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

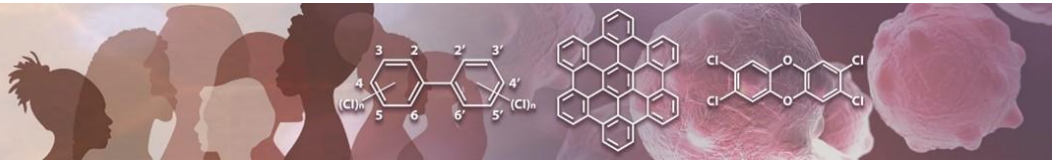
A Virtual Workshop

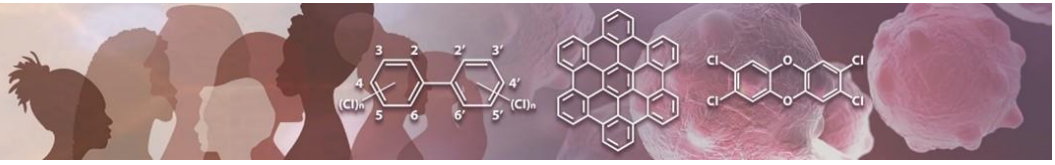
Workshop Report

August 24 – 25, 2022

National Institutes of Health • U.S Department of Health and Human Services

This report was developed by Avanti Corporation in collaboration with NIEHS meeting organizers.





Introduction and Welcome

The National Institute of Environmental Health Sciences (NIEHS) in collaboration with the National Cancer Institute (NCI) hosted a workshop titled "Complex Exposures in Breast Cancer: Unraveling the Role of Environmental Mixtures," August 24 – 25, 2022. This virtual workshop was built on previous NIEHS efforts to understand the health effects of mixtures and bring together experts to discuss the state of the science of environmental chemical mixtures and breast cancer. The workshop goals included:

- Describing the current state of breast cancer research by highlighting cell-based models, animal models, 3-D tissue culture models, epidemiological studies, and approaches for prevention and intervention.
- Determining what research questions and data are needed to improve our understanding of how environmental chemical mixtures influence breast cancer.
- Defining critical research needs and promising approaches for filling data gaps associated with the interaction of environmental chemical mixtures and breast cancer.
- Encouraging complementary publications highlighting the topics described during the workshop.
- Supporting cross-divisional collaboration on the topic of environmental mixtures and breast cancer.

The workshop included six themed sessions and a lighting-talk session to highlight research from trainees. There was also an opportunity for networking and discussion in the form of breakout sessions. Participants were able to select from the following breakout session groups:

- Breakout Group One: Methods for data management and analysis and tools.
- Breakout Group Two: Methods for analysis of biomarkers and *in vitro* or *in vivo* studies.
- Breakout Group Three: Bringing cohort data and health information together.
- Breakout Group Four: Research translation, communication, prevention, and intervention.

Each breakout group was led by two moderators who facilitated group discussion around the following questions:

- What are the challenges associated with your group's topic?
- What do you see as the low-hanging fruit? What can be addressed sooner rather than later?
- Where do we need to place resources on your topic to move research on breast cancer and mixtures forward (i.e., priority setting)?
- What are perceived limitations, and how would overcoming them move the field forward?
- How do we promote translation of research findings (e.g., to other fields of science, to policymakers, to interventions, to move from bench to practice)?
- What are other examples (or good case studies) from other fields that we can use to apply to this topic?
- How can we better integrate experts on basic science, data science, the exposome, and epidemiology to address complex questions?

The four breakout groups reconvened to present their responses and there was an opportunity for further discussion and questions.

Meeting Opening Remarks

Trevor Archer, deputy director for NIEHS, delivered opening remarks. He provided context for the workshop, outlined major workshop goals, and framed the workshop in the context of the NIEHS strategic plan.

Katrina Goddard, director of the Division of Cancer Control and Population Sciences at NCI, welcomed participants by expressing her support for the continued collaboration between NIEHS and NCI on breast cancer and other initiatives. Goddard shared accomplishments of past collaborative research efforts which include community engagement programs, cancer epidemiology cohorts, and a searchable database on cancer cohorts.

Overview of Environmental Mixtures and Breast Cancer
Moderator: Alexandra White

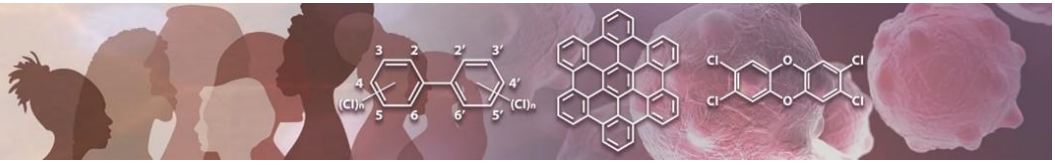
Mhel Kavanaugh-Lynch set the stage for the workshop by discussing primary prevention strategies for breast cancer and the importance of exploring the role of chemical mixtures as exposures. She presented several proof-of-principle studies which demonstrated the impact of chemicals on breast cancer risk. Breast cancer can be considered an environmental disease that can be prevented. There is much geographic heterogeneity in global breast cancer rates and higher income, more industrialized countries have higher incidence. Kavanaugh-Lynch emphasized the need to move beyond our current approach of impacting one individual at a time. The focus should be on informing policy-level decisions that impact the whole of society.

Ruthann Rudel shared her work using toxicology and exposure science to identify and prioritize exposures relevant to breast cancer. She shared findings from her recent publication that sought to identify good candidates for mixture studies by finding chemicals that increase synthesis of estradiol or progesterone. Improving our ability to better detect the chemicals that affect breast development, lactation, and cancer is a priority for prevention. Rudel highlighted the role of experimental studies and risk assessment to inform epidemiological approaches to determine chemicals of interest. By studying toxicology and cancer biology and etiology, we can make chemical inferences about which mixtures are relevant to breast cancer.

Cynthia Rider provided an overview of how toxicology and epidemiology can work synergistically to characterize environmental mixtures. Rider provided considerations for a whole mixture approach and a component-based approach in the context of risk assessment. When deciding which chemicals to include in a cumulative risk assessment, grouping chemicals based on similar mechanisms of action or co-occurrence may not be the most evidence-informed methods. A path forward for encouraging collaboration between epidemiologists and toxicologists would include harmonizing terminology and hosting mixtures-based workshops.

Session One: Setting the Stage for Mixture Exposure Assessment
Moderator: Danielle Carlin

Dale Sandler opened the session by presenting opportunities and challenges in studying environmental contributors to breast cancer in prospective cohort studies. Historically, few cohort studies have used



their resources to study non-lifestyle environmental exposures. Some challenges in studying external exposures include the reliability of self-reported exposure data, the cost of collecting and assaying biological samples, and difficulty in measuring past exposures. Sandler highlighted the Sister Study as an example of a cohort study with extensive data collected across the lifespan. This longitudinal study provided insight into a wide array of risk factors for breast cancer and has helped identify windows of susceptibility. While questionnaires are still a valuable tool for capturing personal and historical exposures, she emphasized that validating this data with Geographic Information System (GIS) and biomarker data will improve its utility. Some considerations for using GIS include the spatial and temporal variability in exposure data and the importance of choosing data sets which are appropriate for the research question.

Tracey Woodruff discussed novel approaches for identifying previously unreported chemical compounds. She presented methods to identify chemicals of importance using biomonitoring and exposure analysis. Echoing comments from previous speakers, Woodruff cautioned against grouping chemicals exclusively by structural similarity or similar mechanisms of action. Developing and investing in chemoinformatics and computational methods to screen large numbers of chemicals can provide solutions for the lack of analytical standards for compounds of interest. Woodruff concluded that the data needed to make breast cancer protective decisions are currently available.

Rena Jones presented her work leveraging geospatially linked data to assess environmental exposures for cancer epidemiology studies. GIS-based data linkage efforts can increase data collection capacity, provide an objective measure of exposure or covariate, and allow for the assessment of multiple exposures at once. Jones provided examples of exposures of interest for breast cancer that are especially well-suited for this approach. Challenges in this area include missing model components, model validation, and the need to reconcile spatial and temporal resolutions.

Session Two: Novel Methods in Analysis of Exposure Mixtures

Moderator: Cynthia Rider

Marianthi-Anna Kioumourtzglou presented an overview of recent advances in methods to evaluate the health effects of environmental mixtures. Several new methods have emerged from the NIEHS program Powering Research Through Innovative Methods for Mixtures in Epidemiology (PRIME), which offers valuable and publicly available informatics tools and training for studying mixtures. Some examples of recent advancements include quantile-based g-computation (qGC) and Bayesian variable selection methods. Kioumourtzglou emphasized the importance of starting with a well-defined research question to identify the appropriate method of data analysis.

Alex Keil provided a detailed look at statistical approaches for leveraging high dimensional data in environmental mixtures health studies. A major challenge in this area is knowing how to analyze data and translate results in a way that is meaningful for health and policy outcomes. Keil discussed how to incorporate machine learning in an interpretable way to identify the most important predictors of an outcome among the variables collected during a study.

Sung Kyun Park shared his work using environmental risk scores (ERS) to integrate the effects of environmental chemical mixtures and exposome. ERS is a predictive risk model as a weighted sum of the pollutant levels from simultaneous assessment of mixtures (i.e., cumulative effects). This presentation focused on estimating the overall effect of a mixture and the magnitude of association as the research

questions of interest. He discussed several tools for statistical approaches to assess chemical mixtures and some examples of their applications.

Session Three: Case studies of Environmental Mixtures in Relation to Cancer Outcomes

Moderator: Curt Dellavalle

Lizbeth López-Carrillo shared her work assessing exposure to multiple chemical-environmental contaminants and breast cancer in Northern Mexico, a region which experiences relatively high rates of breast cancer. She presented results from a population-based case-control study where compounds have been evaluated both individually and as mixtures. More research is needed to assess the response effect of sequential exposure to factors over time and the simultaneous exposure to a subset of factors. Future work should focus on pooling databases and increasing resources to analyze complex data in low- and middle-income countries.

Alexandra White detailed the current evidence supporting the association between outdoor air pollution mixtures and breast cancer risk. White presented data that challenged the conclusion that fine particulate matter (PM2.5) is not consistently associated with breast cancer, including the influence of geographic variability in composition and exposure sources. White shared results and analysis from the Sister Study and the Black Women's Health Study on the heterogeneity of PM2.5 by geographic region. While little is known about the relevant biologic pathways that underly this association, results from the Komen Tissue Bank study suggest that breast tissue characteristics may be a plausible intermediate outcome for breast cancer.

Scarlett Lin Gomez presented her work on the structural and social determinants of health and prostate cancer. She detailed two case studies, including the RESPOND Study, which looked at prostate cancer in African American men and the association with structural racism at a contextual level and an individual level. She also shared results from a latent class analysis to derive social and built environment archetypes. In the context of mixtures, these examples demonstrate modeling approaches to integrate structural and social determinates of health.

Day One Wrap-up

Day one concluded with a discussion led by Kelly Chandler from the Office of Research on Women's Health (ORWH). ORWH is the congressionally mandated focal point for coordinating NIH research on women's health, and they will be leading the next NIH-Wide Strategic Plan for Research on the Health of Women. Participants were asked to identify priority areas of research:

- Prioritizing fragrances, plastics and microplastics, and nanomaterials as exposures.
- Working across disciplines using a team-based science approach.
- Developing methods to evaluate exposures during windows of susceptibility.
- Addressing latency issues between exposure and development of breast cancer.
- Messaging to enlist public support.
- Developing a geospatial risk unit, like the Exposure Risk Unit.

Day Two Introduction

Linda Birnbaum, scientist emeritus and former director of the National Toxicology Program and NIEHS, and scholar in residence at Duke University, provided opening remarks on day two. She welcomed participants and presented a summary of the key messages from day one sessions:

- Worldwide, breast cancer is common, and there is much spatial and temporal variability.
- Breast cancer research requires multidisciplinary and transdisciplinary collaborations.
- Environmental data can come from many sources including questionnaires, external and internal exposures, biomarkers of exposure and response, and 'omics approaches.
- Data needs include developing new methods to analyze big data, applying statistical methods for mixtures, and sharing data across research studies.
- The best solutions involve policy-level changes that impact a wider population.

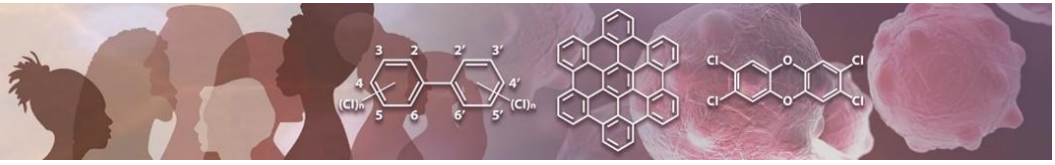
Session Four: Novel Methodologies to Understand the Mechanisms of Breast Cancer

Moderator: Tram Kim Lam

Melissa Troester shared her work studying health equity in breast cancer outcomes using a "cells-to-society" model to explore the difference in breast cancer recurrence rates among white and Black women. She presented findings from her work on the Carolina Breast Cancer study, a population-based sampling of women who developed invasive breast cancer. Troester discussed the complex environmental patterns associated with race which are often compounded by unequal access to health care. She highlighted the importance of recognizing that incidence data are impacted by social factors, likely because of how they are ascertained. The major challenges moving forward to address the role of environment in breast cancer etiology will be to improve data integration and expand the types of data being collected.

Matt Lockett presented his work using 3D tissue- and tumor-like structures in cell cultures to better represent the in vivo environment. Spheroids, organoids, and organ-on-chip devices all represent advances in the 3D environment which can be more representative of physiological phenotypes/ genotypic expression compared to 2D models and single cell type cultures. Tissue type is an important consideration for an extracellular matrix. Lockett also presented results of PFAS exposure in a 3D breast tumor model to characterize the importance of exposure time, oxygen tensions, and tissue type.

Sue Fenton provided an overview of the current state of knowledge for testing chemical mixtures in rodent models. Fenton also discussed the limitations of these current approaches and provided suggestions for making them more human relevant. Breast development and functional assessment are two major areas where traditional test guideline studies fall short. Fit-for-purpose or non-guideline toxicity studies may pave the way for actionable data to address specific issues of public health concern. Focus on early-life markers is especially important for advancing the field of environmental toxicology, especially in the context of exposure to mixtures.



Session Five: Big Data Science Approaches and Challenges
Moderator: Abee Boyles

Doug Walker presented his work establishing a high-resolution mass spectrometry (HRMS) framework for the creation of a cumulative exposome-disease atlas. This work seeks to complement genomic studies with an understanding of how complex mixtures of environmental exposures influence human health. Walker presented three key challenges in the effort to optimize nontargeted HRMS as a cumulative resource for exposure-disease relationships. He emphasized that despite these challenges, the resources and technology base are available to begin the Human Exposome Project.

Julia Rager presented data science approaches to better understand drivers of human disease within the expanding exposome. She detailed three case studies which featured targeted analysis, non-targeted analysis, or chemical database analysis to measure the chemical exposome. The inTelligence and Machine lEarning (TAME) Toolkit is a publicly available tool which can provide data science training to address mixtures. The next steps in this work are to develop a more efficient translation between different layers of 'omic profiling so that data can be integrated in a meaningful way.

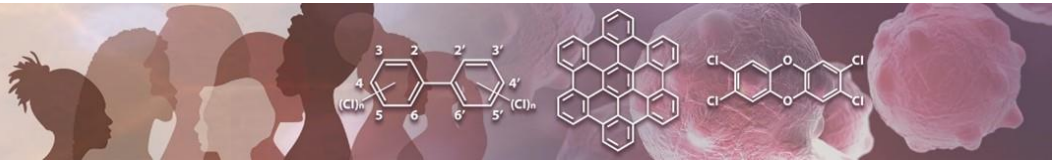
Heather Stapleton shared her work using silicone wristbands to monitor personal exposure to environmental mixtures and how these devices compare to blood and urine analyses. Research has shown that wristband measurements correlate with internal dose, and in one study, wristbands predicted better measures of total mass excreted when compared to spot urine measurements. Stapleton shared examples from a case study on bladder cancer in dogs using silicone tags. Samples were analyzed using both targeted and non-targeted approaches. While silicone samplers do not capture diet or metal exposures, they can serve as affordable, noninvasive tools to support exposomic research.

Trainee Lightning Talks
Moderator: Danielle Carlin

Anna Young presented findings from her work using silicone wristbands to assess exposure to known and unknown chemicals in a cohort of office workers. She also characterized the total hormonal activities of the detected mixtures. The Bayesian kernel machine regression (BKMR) models identified several important known and suspect chemicals which were individual drivers of the mixture effect. Her results demonstrated the prevalence of usually unknown mixtures of chemicals in the environment.

Lauren Koval shared her work using chemical inventory informatics to identify co-exposure patterns between understudied chemicals associated with breast cancer. Her analysis focused on mixtures found in household environments. Using chemical database analysis, she identified 50 priority, but untested, chemicals that co-occur with breast cancer and share structural and physiochemical properties.

Jonathan Boss provided an overview of group inverse-gamma gamma (GIGG) regression as a regularization method for improving estimation of regression coefficients for correlating environmental exposure data. This analysis is necessary when considering the multicollinearity issues in multipollutant models where highly collinear exposures result in unstable regression coefficient estimates and wide confidence intervals. Boss also highlighted the differences between GIGG regression and lasso-style penalized regression methods as two approaches to regularization.



Jennifer Ish shared her work assessing how exposure to multiple correlated carcinogens in mixtures from industrial air emissions may act together to influence breast cancer risk. Ish integrated spatial and temporal data from the Sister Study and the U.S. EPA Toxics Release Inventory to create an exposure continuum map. The next steps in this effort are to refine exposure mixture classification and elucidate mixtures relevant to breast cancer.

Che-Jung (Rong) Chang provided results, using data from the Sister Study, to investigate the joint effect of exposure to personal care product mixtures on breast cancer occurrence. Results showed a positive association between beauty and nail product mixtures, and incidence of postmenopausal breast cancer, as well as inverse associations between skincare product mixtures and incidence of breast cancer. Future work will seek to elucidate a potential third factor correlated with both exposure and outcome.

Ángel Mérida-Ortega presented his work characterizing the association between breast cancer molecular subtypes and exposure to metal mixtures in Mexican women. The positive mixture, characterized by tin, was only associated with one molecular subtype, whereas the negative mixture, characterized by molybdenum, cobalt, and vanadium, was associated with all three subtypes.

Breakout Groups

Breakout Group One: Methods for Data Management and Analysis and Tools

Moderators: Alison Motsinger-Reif and Marianthi-Anna Kioumourtzglou

What are the challenges associated with your group's topic?

- Producing enough understandable and organizable metadata.
- Integrating statistical methods that allow researchers to combine limits of detection issues and flexible modelling.

What do you see as the low-hanging fruit? What can be addressed sooner rather than later?

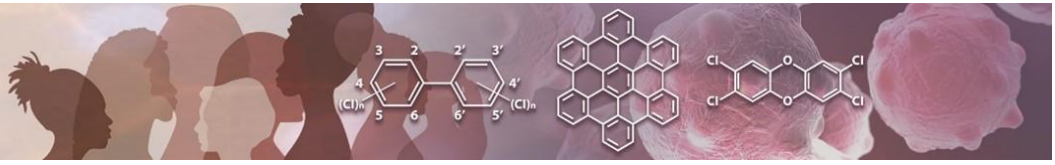
- Standardizing processes across groups/labs, especially for structure data.
- Integrating data science, research software engineering and other disciplines with researchers in the field.
- Training scientists with tools to efficiently generate, collect, and manage data from its inception.

Where do we need to place resources on your topic to move research on breast cancer and mixtures forward (i.e., priority setting)?

- Ensuring that data are securely saved and stored when collecting and managing untargeted exposomic data, such that when annotation tools improve, researchers can go back easily and annotate the data.
- Developing standards across labs to combine data.
- Investing resources to train more biostatisticians to develop integrated methods and manage environmental mixtures in health studies.

What are the perceived limitations, that if alleviated, would move the field forward?

- Training was repeatedly emphasized.
- Recruiting experts on environmental statistics, data science, and related fields to work closely with breast cancer researchers in the development of methods and approaches for our studies.



How do we promote translation of research findings (e.g., to other fields of science, to policy makers, to interventions, to move from bench to practice)?

- Identifying actionable goals and then designing and conducting collaborative studies with that goal in mind.
- Adopting terminology and language that regulators currently use.

What are other examples (or good case studies) from other fields that we can use to apply to this field/topic?

- The field of genomics has developed centralized approaches to translate findings into clinical education.
- Removal of lead in paint and gas are examples of successes.
- Nutritional epidemiology studies that evaluate multiple nutrients at once.

How should we better integrate experts on basic science, data science, exposome, and epidemiology to address complex questions?

- Understanding and rewarding shared and interdisciplinary science through trainees and promotion.
- Implementing exchange programs which enable researchers to learn a new skill, method and/or tool and then bring that experience and knowledge back to their institutions (e.g., K.C. Donnelly Externship awards).
- Having academic department chairs coalesce research faculty from these different disciplines together around a central problem.

Breakout Group Two: Methods for Analysis of Biomarkers and in vitro/in vivo Studies

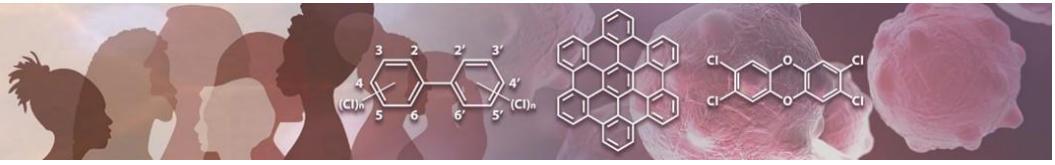
Moderators: Sue Fenton and Heather Stapleton

What are the challenges associated with your group's topic?

- Identifying unknown chemical features using HRMS.
- Screening and characterizing active chemicals in complex mixtures in in vitro methods.
- Developing universal methods for the collection and histopathological evaluation of mammary glands in all test guidelines with prenatal exposures.
- Developing new methods/models to reflect the breast cancer types/subtypes – particularly triple-negative breast cancer (TNBC).
- Developing methods to test different hallmarks of cancer.
- Identifying early biomarkers of carcinogenesis/breast cancer development (move away from two-year studies) and lipophilic chemicals that accumulate in breast tissue.

What do you see as the low hanging fruit? What can be addressed sooner rather than later?

- Modifying toxicity test guidelines to require evaluation of mammary tissue.
- Identifying stored samples from cohorts with breast cancer outcomes.
- Collecting more data for benchmarking hormonal activities measured in complex mixtures.
- Using well characterized carcinogens to examine cell signaling or earlier markers of change before tumor formation and identify "early markers of effect."



- Developing new methods to measure aromatase activity in breast tissues in rodent models and humans (and for other cytochrome P450 enzymes).
- Screening potential carcinogens through the 10 key characteristics of carcinogens, using assays developed for each step, and determining which assays are most sensitive and specific.

Where do we need to place resources on your topic to move research on breast cancer and mixtures forward (i.e., priority setting)?

- Developing a cancer atlas of metabolites/metabolomics.
- Developing a training mixture or a defined mixture that can be shared among researchers.
- Implementing the use of diagnostic tools, particularly for small animals. This would aid in detection of small/early tumors and to detect progression.
- Adding on prospective measures of exposure to environmental mixtures in cohort students, using wearable samples such as the Sister Study.

What are the perceived limitations, that if alleviated, would move the field forward?

- Pursuing data and method harmonization.
- Overcoming some model limitations.
- Identifying mixtures to prioritize for testing.
- Generating toxicokinetic information in a dose-response manner for carcinogens.
- Testing mixtures that may be region specific.
- Developing shorter term models to test individual chemicals and mixtures to evaluate interactions.

How do we promote translation of research findings (e.g., to other fields of science, to policy makers, to interventions, to move from bench to practice)?

- Building databases that can be shared with researchers/programs that build on regional exposures.
- Encouraging more communication/sharing of data/findings between epidemiologists and bench scientists.
- Pooling worldwide data on exposures and cancer subtypes and harmonizing approaches.
- Educating medical students and physicians about environmental exposures.

What are other examples (or good case studies) from other fields that we can use to apply to this field/topic?

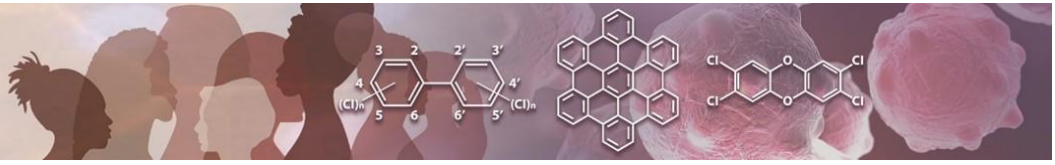
- Bladder cancer and early colorectal cancer.
- The Europe-based FREIA project – Female Reproductive toxicity of EDCs: a human evidence-based screening and Identification Approach – evaluated mixtures and cancer endpoints.
- Obesity studies (i.e., identification of obesogens).

How should we better integrate experts on basic science, data science, exposome, and epidemiology to address complex questions?

- Hosting workshops and encouraging team science between groups that have the right expertise.

Breakout Group Three: Bringing Cohorts and their Data/Health Point Information Together

Moderators: Alexandra White and Mary Beth Terry



What are the challenges associated with your group's topic?

- Obtaining resources and buy-in from funding agencies – overall for research and specifically for data pooling.
- Promoting harmonization of exposures – types of exposures (biomarkers, GIS-based exposures).
- Collecting the "right" samples and banking them for the future.
- Using existing stored biologic samples versus investing in new cohorts.
- Conducting studies focused on repeated measures, early life/windows of susceptibility, and timing of exposures.

What do you see as the low hanging fruit? What can be addressed sooner rather than later?

- Forming concrete questions with integration of medical record data.
- Using existing data resources and stored samples for new analyses.
- Following up with previously studied birth or pregnancy cohorts.
- Recruiting for greater racial and ethnic diversity in cohorts.

Where do we need to place resources on your topic to move research on breast cancer and mixtures forward (i.e., priority setting)?

- Investing in on-going cohorts and preserving existing cohorts to harmonize data.
- Diversifying cohorts and increasing representation.
- Developing untargeted assays to identify new chemicals of interest.
- Improving existing databases through partnerships with data scientists.

What are the perceived limitations, that if alleviated, would move the field forward?

- Providing resources towards harmonization efforts.
- Developing methods to address big data mixtures.
- Acquiring clear lines of evidence for action/policy.

How do we promote translation of research findings (e.g., to other fields of science, to policy makers, to interventions, to move from bench to practice)?

- Investing in education for high school and college educators by developing public curriculum, social media, and citizen scientist programs in the area of mixtures research.
- Bringing policy makers, advocacy organizations and researchers to the discussion table.
- Designing research studies intentionally so that the results will be informative for public health and impact policy-level decisions.

What are other examples (or good case studies) from other fields that we can use to apply to this field/topic?

- Evaluating linkages between the Flint, Michigan, lead crisis and medical record data.
- The drop in breast cancer incidence rates following decreased use of hormone replacement therapy.
- Pooling of questionnaire-based exposure assessments.
- Occupational exposure studies such as female firefighters or nail salon workers.

How should we better integrate experts on basic science, data science, exposome, and epidemiology to address complex questions?

- Hosting workshop and conferences, foster team science, and build interdisciplinary teams of trainees.
- Integrating health behavior and public health practice and partnering with community organizations.
- Communicating directly with GIS/data scientists.
- Contributing to the development of state cancer plans.

Breakout Group Four: Research Translation, Communication, and Prevention/Intervention

Moderators: Abee Boyles and Julia Brody

What are the challenges associated with your group's topic?

- Communicating findings without frightening the public and making it clear that scientific research does not provide yes/no answers.
- Including positive behavior messaging to improve communication.
- Recognizing that research translation regarding environmental factors that are out of personal control requires policy solutions.
- Advising concerned/motivated companies on environmentally safe practices to reduce chemical exposures from their products, with an emphasis on packaging.

What do you see as the low hanging fruit? What can be addressed sooner rather than later?

- Reporting back to study participants – the benefits are greater than the risks.
- Including a mixtures risk assessment factor as conducted by European risk assessors when going from hazard identification to risk estimate.
- Targeting susceptible populations for interventions and prevention messaging.
- Further disseminating existing education materials and informing the public of the choices they can make to reduce certain types of chemical exposures.

Where do we need to place resources on your topic to move research on breast cancer and mixtures forward (i.e., priority setting)?

- Developing resources for clinicians to include chemical mixtures as part of conversation/risk determination.
- Including risk prevention messaging in culturally appropriate ways from trusted messengers – use language that is understandable to a lay audience.
- Rebuilding trust with communities that has been lost from prior extractive research practices.
- Broadening outreach to include new media to reach younger audiences.
- Evaluating combinations of the few known human breast carcinogens listed by the Report on Carcinogens (RoC) and the International Agency for Research on Cancer (IARC).

What are the perceived limitations, that if alleviated, would move the field forward?

- Developing environmental health literacy tools for public health communication that can reach a broader audience.
- Leveraging marketing experience to reach different audiences.

How do we promote translation of research findings (e.g., to other fields of science, to policy makers, to interventions, to move from bench to practice)?

- Improving training for health care providers.
- Applying a "research-based advice" model such as the one used in Denmark to synthesize research and inform the policy makers.
- Incorporating mixtures into risk assessment methods used by policymakers.

What are other examples (or good case studies) from other fields that we can use to apply to this field/topic?

- Tobacco smoke as a mixture with public health intervention on the personal and policy level.
- Occupational exposures (e.g., IARC just evaluated firefighting).
- Regulation of bisphenol A (BPA) as a case study of success for a single chemical.

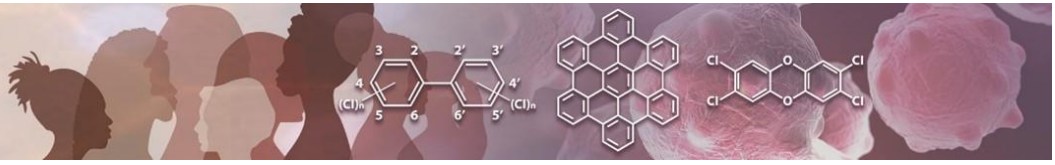
How should we better integrate experts on basic science, data science, exposome, and epidemiology to address complex questions?

- Acknowledging that the community has valuable expertise that should be considered (e.g., Breast Cancer and the Environment Research Program (BCERP) study participants developed communication material for their peers).
- Packaging scientific findings in a way that is easier for journalists, bloggers, and influencers to utilize in the face of the current challenging journalistic arena (i.e., developing relationships with journalists can help facilitate the process).
- Leveraging existing translational centers and their data visualization tools.
- Leveraging history of activities in the breast cancer community.

Session Six: Next steps: Health Disparities, Policy, and Prevention
Moderator: Brittany Trottier

Justin Colacino opened the session by discussing the role of environmental mixtures in breast cancer disparities by focusing on the development of specific breast cancer subtypes and survival outcomes. Disproportionate environmental exposure and environmental justice are important areas to target for health equity and breast cancer prevention. Colacino presented data to show that basal-like breast cancer represents one of the most substantial disparities in health outcomes for African American women. Some causes of breast cancer disparity include ancestry associated genes, access to health lifestyles and care, and systemic racism and social inequality. Colacino emphasized that peoples' zip codes inform their health outcomes more than their genetic codes. One effort to understand the patterns of exposure disparity in American women includes leveraging datasets in the National Health and Nutrition Examination Survey (NHANES). Important next steps in this area of research include quantifying mixtures in diverse populations, generating good life course breast cancer molecular epidemiology, and improving in vitro, in vivo, and in silico modeling technologies.

Sofie Christiansen presented ongoing work in Europe to translate research efforts to policy decisions. This talk focused first on the Organization for Economic Co-operation and Development (OECD) guidelines for testing of chemicals. Christiansen reiterated the critical need to evaluate chemical impact on developing mammary gland, a recurring theme throughout the workshop. The mammary gland whole mount-method is optimal for such assessment and should be included in OECD test guidelines. The FREIA project represents a novel research team, established and funded to assess endocrine



disrupting chemical effects on female reproductive toxicity. Christiansen closed by sharing her new report on risk assessment of endocrine disruptors in products for pregnant women and children.

Vince Cogliano presented methods to identify communities burdened by environmental health disparities. This talk featured a tool called CalEnviroScreen, which was developed by the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment. CalEnviroScreen is a mapping tool to identify communities with disproportionate environmental exposure burdens across California communities. The tool includes 21 indicators including pollution burden and pollution characteristics to look at the combined exposures and map the risks. There is more work to be done to understand the mechanisms of factors that have been identified to modify breast cancer risk.

Workshop Wrap-up

Alexandra White closed the workshop by thanking participants, moderators, and organizers for their efforts in facilitating this workshop.