. Burk, J. Kolling), USGS (Z. Szabo), NOAA (M. Gielazyn), USCG (C. Klarmann), US Public Health Services (C.

Frazier), Indian Health Services (B. Harper, L. Hubbard, R. Martinez), NYSDEC (P. John), NYCDEP (C. Orr) and multiple of other State and local agencies (e.g., AK, CA, CT, FL, ID, IN, KY, MO, MN, NC, NJ, NV, OH, TN, PA, PR, , TX, VA, WA, WI), as well as several international participants (Canada, England, Nigeria, Spain, Turkey) have registered for either our monthly seminar/webinar series and/or our Risk e Learning presentations.

In addition the CU SRP RTC scientists have discussed issues related to arsenic and other heavy metals with researchers and government officials around the world including China and Vietnam. Last August, Beizhan Yan and Steve Chillrud met with Prof. Huang Lei at Nanjing University to discuss her recent findings about exposure from lead-contaminated soils in a village in Nantong, China. In November, Meredith Golden also presented the CU SRP Superfund Footprint Mapper to a delegation from Hanoi Medical University and Public Health School at a meeting hosted by the International Research Institute for Climate and Society (IRI) at Columbia.

Communicating with SRP/NIEHS staff and broad audiences:

At the SRP 2013 Annual Meeting in Baton Rouge, Dr. Braman participated in the RTC day-long session and presented the aforementioned videos on Arsenic in drinking water, eliciting feedback from RTC colleagues. Our SRP trainee Ms. Jing Sun won first prize at the SRP 2013 Annual Meeting for her non-biomedical poster, "Arsenic In-Situ Immobilization by Magnetite Formation within Contaminated Aquifer Sediments". Earlier in the year she gave presentations at the Goldschmidt conference in Florence, Italy and as part of the CU SRP Seminar/Webinar series. Dr. Megan Hall, Former SRP trainee and now Assistant Professor of Epidemiology at Columbia, gave an oral presentation on, “Urinary Creatinine: The Grand Enigma – Implications of Its Use as a Urine Dilution Adjustment Factor in Epidemiologic Studies”. Ms. Brandilyn Peters, another CU SRP trainee, participated in the poster session presenting, "Arsenic Metabolism and Renal Function in an Arsenic-exposed Population in Bangladesh." Both SRP researchers showcased posters on their respective topics at the 15th International conference of the Pacific Basin Consortium for Environment and Health, September 24-27 in Hawaii. CU SRP provides professional training for students affiliated with this program and values the contributions made by this next generation of skilled and creative scientists.

As mentioned under *Partnering with government agencies*, the RTC also worked with the NIEHS organizers in planning the Risk e Learning webinar series “Using GIS Tools to Analyze, Compute, and Predict Pollution” by suggesting key topics and potential presenters. In addition to the Risk e Learning GIS session by Meredith Golden and Tricia Chai-Onn, CU SRP Associate Director Alexander van Geen also gave a talk for the series on "The unrealized potential of field kits to reduce toxic exposures: Case-studies from Bangladesh (arsenic in groundwater) and Peru (lead in mine tailings)". The CU SRP monthly seminars/webinars are another forum for presenting research findings and tools. They are well attended and include bio-medical and geoscience speakers including featured guests, SRP trainees, and our own SRP scientists.

The redesigned and updated Columbia SRP website (superfund.ciesin.columbia.edu) continues to be populated with in-depth descriptions of the projects and cores, contact information for all our scientists and staff, archives of progress reports and publications, upcoming events and announcements, interactive maps, and photo galleries for projects and cores. In addition, the website provides direct links to many SRP and Superfund-related resources, including agency websites, mapping tools, news links, all SRP center websites, and key NIEHS SRP forms and documents. The enhanced website provides easy access to updated information about SRP research and events for many audiences, including our own scientists, colleagues at other SRPs, the NIEHS staff, other government agencies, and the public as well. The Local Water Initiatives section of the enhanced website includes the New Jersey Arsenic Awareness website which hosts the three arsenic awareness videos referenced above as well as lists of local testing and treatment facilities. Private well owners will be accessing this site either through links on state and local environmental, drinking water or health web sites or by googling “New Jersey Arsenic Awareness”.

Columbia SRP scientists make their research findings available through a wide-variety of peer-reviewed publications. Project PIs notify NIEHS either directly or via RTC staff of accepted high profile publications, such as the article on “Retardation of arsenic transport through a Pleistocene aquifer” published in Nature. This

study investigated the rate and direction of water flow, and the coupled chemistry of arsenic and organic carbon. It finds that arsenic contamination moves at a rate of about 10-20 times slower than water travels. This benchmark rate can be used to better understand how fast arsenic will migrate at US contaminated sites. It also helps to understand what affects that rate of migration; changes in organic carbon sources to groundwater can influence the fate of arsenic, and in doing so, can be an important control on water quality. Furthermore, it helps us to understand the sustainability of groundwater resources, and the effects of groundwater use on water quality. The July issue of *Epigenetics* included a paper by our SRP trainee Megan Niedzwiecki and her Columbia SRP colleagues entitled "Blood glutathione redox status and global methylation of peripheral blood mononuclear cell DNA in Bangladeshi adults". In this article, the researchers investigated the relationship between oxidative stress and DNA methylation in humans. Given that redox status and DNA methylation are both potentially modifiable through nutritional and other interventions, a greater mechanistic understanding of these observations could ultimately have therapeutic implications.

RTC continues to help design and participate in innovative bi-directional communications with NIEHS, government agencies, academics, community partners, and the general public. Our activities go beyond simple communications to active participation and leadership in these partnerships. Our SRP Director and RTC co-investigator Joe Graziano has spent considerable effort chairing the National Research Council (NRC) committee to evaluate critical scientific issues to assess effects from oral exposure to inorganic arsenic. The committee also included CU SRP Principal Investigator Habibul Ahsan. Several CU SRP scientists will also participate in the NIEHS and SRP March workshop "Health effects and mitigation of arsenic: current research efforts and future directions".

Conducting technology transfer: Much of projects 4, 5 are focused on developing and understanding enhanced remediation approaches and if successful transfer them to Superfund sites. Furthermore, much of project 6 is focused on interventions in Bangladesh and understanding their long-term implications. As such much of these projects can be said to be directly related to technology transfer effort.

Investigator-initiated research translation (summarized by project):

Project 1: Dr. Habibul Ahsan, PI

a. Dr. Ahsan served on the National Research Council (NRC) committee to evaluate critical scientific issues to assess effects from oral exposure to inorganic arsenic that was chaired by Columbia University SRP Director Joseph Graziano.

Project 2: Dr. Joseph Graziano, PI

a. Columbia SRP Director Dr. Joseph Graziano has carried out a wide range of research translation efforts in both the USA and Bangladesh, but here we highlight the fact that he has been the chair of the National Research Council (NRC) committee to evaluate critical scientific issues to assess effects from oral exposure to inorganic arsenic. The committee also includes CU SRP Principal Investigator Habibul Ahsan and as well as SRP grantees Margaret Karagas, Rebecca Fry, and Robert Wright. The committee has conducted public workshops to gather a variety of perspectives from key stakeholders and the public. It has prepared an interim report providing recommendations on how to address these issues in EPA's Integrated Risk Information System (IRIS) assessment of inorganic arsenic. After the IRIS assessment is revised by EPA, the committee will then review the assessment to determine whether dose-response relationships between inorganic arsenic and cancer and non-cancer effects are appropriately estimated and characterized. The committee will also determine whether the arsenic document implements the recommendations made in Chapter 7 of the 2011 NRC report on formaldehyde for improving descriptions of methods and criteria for selecting studies, approaches to evaluating critical studies, weight-of-evidence analyses, and justification of modeling approaches in IRIS assessments. A final report will be published when the project is completed at the end of 2015.
b. Dr. Graziano served with PI Bostick and Co-I Beizhan Yan on a panel at a public meeting hosted in Orangeburg, NY on July 29th by US Representative Nita Lowey, 17th Congressional District, the Ranking Member on the House Appropriations Committee, which controls the annual budgets of every federal science agency. Dr. Linda Birnbaum also attended and together with Congresswoman

Lowey discussed key environmental health issues and the role of NIEHS. Over 50 people came and stayed for the discussion after the talks and to ask more questions.

c. Dr. Graziano organized and chaired a session devoted to arsenic at the September, 2013, Pacific Basin Consortium on Environmental Health. A small supplement to our SRP was devoted to travel expenses for six speakers, including Drs. CJ Chen (National Taiwan University); Rebecca Fry (University of North Carolina); Craig Steinmaus (University of California, Berkeley); Habibul Ahsan (University of Chicago); Aaron Barchowsky (University of Pittsburgh); and Mary Gamble (Columbia University).

Project 3:
Dr. Mary V. Gamble, PI

a. October 15 to 18, 2013. Dr. Gamble attended the SRP's 25th Annual Meeting in Raleigh, NC. Dr. Gamble's lab was represented by poster presentations by two PhD students. Brandilyn Peters' poster was entitled, "Creatinine, arsenic metabolism, and renal function in an arsenic-exposed population in Bangladesh" and Caitlin Howe's poster was entitled, "Associations between s-adenosylmethionine, s-adenosylhomocysteine and arsenic methylation." In addition, Dr. Gamble's former post-doc gave an oral presentation entitled, "Urinary creatinine: implications of its use as a urine dilution adjustment factor in epidemiologic studies of Metal Exposure."
b. October 30 to November 1, 2013. Dr. Gamble served as a Member of the University of AZ SRP Program's External Advisory Board. September 24 to 27, 2013. Dr. Gamble was an invited speaker at the Pacific Basin Consortium on Environment and Health in Hawaii. "Nutritional Influences on the Metabolism and Toxicity of Arsenic." Dr. Gamble's student, Brandilyn Peters, also presented a poster at this conference. April 4, 2103. Dr. Gamble was an invited speaker at the National Research Council. "Interplay between one-carbon metabolism, arsenic metabolism and epigenetics."
c. December 9, 2013. Dr. Gamble was an invited speaker at Child Health Research Seminar Series at the Icahn School of Medicine at Mount Sinai. "Influence of folate nutritional status on the methylation and toxicity of arsenic."

Project 4: Dr. Benjamin Bostick, PI

a. PI Bostick is actively working to determine how to minimize arsenic exposure in contaminated areas by identifying low-arsenic groundwater sources, through a World Bank supported project in Cambodia in 2013.
b. PI Bostick has been working throughout 2013 with both consultants and EPA officials in Region 2 to identify areas where natural arsenic is being released at landfill sites that have been classified as Superfund sites, and where in situ magnetite formation may be particularly effective to contain the extent and spread of this groundwater contamination.
c. In collaboration with EPA Region 1, PI Bostick worked with the responsible parties including Mike Webster and others at the Dover site to convey the results of our study and to get input from them about their research needs and regarding the best way to make our research relevant to site remediation.
d. PI Bostick also worked in 2013 with NIEHS and EPA Region 2 staff, as well as officials from the City of New York, to examine the relative effects of revising soil lead standards on urban areas heavily affected by legacy contamination.
e. During 2013, Bostick, as a representative to the National User Facility Organization (NUFO), made one trip to Washington DC to present synchrotron research to the congressional delegations of New York.
f. PI Bostick served on a panel with Dr. Graziano at a public meeting hosted in Orangetown, NY on July 29th by US Representative Nita Lowey, 17th Congressional District, the Ranking Member (i.e., senior Democrat) on the House Appropriations Committee, which controls the annual budgets of every federal science agency. Dr. Linda Birnbaum also attended and together with Congresswoman Lowey discussed key environmental health issues and the role of NIEHS. Over 50 people came and stayed for the discussion after the talks and to ask more questions.
g. PI Bostick also gave a presentation on Modern Careers in Environmental Sciences as part of the Columbia SIPA Career Development Workshop. 31 July, 2013.

Project 5:
Dr. Steven Chillrud, PI

a. Project 5 is focused on developing and understanding enhanced remediation approaches and if successful transfer them to Superfund sites. As such almost entire project is a technology transfer effort.
b. Participated on teleconference with NIEHS, EPA on impact of new CDC blood lead standard and *in situ* remediations for lead contaminated soils June 6, 2013.
c. Meeting at LDEO with Steve Parisio from NYSDEC on PAHs and metals in Demolition and Construction Debris that are being assessed for in situ remediation approaches, June 4, 2013,
d. Webinar given by Jing Sun on "Arsenic *In-Situ* Immobilization by Magnetite Formation within Contaminated Aquifer Sediments", Sept 16. 2013.
e. Discussion with Larry Reed, contractor to EPA, on how to improve interactions between EPA, NIEHS SRP scientists and ATSDR at Superfund Sites. January 2014.
f. August 6, 2013, NY: Beizhan Yan and Steve Chillrud provided an on-camera interview with Christine Schiffner, NY correspondent for Chinese Xinhua news to talk about crucial issues related to water and air pollution and sustainable development in China and made comments/suggestions on Chinese government's announcement of spending more than 3 trillion Chinese Yuan to enhance water and air quality. The interview can be seen in the following websites: http://www.cncworld.tv/Lifestyles/v_show/35302_5.shtml (in English) and http://www.xhstv.com/show/Ljwlowtx4RibCAGg.html (in Chinese)
g. Oct. 19, 2013, Nanjing, China: Beizhan Yan and Steve Chillrud met with Prof. Huang Lei from Nanjing University to discuss her recent findings about exposure from lead-contaminated soils in a village in Nantong, China. This village has more than 10 metal wiring plants and elevated levels of Pb were found in soils and blood in children.

Dr. Stute

a. Spring/Summer 2013: Finalized videos on arsenic (and other) contamination issues and testing that were developed in context of a Barnard Workshop in Sustainable Development in collaboration with Stuart Braman. The videos were reviewed by colleagues at the New Jersey Department of Environmental Protection Office of Science and the New Jersey office of the United States Geological Survey. http://njarsenic.superfund.ciesin.columbia.edu/home
b. January 2013: Attendance of a EPA Star grant review meeting at EPA headquarters in Washington, D.C. The main topic of the meeting was CO_2 geosequestration. Water quality issues including elevated As levels in drinking water in the northeastern US were a central theme.

Project 6:
Dr. Lex van Geen, PI

a. January 15-16, 2013 Dhaka : Dr. van Geen was invited present his findings on resilience of deep low-As aquifers based on 10-year time series for community wells in our study area of Bangladesh and more past year's field-kit survey of over 28,000 tubewells. University College London-supported workshop attended by international group of hydrogeologists and government, international organization, and NGO representatives responsible for arsenic mitigation - including government Policy Support Unit.
b. January 22, 2013 Yangon, Myanmar : Dr. van Geen was invited to give a presentation on arsenic mitigation at Symposium on Arsenic in Drinking Water, Myanmar, on the Yangon University campus.
c. July 24-27, 2013 Punjab, India: Dr. van Geen launched a testing campaign of 20,000 wells for arsenic in fluoride by collaborator C.K. Singh from TERI University supported under a new USAID PEER Science grant.
d. August 25-30, 2013 Florence, Italy: Dr. van Geen attended the Goldschmidt Conference sponsored by the Geochemical Society and the European Association of Geochemistry. He convened session entitled "Impact of air, soil, and water geochemistry on human health".

Core C:
Dr. Beizhan Yan, Co-I

a. May 20th, 2013, NY: Dr. Yan gave a lab tour to a delegation of six scientists from the Chinese Research Academy of Environmental Sciences discussed with them about current challenges for environmental protection in China.
b. July 29, 2013, NY: Dr. Yan served with Director Graziano and PI Bostick on a panel at a public meeting hosted in Orangetown, NY on July 29th by US Representative Nita Lowey, 17th Congressional District, the Ranking Member on the House Appropriations Committee, which controls the annual budgets of every federal science agency. Dr. Linda Birnbaum also attended and together with Congresswoman Lowey discussed key environmental health issues and the role of NIEHS. Over 50 people came and stayed for the discussion after the talks and to ask more questions.
c. August 6, 2013, NY: Together with Steve Chillrud, Yan attended an on-camera interview with Christine Schiffner, NY correspondent for Chinese Xinhua news to talk about crucial issue related to water and air pollution and sustainable development in China and made comments/suggestions on Chinese government's announcement of spending more than 3 trillion yuan to enhance water and air quality. The interview can be seen in the following websites: http://www.cncworld.tv/Lifestyles/v_show/35302_5.shtml (in English) and http://www.xhstv.com/show/Ljwlowtx4RibCAGg.html (in Chinese)
d. Oct. 19, 2013, Nanjing, China: Together with Steve Chillrud, Yan met with Prof. Huang Lei from Nanjing University to discuss her recent findings about exposure from lead-contaminated soils in a village in Nantong, China. This village has more than 10 metal wiring plants and elevated levels of Pb were found in soils and blood in children.

Community Engagement Core:
Dr. Yan Zheng, Co-I

a. Community interventions to promote arsenic testing and treatment are being developed based on the results of household surveys and visits in the greater-Augusta, Maine project area and then will be evaluated through an endline survey. Already in collaboration with the RTC, this survey methodology is being expanded into New Jersey, where the NJ Department of Environmental Protection has requested assistance in implementing a similar household well testing and treatment survey in 2014, in the areas of Northern NJ affected by arsenic.

C. Significance:

The CU SRP studies of Arsenic (As) and Manganese (Mn) have contributed to a better understanding of the health consequences of exposure, molecular mechanisms, dose-response relationships, range of impacts, exposure pathways, hydrogeologic environments, and vulnerability of specific populations. Columbia SRP Director and RTC Co-I Dr. Joseph Graziano has successfully chaired the National Research Council (NRC) committee to evaluate critical scientific issues to assess effects from oral exposure to inorganic arsenic. The committee has conducted public workshops to gather a variety of perspectives from key stakeholders and the public. It has submitted its interim report providing recommendations on how to address the critical scientific issues in EPA's Integrated Risk Information System (IRIS) assessment of inorganic arsenic. In the US and Bangladesh, partnerships with government have helped promote effective policies and develop and test remediation strategies. The CEC has also been working closely with local and state agencies in Maine and New Hampshire to encourage testing of private wells by residents. In addition, the RTC has reached out to staff at EPA, ATSDR, NIH, DOE, and state entities concerned with vulnerable populations in proximity to Superfund sites. It has initiated a dialogue among these groups focused on sharing relevant geospatial tools and data. The knowledge and activities generated by our research projects and cores has been guided by and shared with diverse stakeholders.

D. Plans:

We plan on continuing our efforts on all of our aims. However, due to significant cuts in our budget, we most likely will have to continue to scale-back on the extent of our research translation activities. For example, we may also have to scale back on reduce the number of videos to be produced for NJ and other government partnerships. At the same time we have leveraged funds from NJ and taken RTC funds to start working more directly with CEC to carry out a survey in NJ on the impact and perception of groundwater testing in NJ

counties with a high prevalence rate of elevated As groundwaters (As > 5 ppb). Efforts will be made to update the Superfund Footprint Mapper with new NPL sites and with selected 2010 socio-demographic data. Enhancements of the Mapper will be considered in light of continued collaborations with geospatial experts at ATSDR, EPA, and other agencies interested in Superfund sites.

E. Publications from RTC
None

F. Project-Generated Resources:

Stuart Braman and Martin Stute organized a workshop/class on sustainable development that developed videos on arsenic testing for private well owners in New Jersey and edited two previously developed videos to extend them from Hunterdon County to the broader area exposed to naturally-occurring arsenic contamination in Northern New Jersey. The videos are:

Operation: CLEAN WATER, and arsenic awareness video for schoolchildren

What's in your well water? An arsenic awareness video for adults

Testing your well water, a video to help private well owners understand how to go about testing their well water for common contaminants in the area, including arsenic. The videos can be found at: http://njarsenic.superfund.ciesin.columbia.edu/home

Meredith Golden and Tricia Chai-Onn updated the NPL Superfund Footprint: Site, Population, and Environmental Characteristics Mapper. This interactive mapping tool was put into production in 2013 by the CU SRP Research Translation Core. It permits users to visualize critical data about inhabitants and areas near Superfund sites. The Mapper is unique compared to other environmental mapping services. It focuses specifically on NPL Superfund sites and provides key demographic information on communities living within one and four miles of the actual site footprint for most NPL Superfund sites. Golden and Chai-Onn have demonstrated the Mapper at conferences and via webinars to state, local, and federal officials concerned with exposures from Superfund sites. The Mapper will be updated as of March 2014 with the locations of about seventy-five additional NPL Superfund sites that have been finalized since 2010. The CU SRP NPL Superfund Footprint mapper can be accessed at http://superfund.ciesin.columbia.edu/sfmapper.
The locational data for the Superfund sites used in the Mapper have also been made available to the public at no charge: http://sedac.ciesin.columbia.edu/data/collection/superfund