Complex Exposures in Breast Cancer: Unraveling the Role of Environmental Mixtures Virtual Workshop

Trainee Abstracts

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Anna Young, Hormone Receptor Bioactivities of Complex Mixtures of Known and Suspect Chemicals in Silicone Wristband Samplers Worn by Office Workers

People are chronically exposed to complex mixtures of hormone-disrupting chemicals from building materials and consumer products, but traditional laboratory methods typically only measure a small number of known chemicals. Our study sought to advance novel methods that assess our exposures to hundreds of both known and unknown chemicals and that measure the hormone-disrupting potential of those chemical mixtures. For this study, 243 office workers across the U.S.A., U.K., China, and India wore silicone wristbands only during work hours for four days. We then measured extracts of the wristbands for: 1) 99 targeted, semi-volatile organic chemicals, 2) over 1,000 suspect chemical features, and 3) total hormonal bioactivities in three in vitro human hormone receptor activation (CALUX) assays. We found that the chemical mixtures extracted from every wristband sample interfered with at least one of the three hormone receptors: 99% antagonized thyroid hormone receptor (TRb), 96% antagonized androgen receptor (AR), and 58% agonized estrogen receptor (ERa) in human cells. We found strong associations of concurrently increasing chemical concentrations with higher hormonal bioactivities in the wristband extracts, using Bayesian kernel machine regression (BKMR) models separately for subsets of common targeted or suspect chemicals. Certain individual chemicals were identified as strong drivers of the cumulative mixture effects in the BKMR models, including chemicals used for plasticizers, sunscreens, and pesticides, and other tentatively identified chemicals with unknown sources. Our results identify buildings and personal care products as important sources of our exposures to hormone-disrupting chemical mixtures and highlight the prevalence of often unidentified chemicals.

Lauren Koval, Environmental Mixtures and Breast Cancer: Identifying Co-Exposure Patterns Between Understudied vs Breast Cancer-associated Chemicals Using Chemical Inventory Informatics

Although evidence linking environmental chemicals to breast cancer is growing, mixtures-based exposure evaluations are lacking. This study aimed to identify environmental chemicals in use inventories that co-occur and share properties with chemicals that have an association with breast cancer, highlighting exposure combinations that may alter disease risk. The occurrence of chemicals within chemical use categories was characterized using the Chemical and Products Database. Co-exposure patterns were evaluated for chemicals that have an association with breast cancer (BC), no known association (NBC), and understudied chemicals (UC) identified through query of the Silent Spring Institute's Mammary Carcinogens Review Database and the U.S. Environmental Protection Agency's Toxicity Reference Database. UCs were ranked based on structure and physicochemical similarities and co-occurrence patterns with BCs within environmentally relevant exposure sources. A total of 6,793 chemicals had data available for exposure source occurrence analyses. 50 top-ranking UCs spanning five clusters of co-occurring chemicals were prioritized, based on shared properties with co-occurring BCs, including chemicals used in food production and consumer/personal care products, as well as potential endocrine system modulators. Results highlight important co-exposure conditions that are likely prevalent within our everyday environments that warrant further evaluation for possible breast cancer risk.

Jonathan Boss, Group Inverse-Gamma Gamma Shrinkage for Sparse Regression with Applications to Correlated Environmental Exposure Data

Heavy-tailed continuous shrinkage priors, such as the horseshoe prior, are widely used for sparse estimation problems. However, there is limited work extending these priors to regressors with grouping structures. Of particular interest in this talk is regression coefficient estimation in multi-pollutant models where highly collinear chemical groupings are defined by exposure classes. To assuage variance inflation induced by multicollinearity issues, we propose the group inverse-gamma gamma (GIGG) prior, a heavy-tailed prior that can adaptively trade-off between local and group shrinkage. This talk highlights important estimation properties and discusses the differences between GIGG regression and lasso-style penalized regression methods.

Jennifer Ish, Exposure to Carcinogen Industrial Air Emission Mixtures and Breast Cancer Incidence in the United States

Abstract is unavailable.

Che-Jung (Rong) Chang, Personal Care Product Mixtures and Breast Cancer Risk

Abstract is unavailable.

Ángel Mérida-Ortega, Breast Cancer Molecular Subtypes and Supervised Analysis of Urinary Metal Mixtures in Mexican Women

This report develops from a previous work based on a breast cancer study performed in Northern Mexico from 2007 to 2011, that included 498 population-based controls and 497 histologically confirmed cases, with urinary concentrations of ten metals. Information about cases´ hormonal receptors (HR) and epidermal growth factor receptor 2 (HER2) were used to determined breast cancer molecular subtypes as: HR+/HER2-, HER2+ or HR-/HER2-. Through Weighted Quantile Sum Regression, we found two weighted indices of metal mixtures contrastingly associated with molecular subtypes of this tumor. One had tin as the main contributor and showed a positive association with breast cancer, that remained only among HR+/HER2- subtype. The other weighted index was mainly determined by molybdenum followed by vanadium and cobalt. We observed that this second index was negatively related to breast cancer regardless of its molecular subtypes. This work provides evidence of associations between metal mixtures and breast cancer molecular subtypes.