Determining how Placental Epigenetic Machinery Expression is Impacted by Per- and Polyfluoroalkyl Substances

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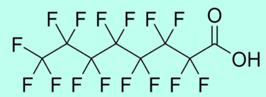
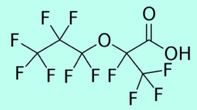
Introduction

- The stability properties of per-and polyfluoroalkyl substances (PFAS) made them desirable for manufacturing [1].
- PFOA and PFOS are the most studied and detected PFAS[2].
- PFAS found to persist in the environment and human body, led to accumulation and exposure became associated with negative health outcomes[3].
- PFOA and PFOS were phased out of production, but they continue to be present in the environment[3].
- Common products containing PFAS include fire-fighting foams, cleaning products, stain and water-repellent fabrics.
- GenX was used to replace PFOA, but its use resulted in water contamination of concern within the NC coast[4].
- PFAS are associated with preeclampsia and reduced birth weight[5,6].
- The effects of PFAS continue to be poorly understood, especially in regards to the placenta, specifically for epigenetic machinery associated genes (EMAGs).

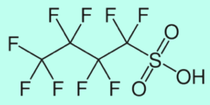
Common PFAS Compounds



Perfluorooctanoic acid: PFOA



2,3,3,3-tetrafluoro-2-(heptafluoro-propoxy)propanoate: GenX

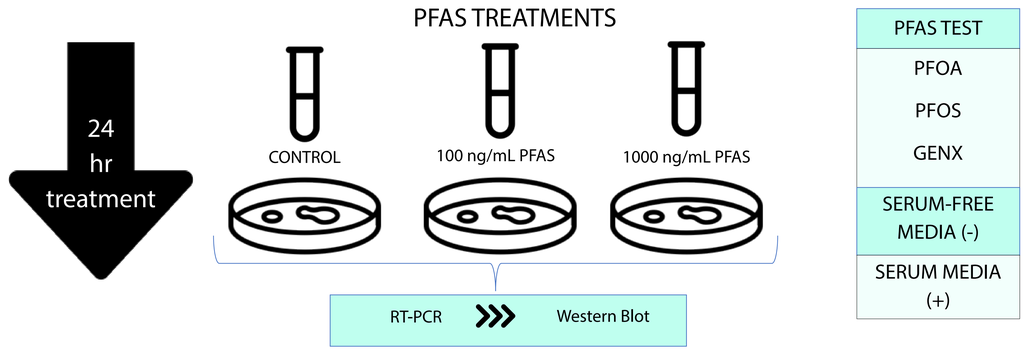


Perfluorooctanesulfonate: PFOS

Hypothesis:

Exposure to PFAS lead to alterations in the expression of EMAGs.

Methods



Results

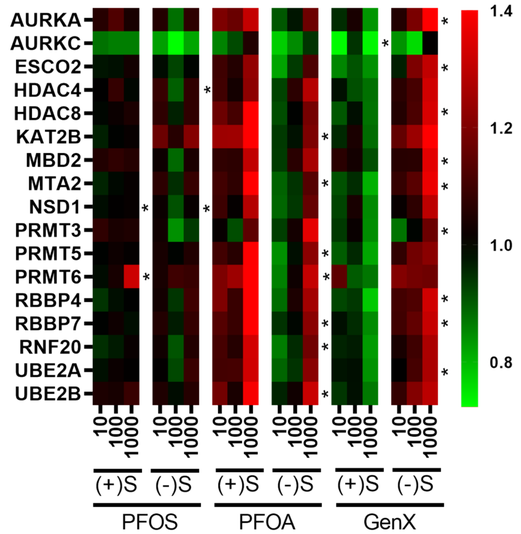


Figure 1: Exposure to PFAS compounds resulted in alterations in the expression of EMAGs. 24 hour treatment of PFOA, PFOS, and GenX, in the presence or absence of 10% fetal bovine serum, (+) S or (-) S. HDAC8 expression is up-regulated above, and AURKC is down-regulated.

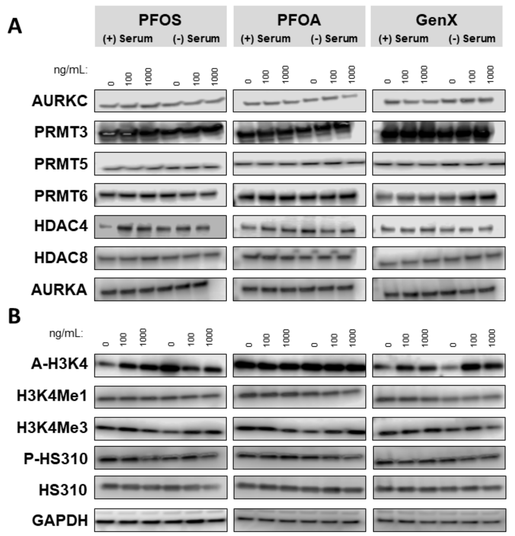


Figure 2: Exposure to PFAS compounds resulted in different protein and histone expression. Western Blots followed a 24 hour treatment, to evaluate for alterations in the expression of epigenetic regulatory protein (A). Alterations in acetylation, phosphorylation, and methylations were found in histones (B).

Conclusions

- PFAS significantly alters the expression of epigenetic regulatory machinery in placental trophoblast cell line JEG-3.
- Alterations include genes related to histone phosphorylation, demethylation, ubiquitination, and deacetylation.
- Differences were found between the presence or absence of 10% fetal bovine serum.
- Protein expression was also altered after exposure to PFAS treatments.
- Significant alterations found in the expression of EMAGs, for Aurora A kinase (AURKA) and Protein Arginine Methyltransferase 3 (PRMT3), after PFAS treatments.

Future Directions

Additional research is needed to determine long-term human health effects due to PFAS exposure and the role of EMAGs.

References

1. Rayne & Forest (2009) J Environ Sci Health A Tox Hazard Subst Environ Eng
2. Wang et al. (2017) Environ Sci Technol
3. Rahman et al (2014) Water Res
4. Stein et al (2009) Am J Epidemiol
5. Sun et al. (2016) Environ Sci & Tech Letters
6. Guerrero-Preston e al (2010) Epigenetics
7. Banister et al. (2011) Epigenetics
8. Clark et al. (2019) Epigenetics
9. Schmidt et al. (2019) Translational psychiatry
10. Meakin et al. (2018) Hormones and behavior

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