Per- and polyfluoroalkyl substances (PFAS) and their effects on gut microbiota

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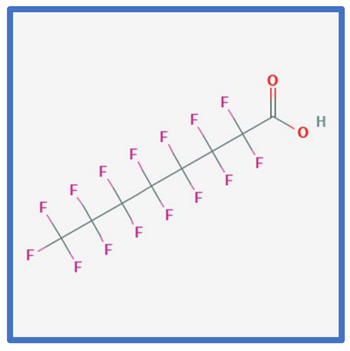

Figure 3. PFOS chemical structure

Executive Summary:

Per- and polyfluoroalkyl substances (PFAS) are man-made contaminants and found throughout our environment. They have been manufactured for almost a century and are used in a variety of commercial and household products. These chemicals are bio-accumulative and have an estimated half-life between 1 and 4 years in the human body and may also cause adverse health outcomes as well as alterations to the gut microbiome.

Problem Statement:

Studies within the last decade have found increasing links between PFAS exposure and developmental problems, liver diseases, kidney problems, and cancer but the mechanisms remain unknown. PFAS have also been found to affect the gut microbiome which may cause the health effects also associated with PFAS exposure. The goal of this study was to determine if current research showed that PFAS exposure altered the gut microbiome.

Background:

PFAS do not naturally occur in the environment and are man-made chemicals that are used in commercial as well as residential environments. There are over 4,700 known PFAS including PFOS, PFOA, and OBS. They do not break down in the environment. Exposure routes of PFAS include ingestion, inhalation, and absorption. The EPA recommends 70ng/L of PFAS in drinking water but there is no federal guideline level. However, Michigan required PFAS levels to be 8ng/L for PFOA and 16ng/L for PFOS. PFAS exposure has also been linked to health problems such as liver disease, cancer, and effects on the gut microbiome. The gut microbiome is the collection of bacteria found in the gastrointestinal system of organisms. It plays an integral role in the metabolism of dietary compounds and foreign substances. One measure of the health of the gut microbiome is diversity.

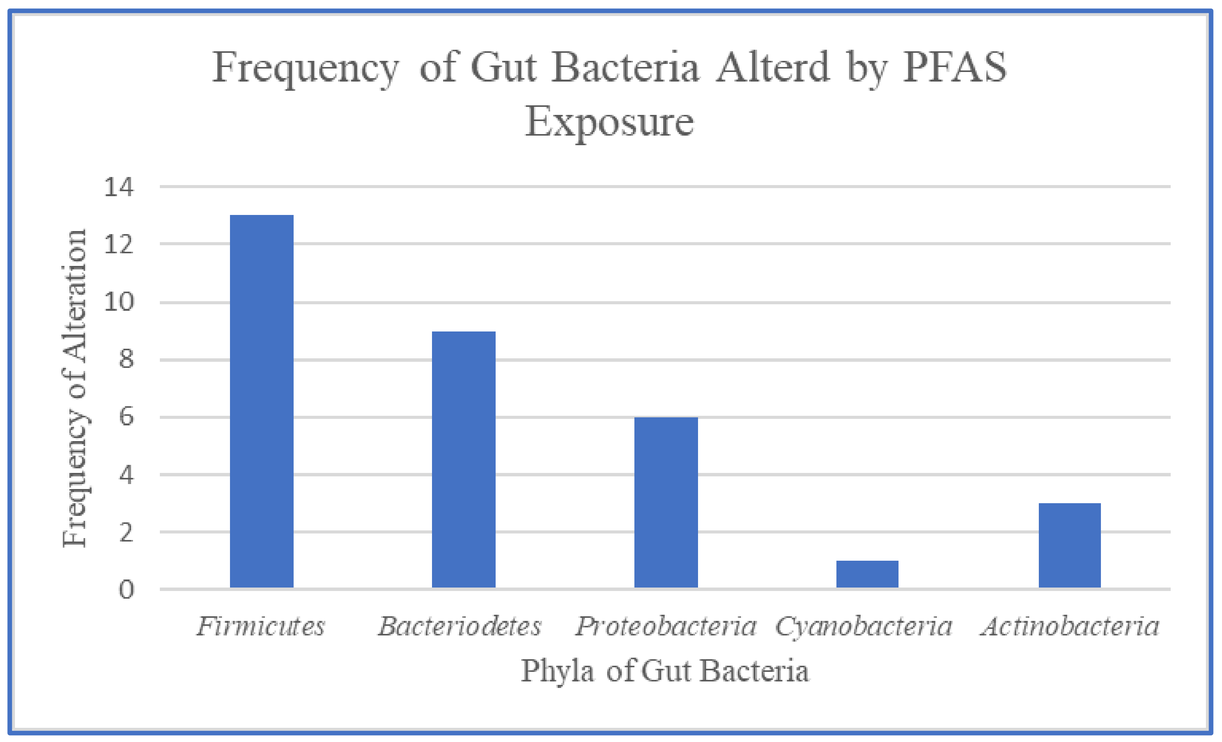

Figure 2. Frequency of alteration to gut bacteria after exposure to PFAS.

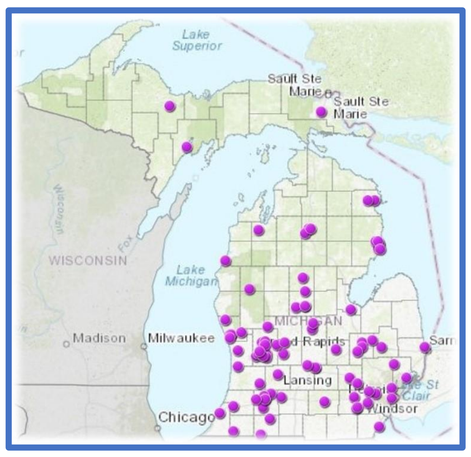

Figure 1. PFAS contamination sites in Michigan according to Michigan Department of Environment, Great Lakes, and Energy.

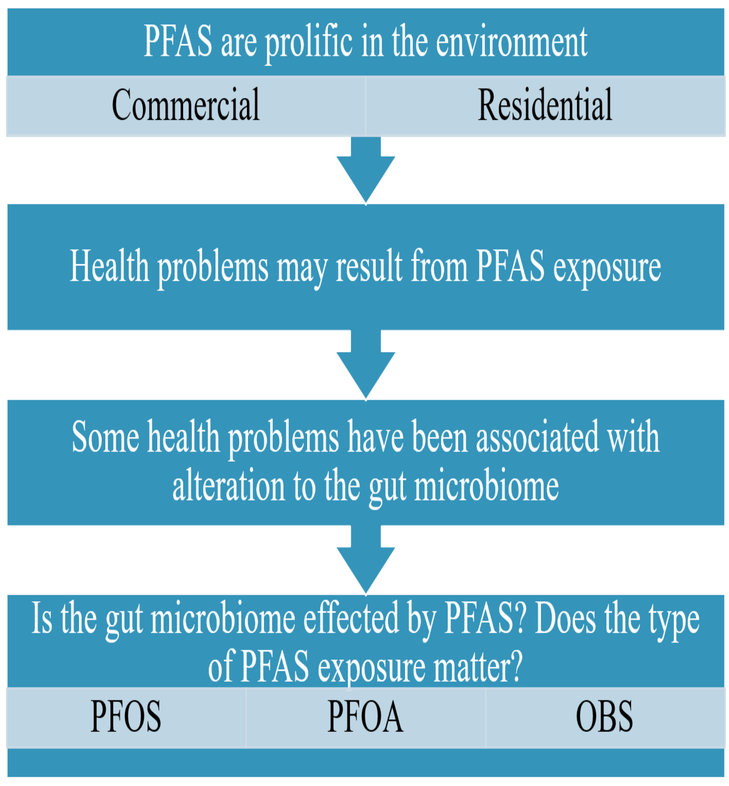

Figure 4. Flowchart of research plan.

Table 1. Varying concentrations of PFAS chemicals (PFOS, PFOA, and OBS) and gut bacteria affected organized by phyla.

Species	Type of PFAS exposed to	Concentration	Gut bacteria affected (by Phyla)
Human	PFOS	Max: 370.63 ng/L Min: 158.05 ng/L Max: 182.55 ng/L	*Firmicutes*
Human	PFOA	Min: 2.19 ng/L	*Firmicutes*
Mouse	PFOS	3 µg/g	*Bacteroidetes, Firmicutes*
Mouse	PFOS	0.3 µg/g	*Bacteroidetes, Cyanobacteria, Firmicutes, Proteobacteria*
Mouse	PFOS	5 µg/g	*Bacteroidetes, Firmicutes*
Mouse	PFOS	25 µg/g	*Bacteroidetes, Firmicutes*
Mouse	PFOS	50 µg/g	*Bacteroidetes, Firmicutes*
Mouse	PFOS	2 mg/kg	*Firmicutes*
Zebrafish	OBS	3 µg/L	*Actinobacteria*
Zebrafish	OBS	30 µg/L	*Actinobacteria, Proteobacteria*
Zebrafish	OBS	300 µg/L	*Actinobacteria, Bacteroidetes, Proteobacteria, Verrucomicrobia*
Mouse	PFOS	5 mg/kg	55 common species (phylum not specified in the article)
Mouse	PFOS	0.3 µg/g	*Bacteroidetes, Firmicutes, Proteobacteria*
Mouse	PFOS	3 µg/g	*Bacteroidetes, Firmicutes, Proteobacteria*
Mouse	PFOS	30 µg/g	*Bacteroidetes, Firmicutes, Proteobacteria*

Approach:

An in depth literature review was conducted using the PubMed database and Google Scholar. The type of literature identified were studies that had experimented to see what effect different PFAS had on the gut microbiome. Many of the known forms of PFAS were searched for including: PFOS, PFOA, OBS, and PFAS in general. Studies were selected because they talked about the potential links between PFAS exposure and resulting effects on the gut microbiome.

Outputs & Outcomes:

Bacteria in the phyla *Bacteroidetes*, *Firmicutes*, *Proteobacteria*, and *Verrucomicrobia* decreased in mice, zebrafish, and humans after PFAS exposure. The typical levels of PFAS found in human blood plasma is 2100-6300 ng/L. These studies used concentrations varying between 0.3µg/g of body weight and 370.63 ng/L. There is no definitive evidence linking PFAS exposure directly to pathology, however, alteration of the gut microbiome may lead to increased risk of disease. The bacterium *Bacteroides vulgatus*, which is in the phyla *Bacteroidetes*, is inhibited in the progression of liver disease. Bacteria in the phyla *Bacteroidetes*, *Actinobacteria*, *Firmicutes*, and *Verrucomicrobia* are helpful for the immune system and may help with anti-tumor immunity and control of tumor growth. Disturbances in the gut microbiome make-up may result in increased risk of cancer in the epithelial barrier tissues.

Future Research Directions:

More human studies need to be performed in order to determine which gut bacteria are affected by PFAS exposure. Research into diseases that are affected by the composition of the gut microbiome should also be done to assess downstream effects of PFAS exposure. Additional research into the PFAS, PFOA should be done as there is limited research on the effects of this type of PFAS. PFAS replacements (Ex: GenX) should also be tested to determine if they are safer than current PFAS. Lastly, combination studies should be done to test multiple different PFAS exposures simultaneously.

Lessons Learned:

PFAS exposure is a much larger problem than originally thought. They can effect the gut microbiome of humans and animals alike. There is a lack of research on the potential health risks and downstream effects of PFAS exposure for humans. Many of the levels of PFAS used in current studies are not realistic to human exposure levels as they were much lower than the average blood serum in humans. It is unknown how long these chemicals can stay in the environment and the human body. The extent to which PFAS can cause long term deleterious effects is still unknown.

Acknowledgements:

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