

PFAS AND PLACENTAL TOXICITY

Rebecca Fry

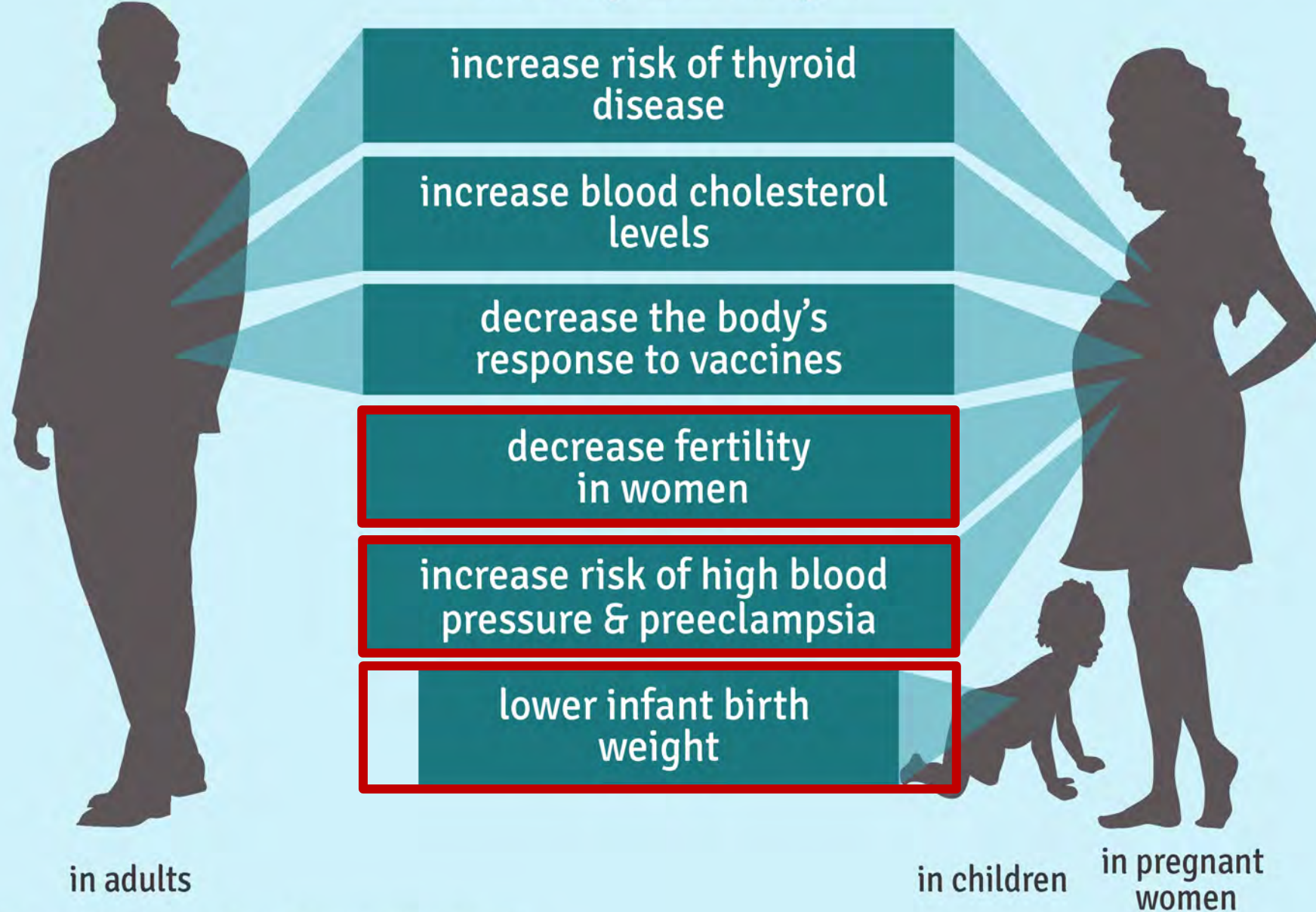
Environmental Sciences and Engineering
UNC-Chapel Hill

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Environmental Health Collaborative 2019 Summit
PFAS: Integrating Science and Solutions in NC



Human studies suggest PFAS exposure may...



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increase risk of thyroid
disease

increase blood cholesterol

Do PFAS in drinking water pose a risk to pregnant women and could they affect the health and function of her placenta?

decrease fertility
in women

increase risk of high blood
pressure & preeclampsia

lower infant birth
weight

in adults

in children

in pregnant
women

Do PFAS in drinking water pose a risk to pregnant women and could they affect the health and function of her placenta?

Human



What are the levels of PFAS in the placenta??

PFAS

CCCCCCCC(=O)O

Perfluorooctanoic acid (PFOA)

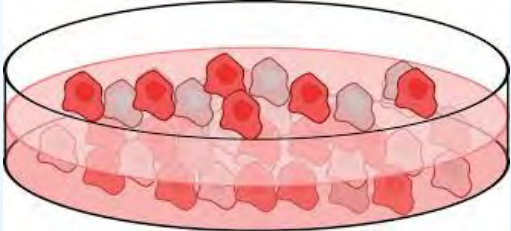
CCCCCCCC(S(=O)(=O)O)F

Perfluorooctanoic sulfate (PFOS)

CCCC(F)(F)OC(=O)O

2,3,3,3-tetrafluoro-2-(hepta fluoropropoxy) propanoate (GenX)

Cells



What is the effect of PFAS on placental health and function?

What are the levels of PFAS in the placenta?

| | PFPeS | PFHxS | PFHpS | PFOS | PFHxA | PFOA | PFNA | PFDA | PFUnA | PFTriA | PFTA |
|---------------------|---------|---------|---------|---------|--------|---------|---------|---------|---------|---------|---------|
| Chain length | 5 | 6 | 7 | 8 | 6 | 8 | 9 | 10 | 11 | 13 | 14 |
| %> LOD | 31.1 | 74.6 | 54.9 | 99.2 | 1.6 | 27.0 | 21.3 | 39.3 | 49.2 | 29.5 | 6.6 |
| Maximum | 0.035 | 0.446 | 0.063 | 4.87 | 5.87 | 1.23 | 0.494 | 0.465 | 0.24 | 0.336 | 0.111 |
| Minimum | < 0.005 | < 0.033 | < 0.008 | < 0.001 | < 1.32 | < 0.290 | < 0.148 | < 0.030 | < 0.033 | < 0.050 | < 0.049 |
| Median | < 0.005 | 0.067 | 0.009 | 0.48 | < 1.45 | < 0.315 | < 0.163 | < 0.031 | < 0.031 | < 0.057 | < 0.054 |
| n | 122 | 122 | 122 | 122 | 122 | 122 | 122 | 122 | 122 | 122 | 122 |

- 122 placentas from high-risk pregnancies at UNC Hospitals
- Pre-Term Birth cohort
- Monitored for a total of 26 PFAS
- Including GenX, Nafion BP2 previously seen in Wilmington serum
- **11 legacy PFAS found above limit of detection (LOD)**

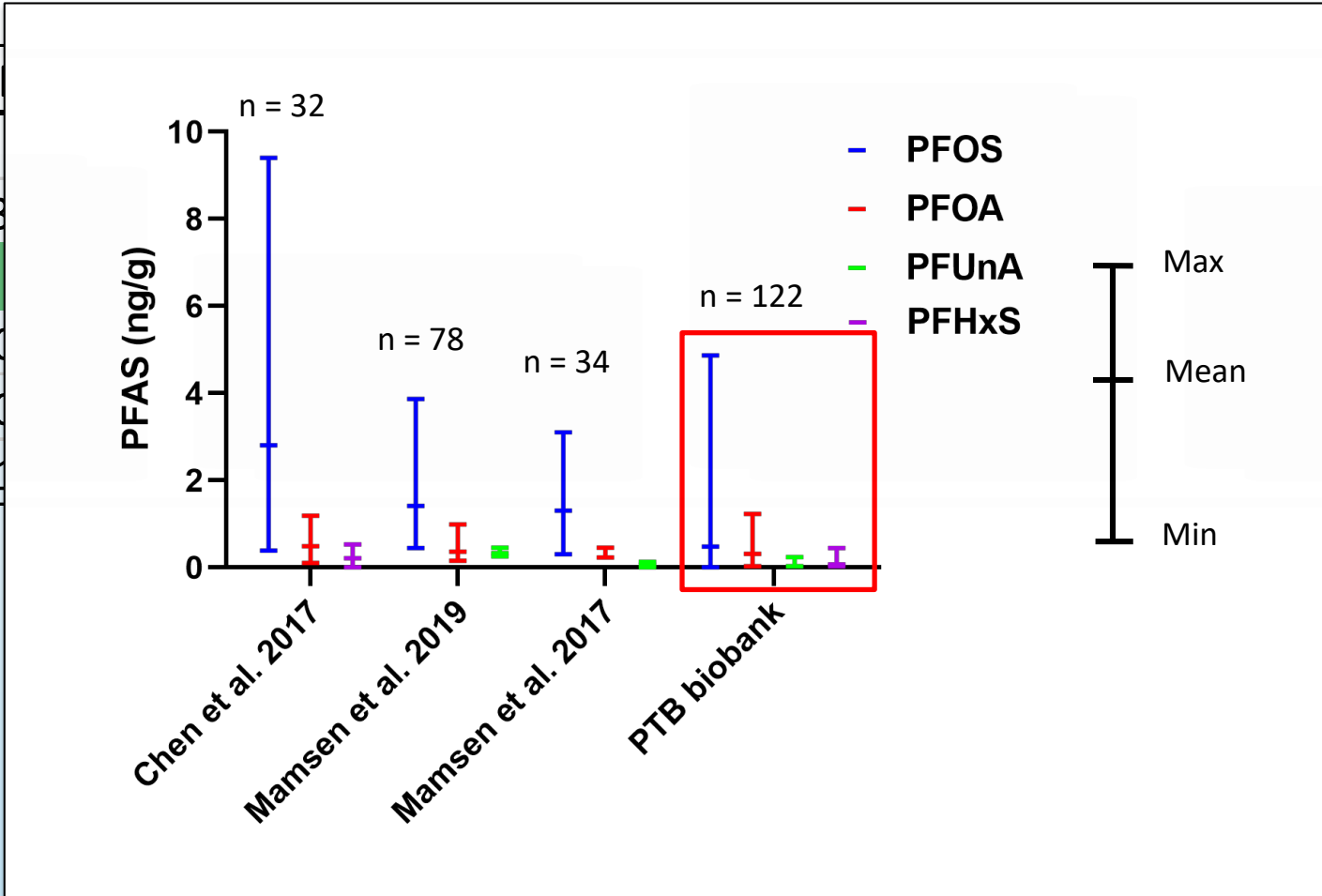


PFAS results are presented as ng/g wet weight



What are the levels of PFAS in the placenta?

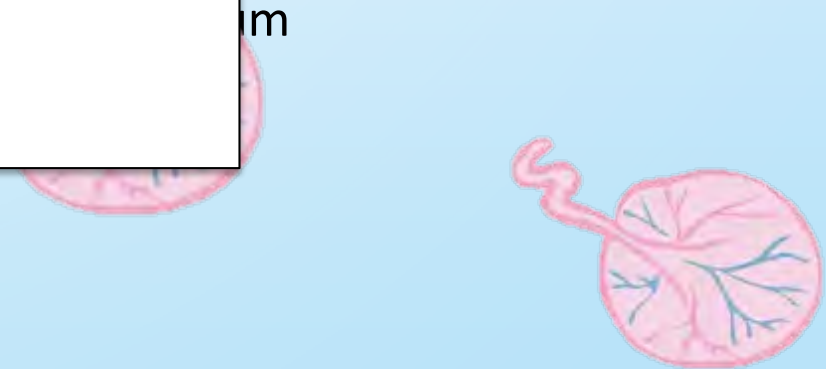
| | PFAS |
|--------------|------|
| Chain length | |
| % > LOD | 3 |
| Maximum | 0 |
| Minimum | < 0 |
| Median | < 0 |
| n | 1 |



| | PFUnA | PFTriA | PFTA |
|--------------|-------|---------|---------|
| Chain length | 11 | 13 | 14 |
| % > LOD | 49.2 | 29.5 | 6.6 |
| Maximum | 0.24 | 0.336 | 0.111 |
| Minimum | 0.033 | < 0.050 | < 0.049 |
| Median | 0.031 | < 0.057 | < 0.054 |
| n | 122 | 122 | 122 |



PFAS results are presented as ng/g wet weight



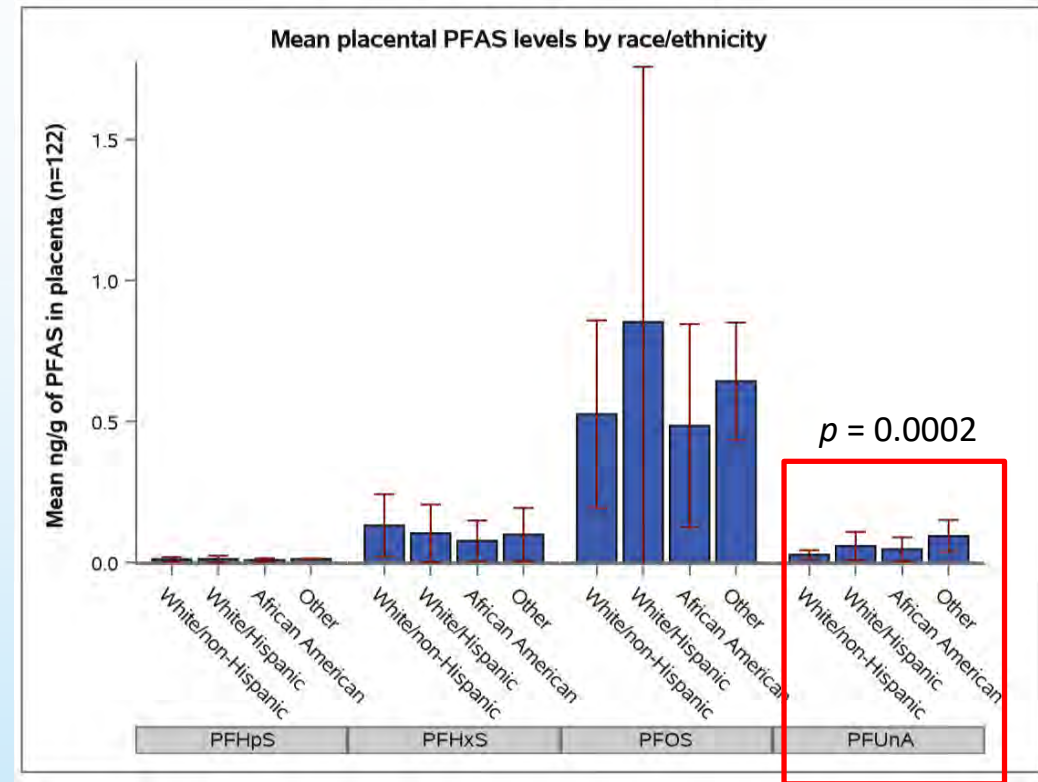
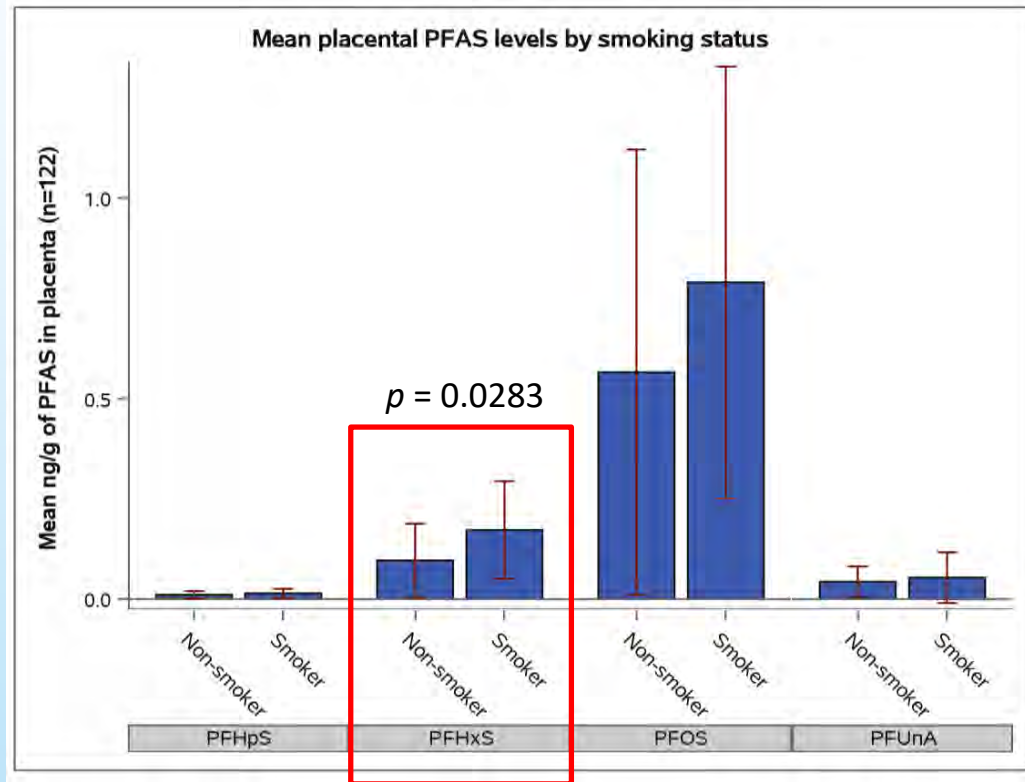
Risk factors associated with elevated PFAS in PTB placenta

PFOS, PFHxS, PFHps, and PFUnA were investigated for associations with risk factors including:

- Maternal age
- Maternal smoking status
- Maternal race/ethnicity
 - Child's gender
- Maternal pre-pregnancy BMI
- Maternal medical insurance
 - Maternal education
 - Marital status

Risk factors associated with elevated PFAS in PTB placenta

- PFOS, PFHxS, PFHpS, and PFUnA were investigated for associations with risk factors including:



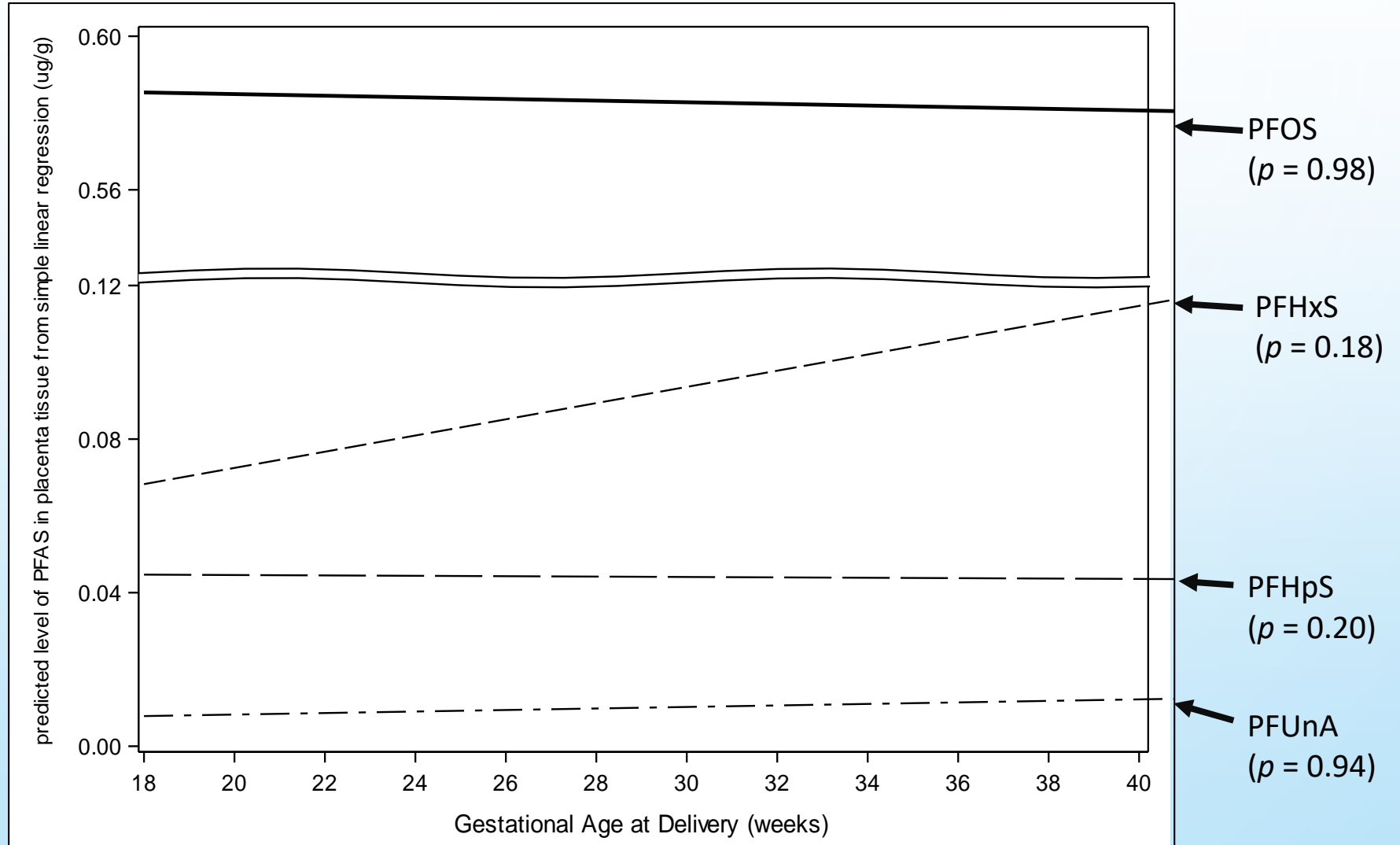
PFAS in relation to pregnancy outcomes and birth outcomes

PFOS, PFHxS, PFHps, and PFUnA in relation to adverse outcomes:

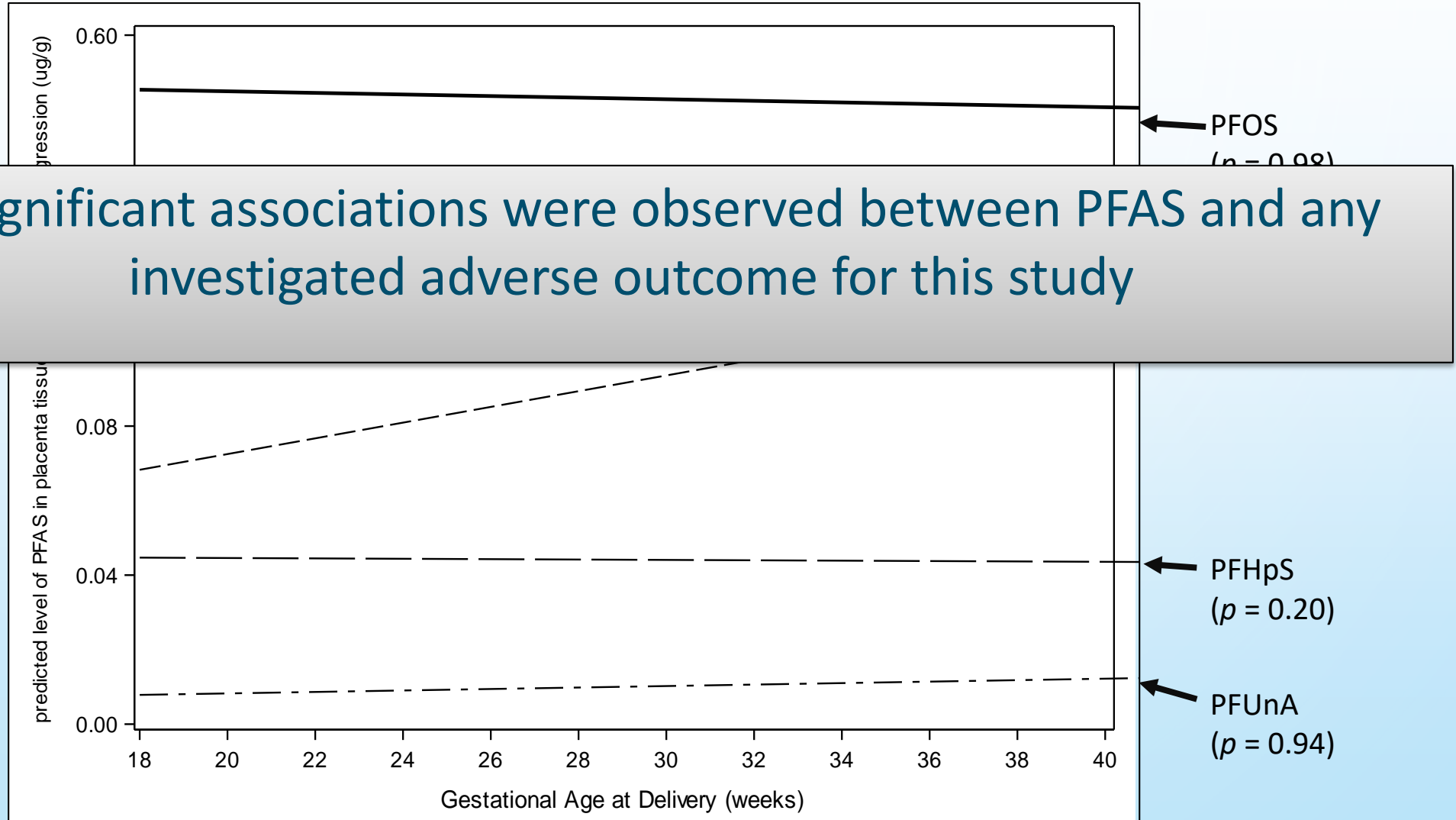
- Preeclampsia
- Birthweight
- Gestational age at delivery



PFAS and adverse outcomes

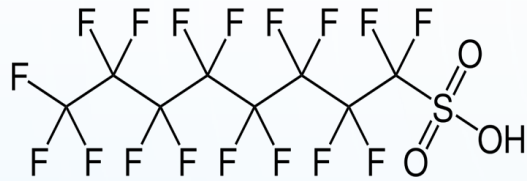


PFAS and adverse outcomes

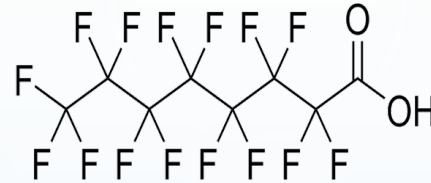


No significant associations were observed between PFAS and any investigated adverse outcome for this study

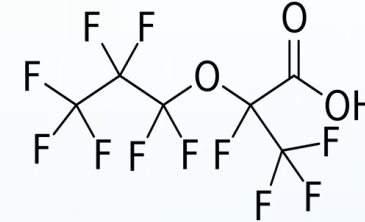
Examining the effects of PFAS in cell culture



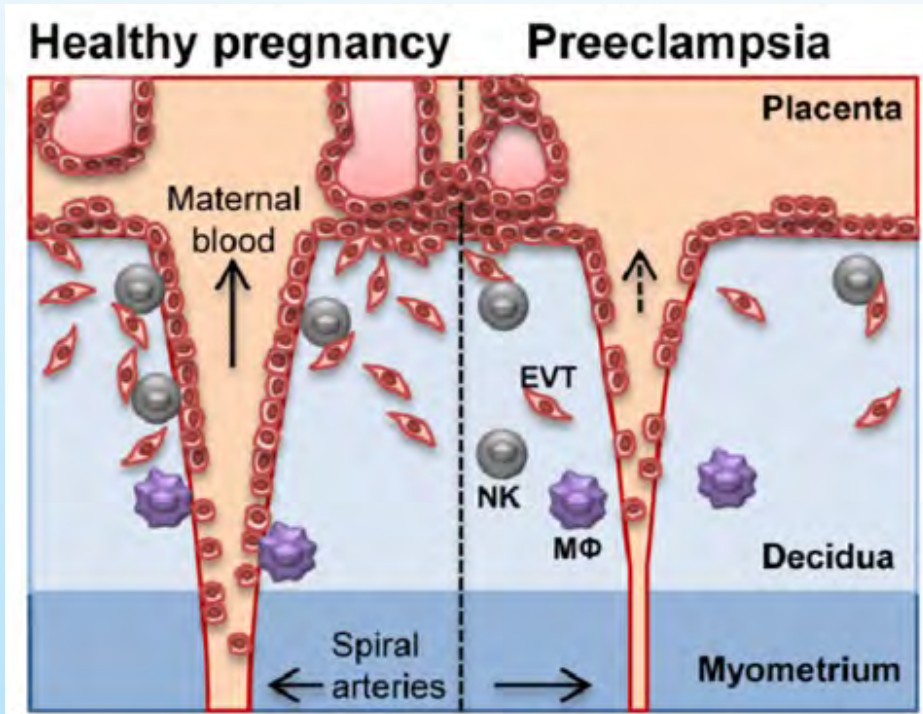
Perfluorooctanoic sulfate
(PFOS)



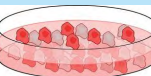
Perfluorooctanoic acid
(PFOA)



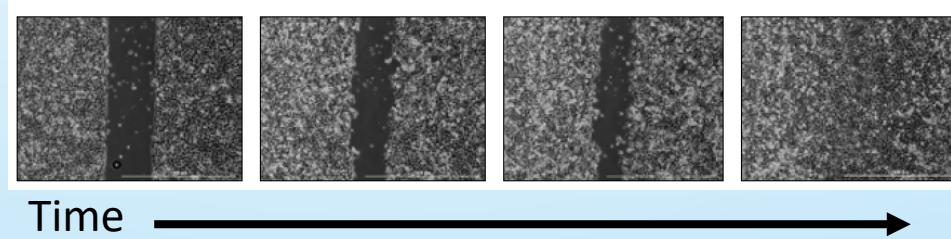
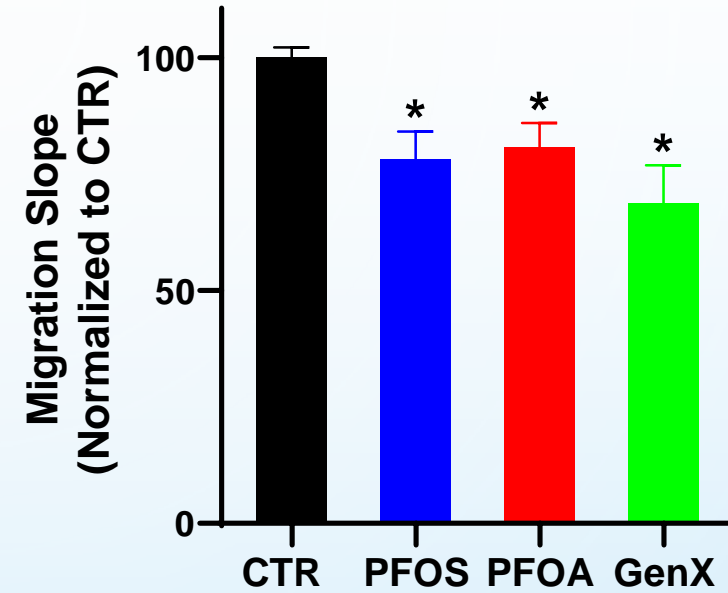
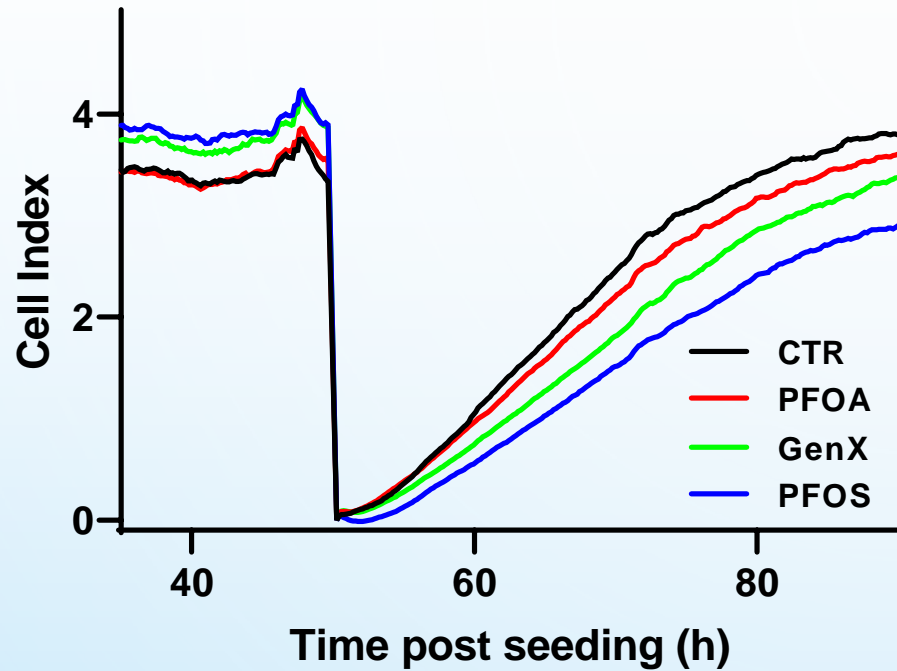
2,3,3,3-tetrafluoro-2-
(hepta fluoropropoxy)
propanoate
(GenX)



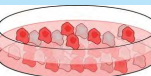
- Late in the first trimester, cells of the placenta known as trophoblast cells migrate to invade and remodel the arteries of the uterine wall.
- Remodeling allows for increased blood flow to the placenta and growing fetus.
- When this migration and invasion of trophoblast is compromised, pregnancy complications develop like Preeclampsia.



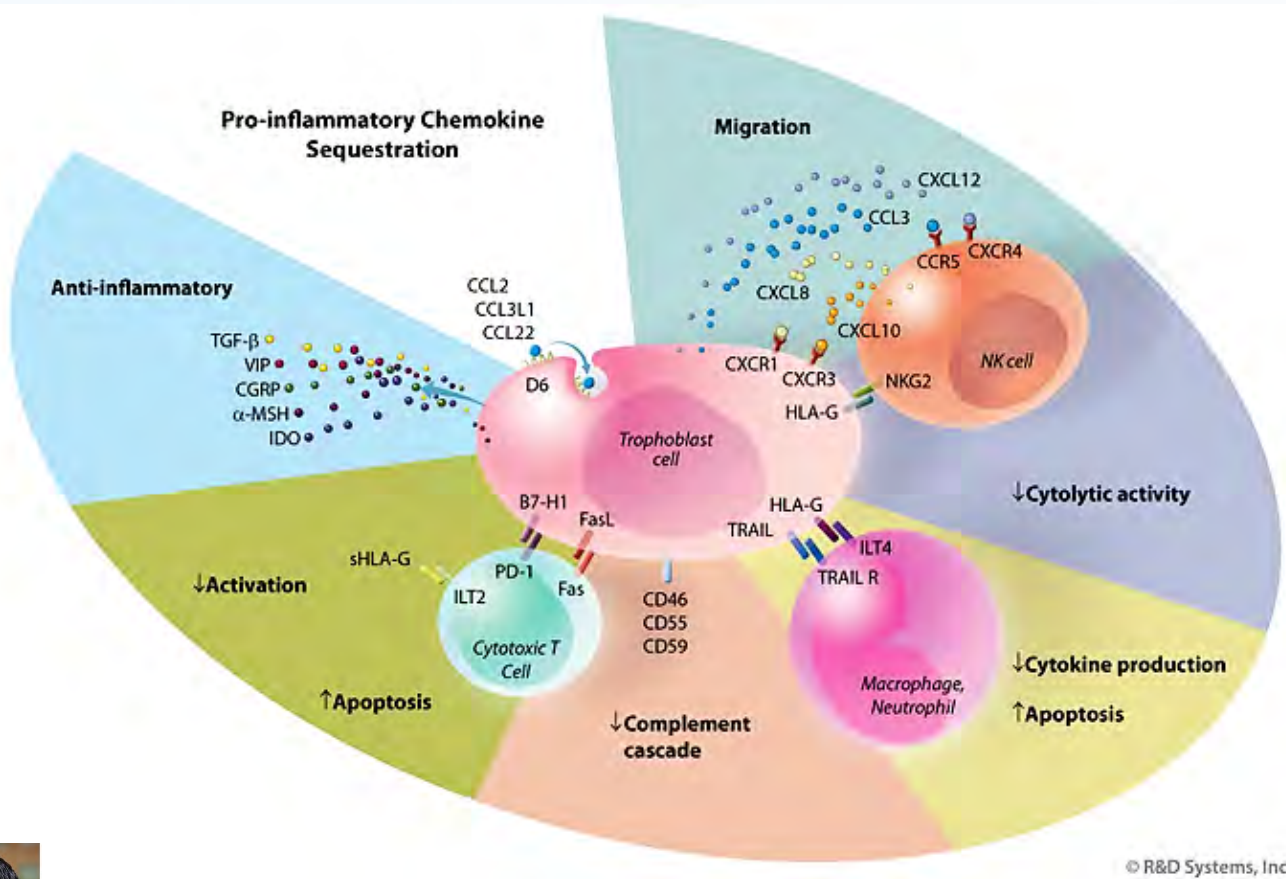
PFAS reduce migration in SVneo/HTR8



N = mean of 3 experiments
* p < .05 compared to control



Immune regulation of trophoblast migration

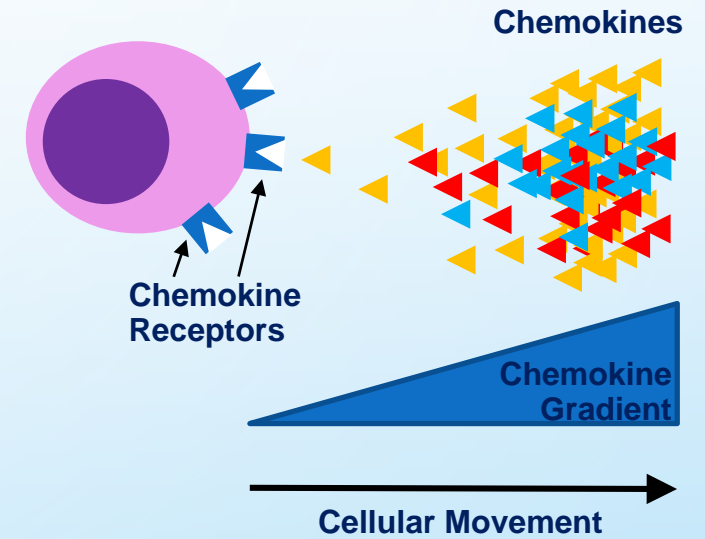
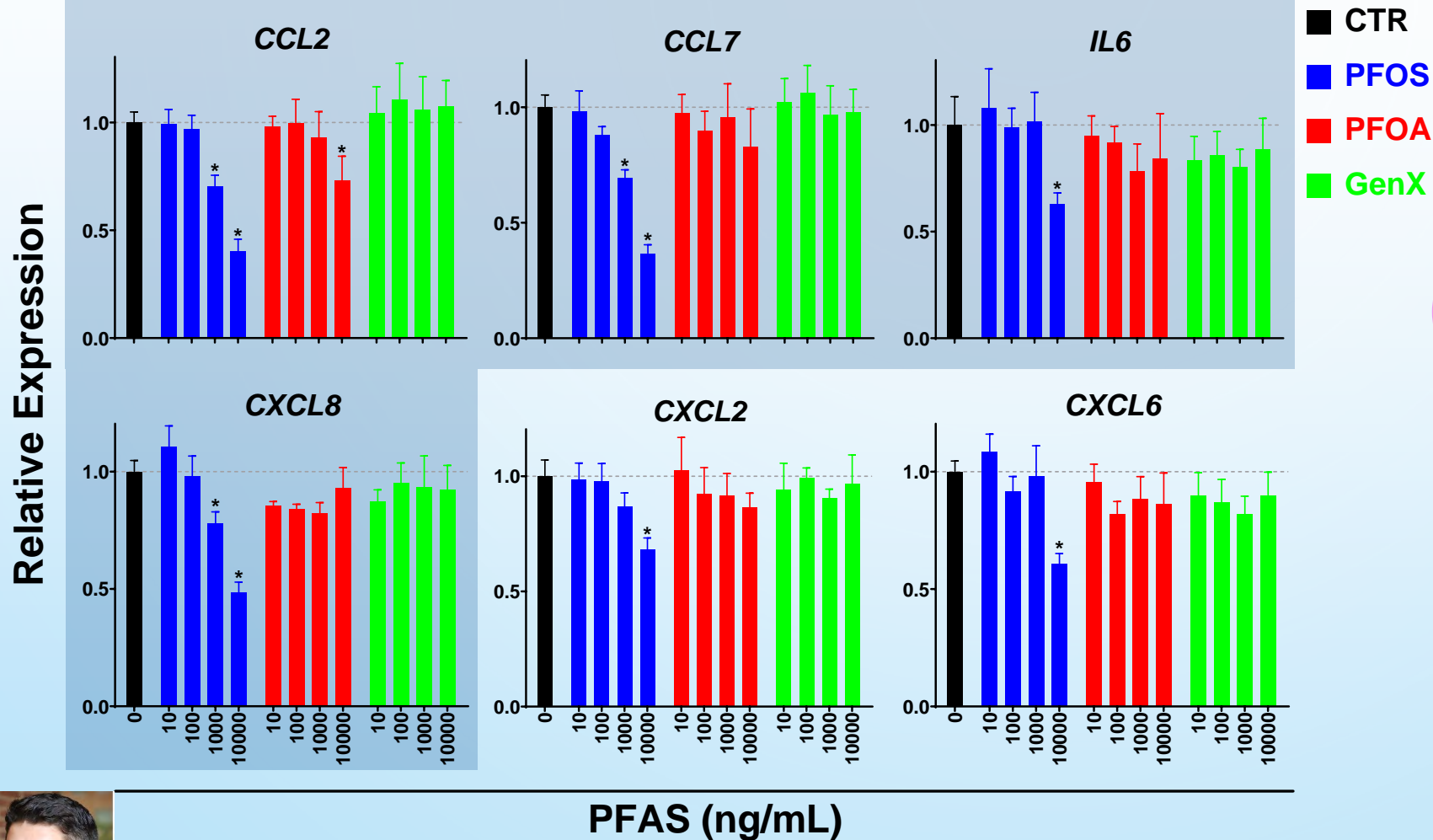


- Trophoblast-immune crosstalk
 - Prevents maternal immune cells from attacking fetal tissue
 - Protects fetus against pathogens
 - Controls trophoblast invasion/migration
- PFAS modulate immune signaling in other tissues

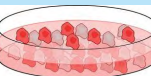


Chemokine expression

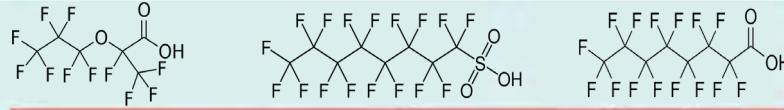
Involved in preeclampsia



N = mean of 4 experiments
* p < .05 compared to control



Environmental exposure to PFAS in the placenta at UNC



Potential Toxicological Changes

PFAS induced changes in migration

Potential Disease Outcomes

Maternal
Health

Pregnancy
Disorders

Fetal Growth and
Development

Later-in-Life
Health Effects



OUR TEAM: UNC at Chapel Hill



*Dr. Rebecca
Fry*



*Dr. Tracy
Manuck*



*Dr. Jackie
Bangma*



*Dr. Martha
Scott
Tomlinson*



*Dr. John
Szilagyi*



*Lauren
Eaves*



*Kirsi
Oldenburg*



EXTRA SLIDES

Discussion Questions

- Who needs to know about this research?
- How can these results inform clinical practice?
- Can we use these data to drive in vivo work?