ABSTRACT

Per- and polyfluoroalkyl substances (PFASs) are persistent organic contaminants that are widespread in human blood worldwide. At least 98% of people in the United States are estimated to have detectable levels of PFASs in their blood. While a subset of highly persistent perfluoroalkyl acids (PFAAs) have been studied extensively, there are thousands of other PFASs in our environment that have not been studied in detail with respect to major sources of exposure, toxicokinetics, or toxic effects. A significant portion of the total PFAS content in human blood appears to be comprised of compounds with unknown structures. Women appear to have a greater portion of unidentified PFAS in their blood compared to men, suggesting that products marketed towards women (e.g., cosmetics) may be a significant source of novel PFAS exposure. Uncovering the identities of these unidentified PFASs is crucial to closing the mass balance on PFAS in human blood and gaining a comprehensive understanding of human exposure to PFASs, and potential health risks associated with PFAS exposure. The majority of these unknown compounds are "pre-PFAAs," a sub-class of PFASs widely used in consumer products. Pre-PFAAs can be transformed into PFAAs as well as other intermediate transformation products due to environmental and biological processes. **The over-arching objective of this seed grant proposal is to identify pre-PFAAs that are prevalent in consumer products that are marketed towards women, and assess their metabolic transformation and toxicity in the liver, a major target organ for PFAS toxicity**. We will accomplish this by [1] screening commercially-available cosmetics for known and novel PFASs as well as total pre-PFAA content using a combination of high-resolution mass spectrometry and total oxidizable precursor assay, [2] tracking the transformation of pre-PFAA mixtures isolated from these cosmetics via incubation with liver sub-cellular fractions, and [3] measuring the toxicity (DNA damage and disruption of mitochondrial functions) in liver cells dosed with pre-PFAAs and their transformation products. Expected outcomes include identification of predominant pre-PFAAs in several cosmetics products, and insights into the mechanisms by which these pre-PFAAs may be transformed in the human body and elicit toxic effects. This project is an exciting multidisciplinary effort that will offer valuable training in environmental health engineering research for a graduate student. **The project will generate compelling data for an R01 proposal that the team plans to submit in June 2022**.