Title: Use of non-targeted metabolomics to identify chemical exposures that affect metabolic processes
Category: Chemical Environment in Breast Cancer

Abstract:
A limitation of current biomonitoring for environmental chemicals is that targeted analytic methods require a priori selection of compounds to study. As a result, significant time and resources are expended to develop methods for chemicals that may or may not be present in biological specimens, and important exposures may be missed if not anticipated. One way to circumvent this issue is to perform non-targeted analysis of biospecimens using high-resolution mass spectrometry to measure environmental exposures (chemical exposome) and to assess which chemicals are associated with biological changes (metabolome).

In the Women Firefighter Biomonitoring Collaborative study, we conducted non-targeted analysis of serum samples using liquid chromatography and quadrupole time-of-flight mass spectrometry (LC-QTOF/MS) to identify exposures for potential breast carcinogens among women firefighters and office workers. By matching compounds against an in-house library of 720 environmental chemicals, we detected 620 chemicals that matched 300 different molecular formulas, including phthalates metabolites, phosphate flame retardants (PFR) metabolites, phenols, pesticides, nitro and nitroso compounds and perfluorinated alkyls substances (PFAS). We also identified more than 90 endogenous molecules in serum samples by matching detected peaks against public mass spectral libraries.

Partial correlations analysis of chemical exposures and the metabolome revealed many direct associations between environmental chemicals and endogenous molecules. For example, we observed direct associations between perfluorohexanesulfonic acid (PFHxS) and 4-hydroxyphenone and bile acids, and perfluoroctane sulfonic acid (PFOS) and inflammatory signaling molecules. Several exposure-metabolite associations were further confirmed using NHANES. For example, exposure to PFOS was associated with a significant increase in serum C-reactive protein and lymphocyte count in women 20-80 years of age, after adjusting for age, race/ethnicity, socioeconomic status and body mass index, suggesting that PFOS may affect inflammation and immunity in women. Non-targeted metabolomics analysis is effective in revealing environmental exposures associated with metabolic changes.