COLUMBIA PRECISION MEDICINE INITIATIVE

PRECISION MEDICINE & SOCIETY

EXPOSOMICS & SOCIETY: BIOLOGICAL, SOCIAL & ETHICAL PERSPECTIVES

FOURTH ANNUAL CONFERENCE

MAY 11, 2022

COLUMBIA | PRECISION MEDICINE

Welcome Letter

Welcome to the fourth annual Precision Medicine & Society Conference at Columbia University. This year's conference is entitled "Exposomics & Society: Biological, Social & Ethical Perspectives." We will explore how environmental factors interact with genomic, epigenetic, and cellular processes in affecting a population's health, which in some cases may have a disproportionate impact on marginalized communities, leading to lifelong health disparities.

The Precision Medicine & Society Program is an integral part of Columbia's Precision Medicine Initiative. This University-wide collaboration was created to support academic discussion and research about the interplay between the biomedical advances of precision medicine and the social sciences, humanities, law, and business. It brings together biomedical and public health researchers, clinicians, and bioethicists working at our Medical Center with social scientists, legal scholars, and humanists in the Faculty of Arts and Sciences, the Law and Business Schools, and Barnard College.

This year's conference will expand beyond genomics to consider the rapidly evolving field of exposomics. We believe that the set of phenomena captured under the rubric of exposomics are best understood by bringing biomedical researchers, specializing in genomics, epigenetics, and cellular processes, together with social scientists and epidemiologists, who have worked closely with affected communities.

We have organized the conference around three thematic sessions that were selected to introduce cutting-edge research that is pertinent to the key concerns of precision medicine and exposomics. The first session explores the ethical and methodological issues that are raised by research on the causes and mechanisms of environmental exposure, especially in vulnerable communities. The second session considers gene-environment interactions in the context of environmental exposures, and how the contributions of genomic vs. environmental factors may be understood. The final session includes scholars who consider how social and physical factors interact in the causation and impact of environmental exposures.

We believe that Columbia University is ideally positioned to lead this conversation, as it was among the first academic institutions to create a program dedicated to precision medicine and society. Our thanks to President Lee C. Bollinger, the Columbia Precision Medicine Initiative, and its director, Tom Maniatis, for supporting the Precision Medicine & Society Program and making possible this fourth annual conference. We are also grateful to Roy Vagelos for his vision and support for precision medicine at Columbia.

Paul S. Appelbaum, MD, Elizabeth K. Dollard Professor of Psychiatry, Medicine and Law
Gil Eyal, PhD, Professor of Sociology
Co-Directors of the Columbia Precision Medicine & Society Program

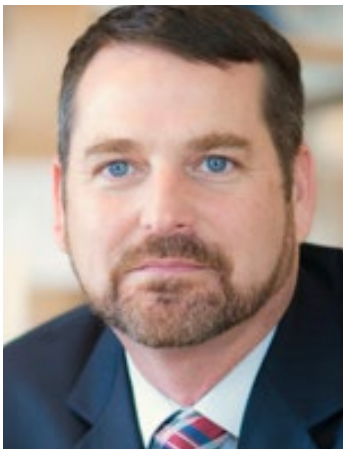
Conference Schedule

EXPOSOMICS & SOCIETY: BIOLOGICAL, SOCIAL & ETHICAL PERSPECTIVES

Columbia University, New York

May 11, 2022

9:00 a.m.	**Opening Remarks by Gil Eyal, PhD**
9:10–10:10 a.m.	**Keynote Speakers** Gary W. Miller, PhD, Columbia University Sarah S. Richardson, PhD, Harvard University
10:20–11:30 a.m.	**Ethical and Methodological Issues** Susan M. Pinney, PhD, FACE, and Jack Rubinstein, MD, University of Cincinnati Phil Brown, PhD, Northeastern University
11:30 a.m.–12:30 p.m.	**Lunch Break**
12:30–2:00 p.m.	**GxE Interactions and Parsing Genomic vs. Environmental Influences** Chirag Patel, PhD, Harvard Medical School Laura Senier, PhD, MPH, Northeastern University Andrea Baccarelli, MD, PhD, Columbia University
2:10–3:20 p.m.	**Social x Physical Interactions** Rosalind Wright, MD, MPH, Mount Sinai Institute for Exposomic Research Robert Wright, MD, MPH, Mount Sinai Institute for Exposomic Research
3:20 p.m.	**Closing Remarks by Paul S. Appelbaum, MD**



Gary W. Miller, PhD

Columbia University

Gary W. Miller serves as Vice Dean for Research Strategy and Innovation and professor of environmental health sciences at the Mailman School of Public Health and professor of molecular pharmacology and therapeutics in the Vagelos College of Physicians and Surgeons at Columbia University. Professor Miller founded the first exposome center in the U.S. and wrote the first book on the topic. He has helped develop high-resolution mass spectrometry methods to provide an omic-scale analysis of the human exposome. He serves as co-director of Columbia's Irving Institute Precision Medicine Resource, which supports integration of exposomics and environmental measures into clinical and translational research projects. He is a member of the NIH All of Us Research Program Advisory Panel, serves on the NIEHS Council, and is the founding editor of the new journal *Exposome,* published by Oxford University Press.

Exposomics: The Environmental Complement to Genomics

ABSTRACT

Advances in high-resolution mass spectrometry have led to an increased ability to measure small molecules in biological samples. Although the field of metabolomics has progressed in its ability to measure endogenous small molecules, little attention has been given to the detection of environmental chemicals and other xenobiotics in human samples using these high-resolution approaches, which we refer to as "exposomics." Several major research initiatives have been established to identify causes of human disease with massive biobanks created. Development of techniques that can provide omic-scale analysis of environmental chemicals in biobanked samples could rapidly increase our understanding of environmental influences of disease. Professor Miller's group is focused on the use of liquid chromatography (LC) and gas chromatography–based high-resolution mass spectrometry to detect a wide range of xenobiotics and their metabolites. His team is working to develop an exposomic analysis framework for human clinical, translational, and population studies, which will allow seamless integration into multi-omic studies of human disease that can be used within large-scale efforts. Professor Miller will share recent results from several ongoing studies and discuss the implications of having access to exposomic-scale data.

Sarah S. Richardson, PhD

Harvard University

Sarah S. Richardson is professor of the history of science and of studies of women, gender, and sexuality at Harvard University and directs the Harvard GenderSci Lab. A historian and philosopher of science, Richardson is a leading scholar of gender and science whose work argues for conceptual rigor and social responsibility in scientific research on sex, gender, sexuality, and reproduction. Richardson serves on the Standing Committees for Degrees in Social Studies and for the Mind, Brain, and Behavior Interfaculty Initiative at Harvard.

Professor Richardson is the author of *The Maternal Imprint: The Contested Science of Maternal-Fetal Effects* and *Sex Itself: The Search for Male and Female in the Human Genome*. She has published two edited volumes, *Revisiting Race in a Genomic Age* and *Postgenomics: Perspectives on Biology after the Genome;* articles in *Signs: Journal of Women in Culture and Society, Studies in History and Philosophy of Science, BioSocieties, the Hastings Report,* and *Biology and Philosophy;* and commentaries in *Nature, Proceedings of the National Academy of Sciences,* and the *Journal of Neuroscience*. Her work has also appeared in popular forums such as *Slate,* the *New York Times,* and the *Boston Globe*.

Professor Richardson's research has been supported by the Wissenschaftskolleg zu Berlin, the Radcliffe Institute for Advanced Study, the American Council of Learned Societies, and the American Association of University Women. She has served on the governing board of the International Association for the History, Philosophy, and Social Studies of Biology and is a member of the editorial boards of *Signs* and *Bulletin of the History of Medicine*.

Categories of Concern, Patterns of Risk: Reduction, Mechanism, and Causal Crypticity in the Biosocial Sciences

ABSTRACT

"Causal crypticity" characterizes the knowledge landscape and knowledge practices endemic to data-rich, 21st-century postgenomic biomedical life science endeavors operating in complex biosocial causal spaces. Cryptic effects are findings of health outcomes in exposed compared to unexposed populations that are small in effect size and that present inconsistently across different study cohorts; moreover, such crypticity in reported outcomes is persistent and unresolved despite expanding volumes of data. Because biosocial sciences such as exposomics record traces of complex, multiply-confounded causal chains, with outcomes frequently occurring at great temporal distance from the hypothesized initial exposure, causal crypticity is and will likely continue to be a persistent feature of this field. Contending with that likelihood demands reflection on strategies for ethical and accountable practices of claims-making in exposomics, in a world in which this science carries powerful implications in arenas ranging from reproductive autonomy to efforts to redress the health implications of racism and intergenerational trauma.

Susan M. Pinney, PhD, FACE, and Jack Rubinstein, MD

University of Cincinnati

Susan M. Pinney is a professor in the Department of Environmental Health in the College of Medicine, University of Cincinnati; the director of the Center for Environmental Genetics; and the Cancer Risk, Control and Prevention program leader for the Cincinnati Cancer Center. She conducts a variety of large molecular epidemiology studies, with research focused on the environmental factors that influence the age of pubertal events such as breast development (and risk of breast cancer later in life), cancer, and other complex diseases. Since 1990, she has been the research director of the Fernald Community Cohort, with data and biospecimens collected over 18 years that have been used in more than 85 research studies. Professor Pinney received her PhD in epidemiology from the University of Cincinnati and her MS from the University of Michigan, Ann Arbor.

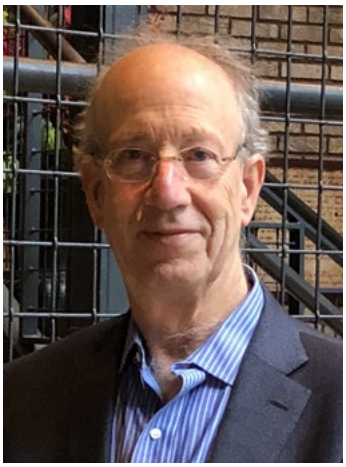
Jack Rubinstein is a board-certified cardiologist at the University of Cincinnati. He was born and raised in Mexico City and completed his residency at Albert Einstein Medical Center in Philadelphia and his fellowship at Michigan State University. He is currently an associate professor of medicine and the associate director of cardiology at the Cincinnati VA Medical Center. He has a translational cardiovascular science laboratory that has been funded by the AHA, NIH, and the VA. He also directs the PSTP and the R38 training programs at the University of Cincinnati. He is the founder of a start-up pharmaceutical company, TRPV Pharmaceuticals; wrote a medical novel titled *The Perfect Dose,* and enjoys playing polo.

Which Population Groups Are Most Susceptible to the Effects of BPA on Cardiac Electrophysiology?

ABSTRACT

This presentation highlights an example in which a precision health approach to investigating the effects of environmental phenols on cardiac electroconductivity led to identifying population strata at heightened risk, so that clinical and public health interventions could be applied. Bisphenol A (BPA) was used extensively around the world in the production of polycarbonate plastics, epoxy resins, and other additives to other plastics and is a known endocrine disruptor. In vitro and in animals, BPA has also been demonstrated to affect cardiac function, primarily through inhibitory effects on key ion channels involved in cardiac electrophysiology. We measured BPA and other phenols in urine of 600 members of a large cohort and used electrocardiogram data obtained the same day to determine if key electrocardiographic parameters were associated with exposure. Heightened susceptibility was observed in those of increased age as it pertained to sinus and atrial node function, as well as QTc prolongation, with specific effects in females as it pertained to sympathetic regulation of heart rate.

No significant susceptibility was observed when BMI was evaluated. These patterns are consistent with the effects observed in vitro and in animal studies and point to the importance of limiting exposure to BPA (even at current, very low levels) and its replacement chemicals in our aging population. Findings such as these can shape information dissemination to clinicians and public health officials, and to the general population as well.



Phil Brown, PhD

Northeastern University

Phil Brown directs the Social Science Environmental Health Research Institute at Northeastern. He is the author of *No Safe Place: Toxic Waste, Leukemia, and Community Action* and *Toxic Exposures: Contested Illnesses and the Environmental Health Movement,* and co-editor of *Social Movements in Health* and *Contested Illnesses: Citizens, Science, and Health Social Movements.* He studies biomonitoring and household exposure and reporting back that data to participants, health social movements, and chemical policy. His work on PFAS—per- and polyfluorinated compounds (https://pfasproject.com/)—examines activism, governance, policy, mapping of contaminated sites and potential exposure locations, water monitoring, immunotoxic effects, and economic costs. He directs the NIEHS T32 training program "Transdisciplinary Training at the Intersection of Environmental Health and Social Science." He co-directs the Community Outreach and Translation Core of Northeastern's Children's Environmental Health Center (CRECE) and is the research translation coordinator and co-director of the Community Engagement Core of Northeastern's Superfund Research Program (PROTECT).

The "Research-Right-to-Know" via Report-Back of Environmental Health Data

ABSTRACT

Exposomics opens up the potential for an exponential increase in data about human health and the social factors underlying a person's health status. There is much promise for the socio-exposome to reduce human exposures to toxics and other detrimental factors. Like all health data, the enormous amount of information generated by these efforts can be used in both positive and negative ways. To accentuate the positive ways and prevent the negative ones, people need to have full awareness of the data collected on them and their communities.

This presentation applies to exposomics and precision medicine the "research-right-to-know" approach developed over the last two decades, in which researchers provide full report-back of environmental health data from biomonitoring and household exposure studies. This report-back process is often tied to community-based participatory research but can be used in other settings as well. It offers information on personal exposures and their relation to various benchmarks and averages, describes the sources and uses of contaminants, and offers both personal and societal exposure-reduction practices. This talk traces two decades of work in this field, in collaboration with colleagues at Silent Spring Institute (Newton, MA), culminating in the Digital Exposure Report-Back Interface (DERBI). It shows how this approach has spread throughout the environmental health community, looks at the ethical and scientific benefits that have been recognized by national health projects and agencies, and shows the individual and social empowerment outcomes for people and communities. This presentation concludes with recommendations for applying the research-right-to-know to exposomics and precision medicine.

Chirag Patel, PhD

Harvard Medical School

Chirag Patel is an associate professor in the Department of Biomedical Informatics at Harvard Medical School. His primary research interests include developing multiscale computational and data science methods to dissect the role of environmental exposures and genetic factors in complex traits and disease, with an emphasis on the trajectory from metabolic disease and its complications. His portfolio is supported by the National Science Foundation and the National Institutes of Health (National Institutes of Environmental Health Sciences, National Institutes on Aging, and National Institutes of Allergy and Infectious Disease). Professor Patel is a leader in exposome science, developing methods to map systems of dietary and environmental exposure factors with disease (as seen in *JAMA,* 2015; *Circulation,* 2012; *Nature Genetics,* 2019; and *Nature Communications,* 2021 and 2022). He is an active researcher in "meta-science," studying the science of science, to make results more robust. He received his PhD in biomedical informatics from Stanford University.

Partitioning Exposome and Genome Interactions with the Tools of Data Science

ABSTRACT

It is hypothesized that genes and environments "interact" or conspire to influence our health. This talk discusses current and new definitions of gene-by-environment interactions, the role of the exposome in elucidating gene-by-environment interactions, new machine learning approaches to extract signal from noise, and challenges to translate genome-by-exposome interactions for the bedside.

Laura Senier, PhD, MPH

Northeastern University

Laura Senier is an associate professor of sociology and health sciences at Northeastern University. Her research interests include the sociology of medicine and public health, community environmental health, and environmental justice. She has studied how political barriers hinder research translation or the effort to migrate scientific discoveries into clinical and public health practice. Her current work explores how access to green and blue spaces affects teens in environmental justice communities. Her work has appeared in *Social Science & Medicine, Sociological Inquiry, Organization & Environment,* and *Environmental Science & Technology.*

The Socio-Exposome: Advancing Exposure Science and Environmental Justice in a Postgenomic Era

ABSTRACT

Environmental scientists coined the term "exposome" with the goal of inventorying and quantifying environmental exposures as precisely as scientists measure genes and gene expression. This talk explains how the notion of the exposome advances gene-environment research and suggests how it could be made even more relevant to public health scholarship and environmental justice activism. To fully realize the potential of research on gene-environment interactions, we need not only more comprehensive data on more and different kinds of environmental exposures and social determinants of health, but also we must be able to characterize the economic conditions and political inequities that allow hazards to continue unchecked. The socio-exposome is a multidimensional framework oriented around three axes: individual, local, and global exposures. This presentation suggests some sociomarkers that could characterize social phenomena at each level and identifies some existing administrative databases that could be leveraged to advance population-level research on gene-environment interactions. The socio-exposome can guide both research and policy, by creating a predictive framework that helps communities understand the repercussions of corporate and regulatory practices for public health and social justice.

Andrea Baccarelli, MD, PhD

Columbia University

Andrea Baccarelli is the Leon Hess Professor and chair of the Department of Environmental Health Sciences at the Columbia University Mailman School of Public Health and director of the NIH/NIEHS P30 Center for Environmental Health in northern Manhattan, one of such 21 centers across the country. His work has supported international best practices for air pollution control developed by multiple agencies worldwide, and his findings have served as the basis for the Environmental Protection Agency's decision to enforce stricter guidelines for human exposure. Dr. Baccarelli's research investigates molecular mechanisms as pathways linking environmental exposures to human disease. Current projects investigate a range of mechanisms, including epigenomics, epitranscriptomics, extracellular vesicles and small noncoding RNAs, mitochondrial DNA, and the microbiome. His research interest lies in the investigation of the effects of environmental exposures to human disease and processes, particularly age-related diseases and environmentally induced age acceleration. Dr. Baccarelli was elected to the National Academy of Medicine for his pioneering work showing that environmental exposures adversely affect the human epigenome and has been included in the Web of Science list of highly cited, world's most influential scientists of the past decade. In addition to his research activities, Dr. Baccarelli has a long history of mentorship and aims to support future leaders in public health.

Precision Environmental Medicine and Society

ABSTRACT

Precision medicine is "an approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person." In practice, however, modern precision medicine primarily emphasizes the genetic underpinnings of disease, while environmental components have received less attention. Accordingly, although we have had success guiding treatment for diseases with genetic-based approaches, integration of environmental components into precision medicine and prevention of disease linked to environmental exposures have lagged far behind. Addressing these gaps is an untapped opportunity, particularly when considering that 70 to 90 percent of human disease is attributable to differences in environmental and lifestyle factors.

Furthermore, harmful environmental exposures disproportionately affect marginalized, disadvantaged groups. Environmental factors that affect human health can be invisible or hard to characterize. Therefore, we need new strategies to better capture environmental exposures, learn how these exposures affect the health of individuals and disadvantaged groups, and move toward more precise and effective disease prevention and intervention. This presentation will discuss recent evidence that demonstrates how epigenetic mechanisms can be used to identify individuals who are impacted by environmental exposures. It will also review examples based on DNA methylation studies and then illustrate emerging research on miRNAs packaged in extracellular vesicles. By integrating the power of big data with epigenetics and environmental health research, precision environmental health offers an unparalleled opportunity to develop new approaches and practices to prevention and treatment based on precise assessments of individual risk for environmentally linked disease.

Rosalind Wright, MD, MPH

Mount Sinai Institute for Exposomic Research

Rosalind Wright is the Horace W. Goldsmith Professor of Life Course Health Research in the Departments of Pediatrics and Environmental Medicine & Public Health at the Icahn School of Medicine at Mount Sinai (ISMMS) Kravis Children's Hospital, dean for translational biomedical sciences, and director of Conduits (the Mount Sinai Health System CTSA). She is a physician and internationally recognized life course epidemiologist with transdisciplinary training in perinatal environmental programming of chronic disease risk. Dr. Wright is also the founding co-director of the Institute for Exposomic Research at the ISMMS. She has led and been a part of pregnancy cohort studies for more than 23 years.

Dr. Wright has a primary interest in early life (prenatal and early childhood) predictors of developmental disorders, including asthma and lung development, sleep, and neurobehavioral development. A particular focus of her research has been on the implementation of studies considering the role of social (e.g., psychosocial stress, trauma, other socioeconomic risk factors); nutritional; and physical (e.g., air pollution, chemical, allergens) environmental factors in explaining health disparities among lower-SES ethnically mixed populations. Her group also has a growing interest in elucidating sex-specific programming effects of environmental toxins. Her research program also explores underlying mechanisms through which chemical and nonchemical stressors program adverse health and development by incorporating biomarkers of physiological pathways (e.g., altered hypothalamic-pituitary-adrenal axis functioning, shifts in maturation of the immune system, disruption of the autonomic nervous system, telomeres, mitochondriomics, epigenetics, and, more recently, extracellular vesicles). Finally, this work examines resiliency factors that mitigate toxic effects of chemical and nonchemical stressors, including enhancing the social/caregiving environment in early childhood and identifying nutritional factors that mitigate risk in pregnant women and young children. This work has been supported by uninterrupted funding from the NIH for more than 23 years.

Disentangling the Complexities of Social and Chemical Factors Contributing to Health Disparities: Moving Toward Exposomics

ABSTRACT

Advancements in the understanding of disparities in health require attention to both physical environmental hazards and social conditions. Moreover, when considered only at the individual level, it remains difficult to fully explain how exposure to health-relevant environmental factors contributes to observed disparities. The role of neighborhood social context in shaping individual exposure, resilience, and vulnerability to a host of harmful health effects has received increasing attention. Health risks and resources appear to be spatially and socially distributed across neighborhoods, with pathogenic risk factors concentrated in poorer, segregated neighborhoods. The increasing understanding of what begets health disparities has moved researchers toward an exposomics framework that considers complex mixtures for both social and chemical determinants.

Robert Wright, MD, MPH

Mount Sinai Institute for Exposomic Research

Robert Wright is the Ethel H. Wise Professor and chair of Environmental Medicine and Public Health at the Icahn School of Medicine at Mount Sinai, director of the Lautenberg Environmental Health Sciences Laboratory, and co-director of the Institute for Exposomic Research. He has a transdisciplinary background in pediatrics, toxicology, genetics, and environmental epidemiology. He has served on numerous national committees and is board certified in medical toxicology. Dr. Wright co-founded the PROGRESS cohort with Dr. Mara Tellez-Rojo in 2006 and the Lautenberg Laboratory of Environmental Health in 2014. He also established the Mount Sinai Institute for Exposomic Research in 2017. As a physician, he is a leading advocate of incorporating exposomics into precision medicine initiatives. He directs the Mount Sinai NIEHS P30 Core Center and an Optional Function in the CTSA program on Exposomics in Precision Medicine and Public Health. His research seeks to link exposomics, genomics, and phenomics with life stage, employing big data methods that address complex problems in human health and disease research.

How and Why to Bring Exposomics to Precision Medicine

ABSTRACT

The exposome is an omic-scale characterization of the environmental drivers of health and disease across the life course. Exposomics is a particularly diverse science that includes state-of-the-art high resolution mass spectrometry that can measure thousands of chemicals in urine, blood, or unconventional biomatrices, such as hair and teeth, as well as computer scientists, geographers, and statistician experts in database mining and big data science. Exposomics applies systems biology, informatics, computation tools, and omic technologies to the methodologies of environmental exposure assessment. Exposomics also epitomizes transdisciplinary translational medicine, as it can delineate new pathways, networks, risk factors, and vulnerable time periods, thereby catalyzing the discovery of novel prevention and treatment strategies.

Research should promote and integrate clinical and translational research in special populations across the life course, e.g., children, the elderly, individuals from disadvantaged ethnic/racial minority groups who bear a disproportionate burden of disease, and most critically regarding precision medicine—*children and adults with chronic diseases*. This discussion focuses on four areas: (a) untargeted chemical assays that can be used for discovery research in precision medicine and prevention; (b) targeted chemical assay panels that inform risks for treatment response or disease prevention; (c) geomedicine research that creates spatial models of disease patterns and environment (temperature, air pollution, green space, etc.) that link to the EMR and patient response to treatment or disease progression; and (d) the need for expert consultation on sample collection/preparation/storage and exposomic assays, as well as expert consultation on geospatial environmental models that can be linked to clinical data from the EMR. All these efforts will enhance exposomic and gene-environment interaction research in precision medicine.