**Mechanisms of uptake and negative health effects of per and polyfluorinated alkyl substance**

Judith R. Cristobal, Logan Running, Michelle Camdzic, Diana S. Aga, G. Ekin Atilla-Gokcumen

Per- and polyfluorinated alkyl substances (PFAS) are a class of widely used compounds in various commercial and industrial applications. Due to their extensive use and chemical stability, PFAS persist in the environment and bioaccumulate in humans and wildlife. PFAS exposure has been linked to several diseases and pathologies, including the formation of various cancers, disruption of the endocrine system, and obesity. PFAS can cross the blood-brain barrier, bioaccumulate the brain, and exert neurotoxic effects; however, the mechanisms of how they bioaccumulate in the brain and the mechanism of their neurotoxicity are unknown. We will discuss the interactions of different classes of PFAS with biomolecules, with a focus on lipids and lipid-related proteins, using in vitro cell line-based models and differentiated neuronal cells. Specifically, we have recently shown the interactions of PFAS and cellular transport proteins and demonstrated that these interactions vary depending on the precise chemical structures of PFAS. We have also shown that exposure of neuronal cells to PFAS results in significant changes in the cellular lipidome, indicating that PFAS might perturb lipid homeostasis in cells. Integration of lipidomics results with gene expression analysis revealed potential biological pathways that might be impacted by PFAS exposure. Overall, our results provide insights into the cellular interaction of PFAS and pave the way for the prioritization of biological pathways that cause adverse health effects of PFAS.