

Exploring Potential Differences in Developmental Toxicology of Per- and Polyfluoroalkyl Substances (PFAS) Through Targeted Metabolomics Denise K. MacMillan,¹ Nicola Evans, ² L. Earl Gray,² Christy S. Lambright,² and Justin M. Conley²

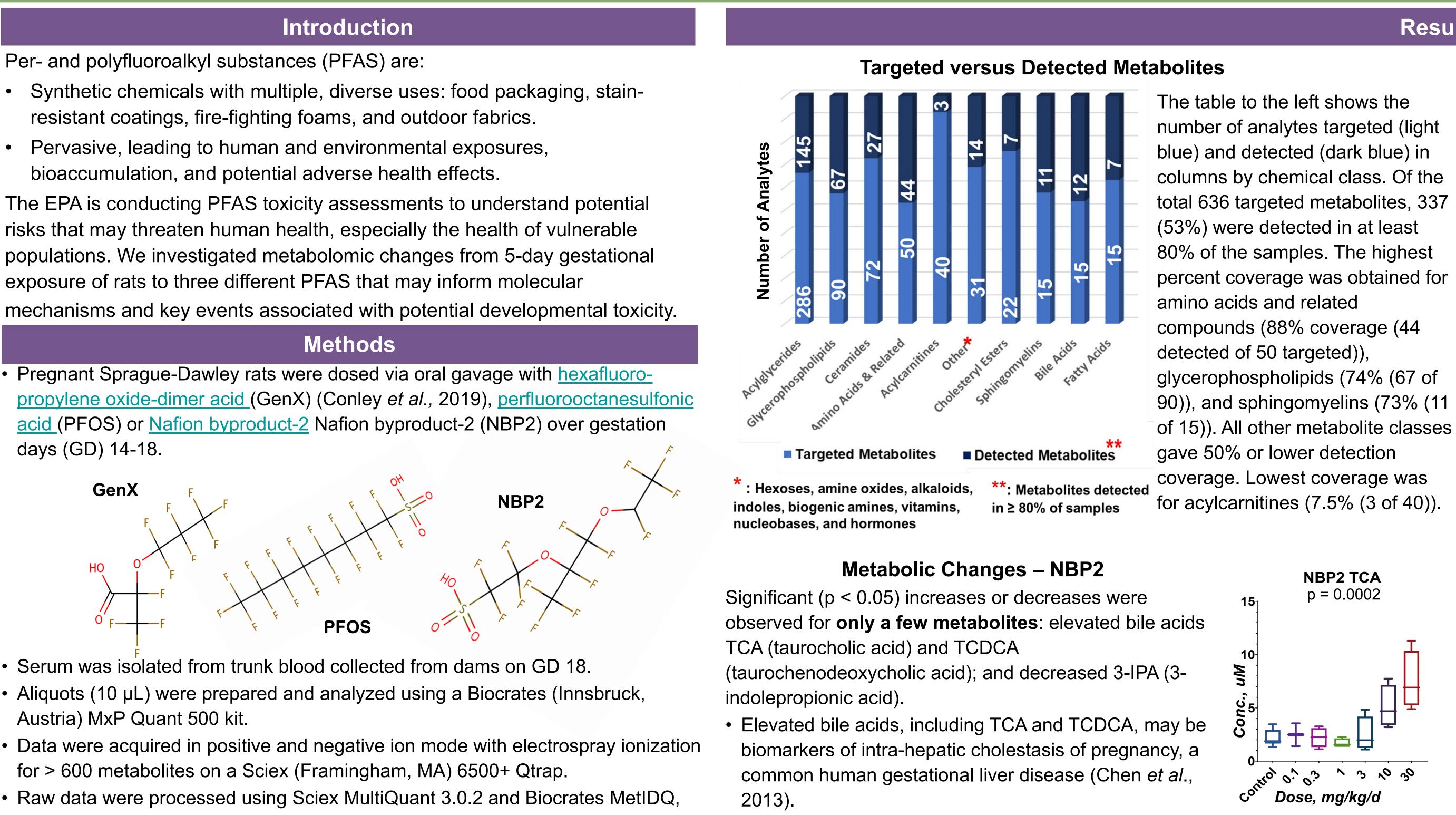
1 – U.S. Environmental Protection Agency, Center for Computational Toxicology and Exposure 2 - U.S. Environmental Protection Agency, Center for Public Health and Environmental Assessment

Per- and polyfluoroalkyl substances (PFAS) are:

- Synthetic chemicals with multiple, diverse uses: food packaging, stainresistant coatings, fire-fighting foams, and outdoor fabrics.
- Pervasive, leading to human and environmental exposures, bioaccumulation, and potential adverse health effects.

The EPA is conducting PFAS toxicity assessments to understand potential risks that may threaten human health, especially the health of vulnerable populations. We investigated metabolomic changes from 5-day gestational exposure of rats to three different PFAS that may inform molecular

Pregnant Sprague-Dawley rats were dosed via oral gavage with <u>hexafluoro-</u> days (GD) 14-18.



- Serum was isolated from trunk blood collected from dams on GD 18.
- Aliquots (10 μL) were prepared and analyzed using a Biocrates (Innsbruck, Austria) MxP Quant 500 kit.
- for > 600 metabolites on a Sciex (Framingham, MA) 6500+ Qtrap.
- Oxygen version.
- Analytes observed in ≥80% of samples were evaluated for changes relative to controls and one-way ANOVA analysis using GraphPad Prism and MetIDQ.

• 3-IPA is an anti-oxidant formed during tryptophan metabolism by gut microbiota.

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Results

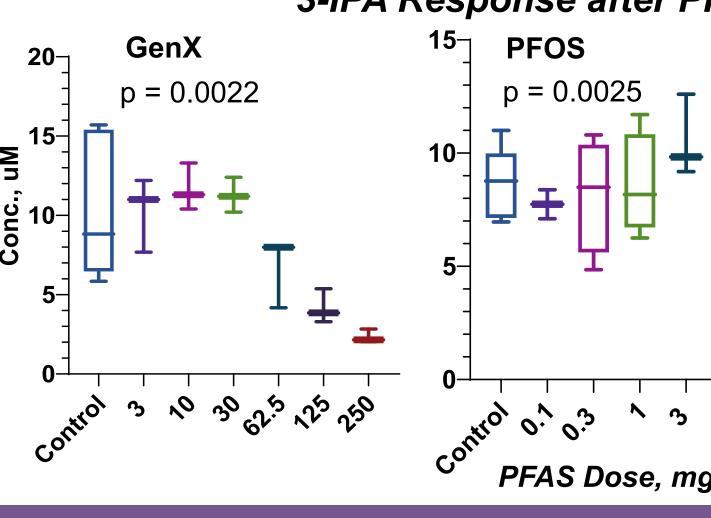
Significant changes (p < 0.05) were observed for **many metabolites**.

- GenX-exposed serum: decreased amino acids Arg, Thr, and Trp, bile acid TCDCA, indole derivatives 3-IAA (3-indoleacetic acid) and 3-IPA, several phosphatidylcholines (PCs), and others.
- PFOS-exposed serum: decreased Trp, TCDCA, 3-IAA, 3-IPA, several PCs, and others.

Metabolic Changes Common to GenX, PFOS, and NBP2

Changes were observed for several metabolites, but often not in the same direction. For example, bile acids increased for NBP2 and decreased for GenX and PFOS.

• 3-IPA, an anti-oxidant formed during tryptophan metabolism, decrease was consistent for the three PFAS.



3-IPA Response after PFAS Exposure 151 NBP2 p = 0.00270° 0° ° ° ° ° ° ° ° ° ° PFAS Dose, mg/kg/d

Conclusions

Metabolic changes observed here after PFAS exposure suggest dose-related impacts to bile acid, lipid, and amino acid metabolism. Additional research is needed to investigate health effects, if any, of these changes to pregnant rats.

References

Chen et al., (2013) Int J Gynecol Obstet **122**(1):5. doi: 10.1016/j.ijgo.2013.02.015. Conley et al. (2019). Environ Health Perspect **127**(3): 37008. doi: 10.1289/EHP4372.



Metabolic Changes – GenX and PFOS

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