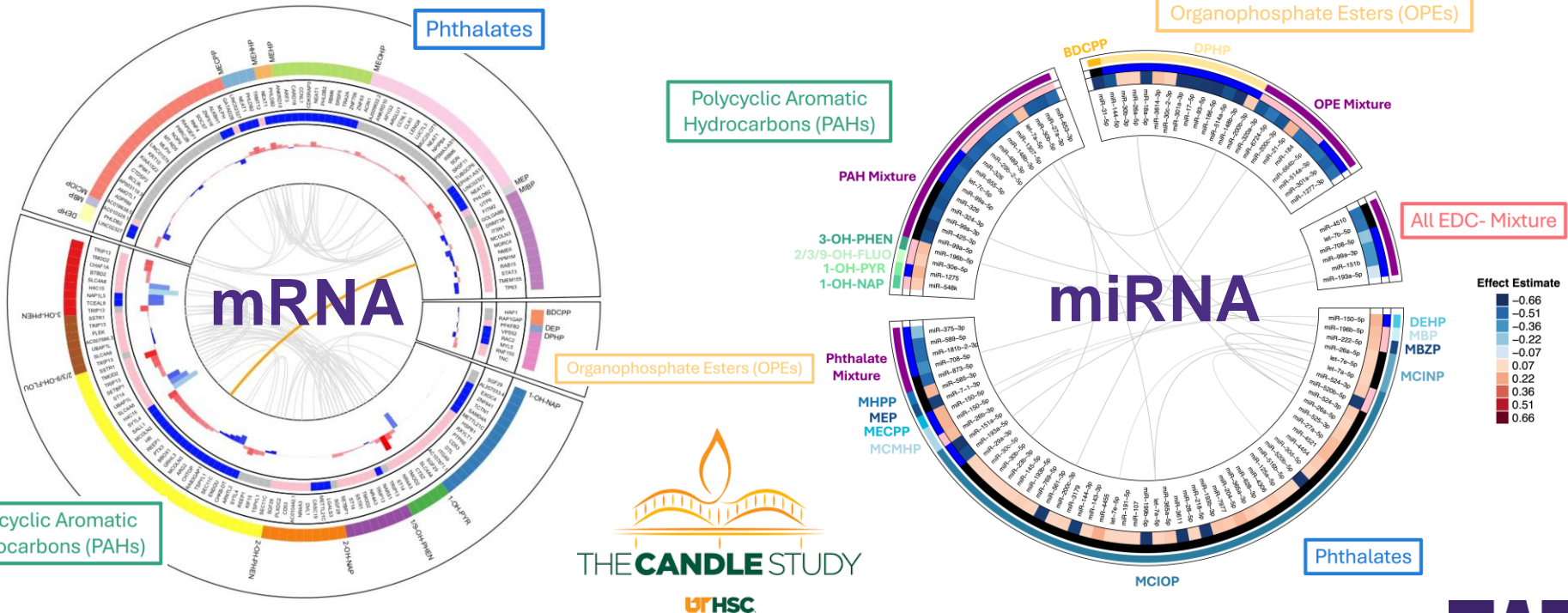


Development of a phthalate-disrupted placental multi-omic network

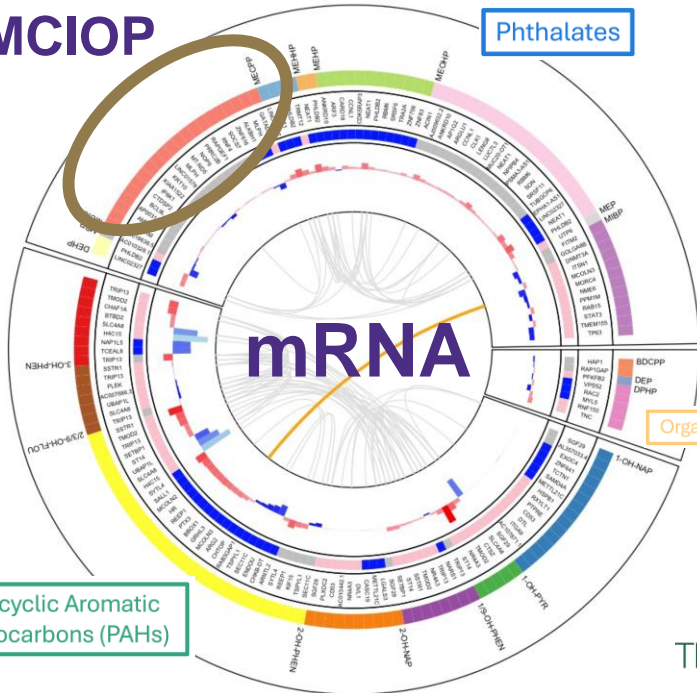
Samantha Lapehn, PhD and Alison Paquette, PhD
Seattle Children's Research Institute

mRNA & miRNA Signatures of EDC Exposure in CANDLE



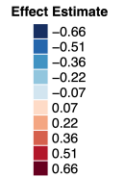
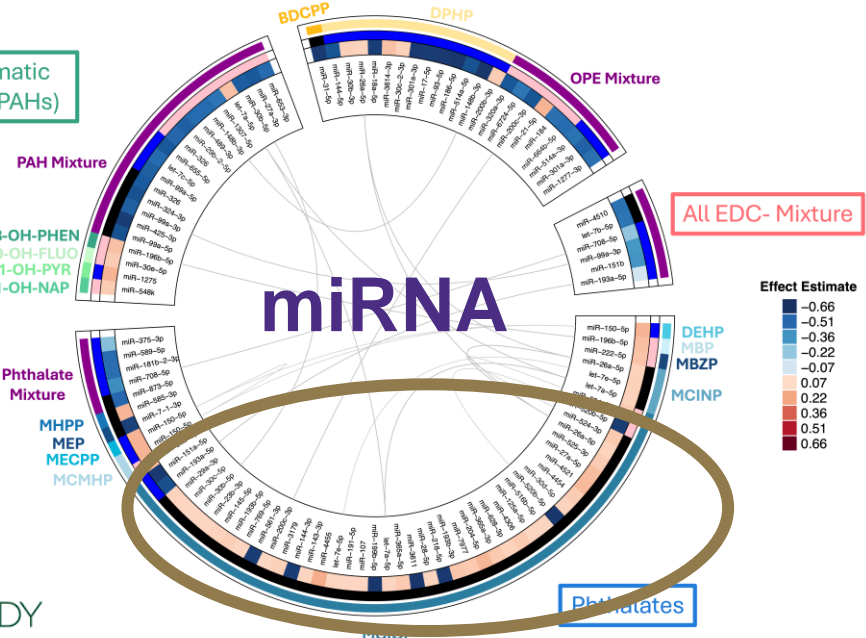
mRNA & miRNA Signatures of EDC Exposure in CANDLE

MCIOP



Polycyclic Aromatic Hydrocarbons (PAHs)

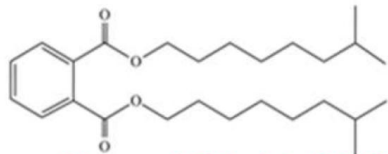
Organophosphate Esters (OPEs)



MCIOP

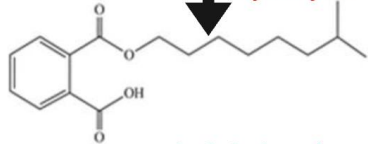


Diisononyl Phthalate (DINP)



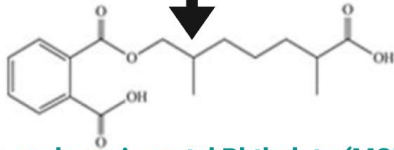
Diisononyl Phthalate (DINP)

Hydrolysis

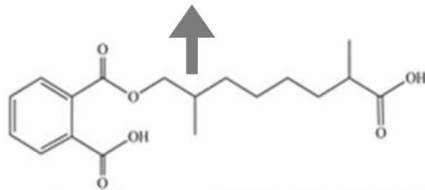


Monoisononyl Phthalate (MINP)

Oxidation



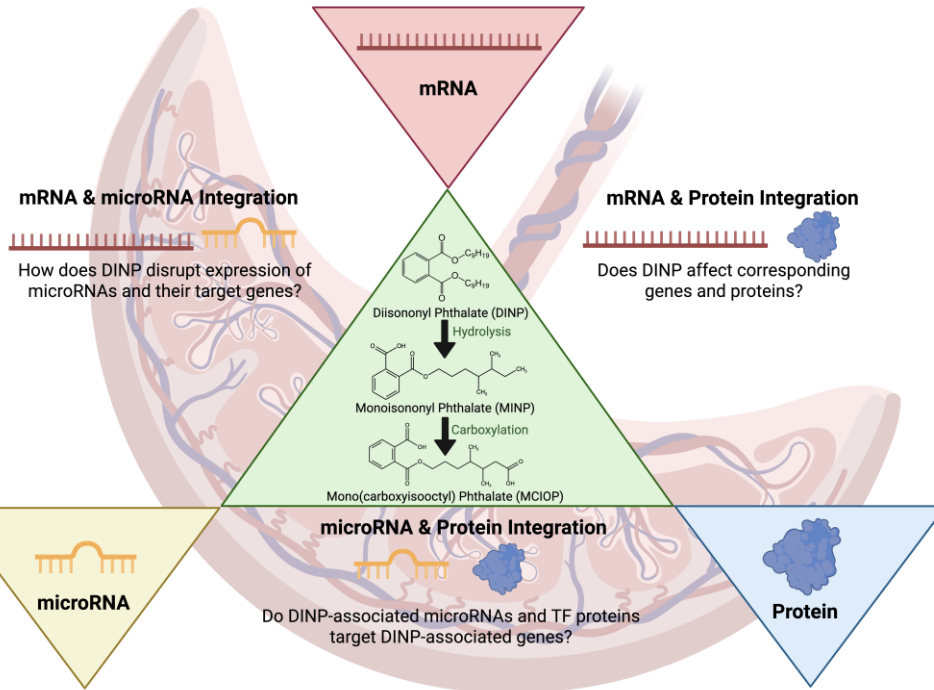
Mono-carboxy-isoocetyl Phthalate (MCIOP)



Mono-carboxy-isononyl Phthalate (MCINP)

- Limited in vitro or animal studies focused on DINP and its metabolites.
- 1.88 million global PTBs in 2018 attributed to DINP exposure (similar in magnitude to DEHP- 1.97 million) (Hyman et al. 2026).
- In 2017, US Consumer Product Safety Commission named DINP as 1/8 phthalates that would be concentration-limited in children's toys due to risk of male reproductive harm.
- In 2025, the US EPA concluded that certain industrial uses of DINP posed an, "unreasonable risk of injury to human health."

EDGE Pilot Aims

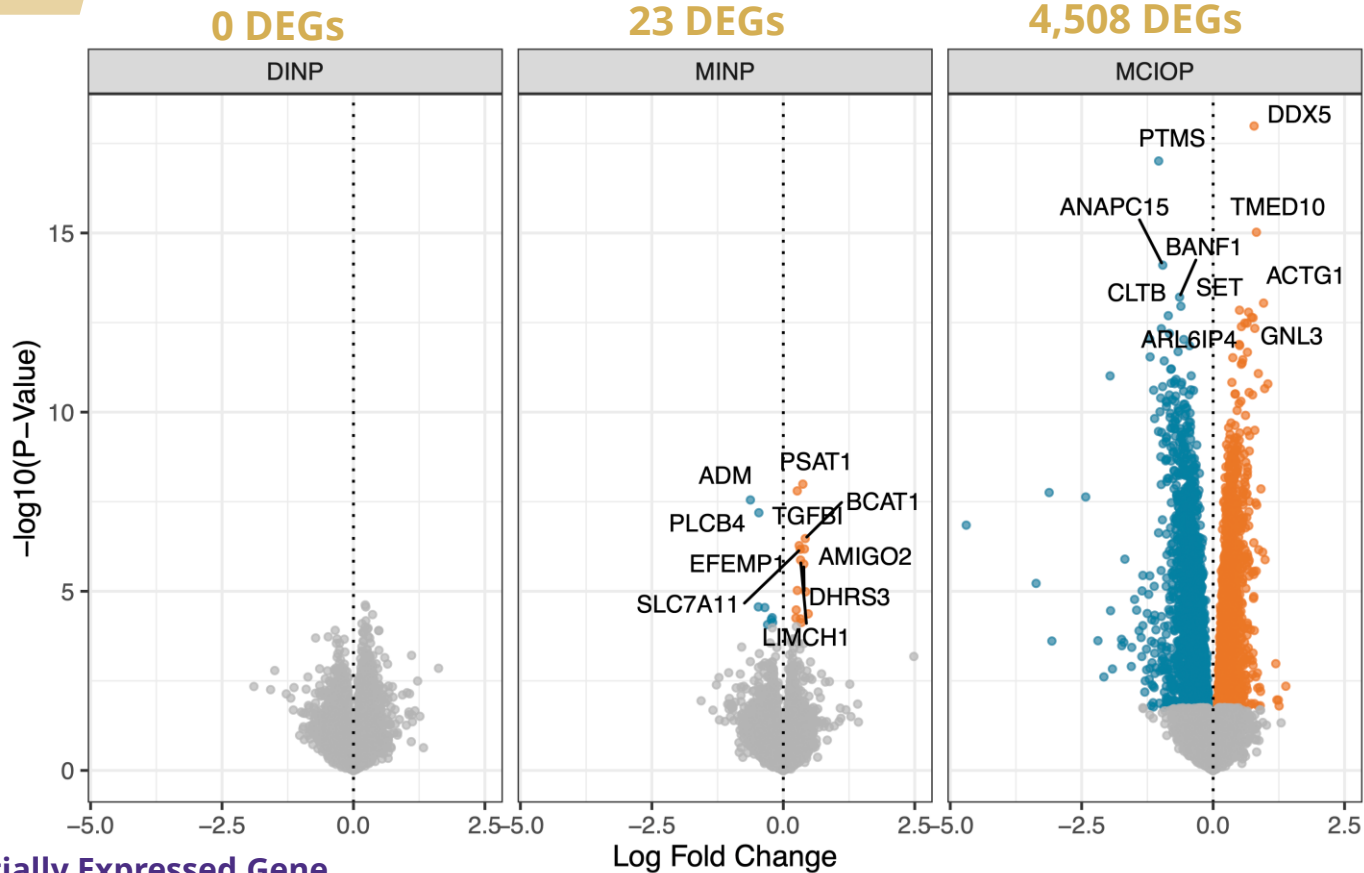


Aim 1: Evaluate the effect of DINP and metabolites on placental transcriptome (mRNA and microRNA).

Aim 2: Evaluate the effect of DINP or metabolites on placental protein expression.

Aim 3: Build a multi-omic network of phthalate-disruption in the placenta.

Differential Expression Analysis - mRNA

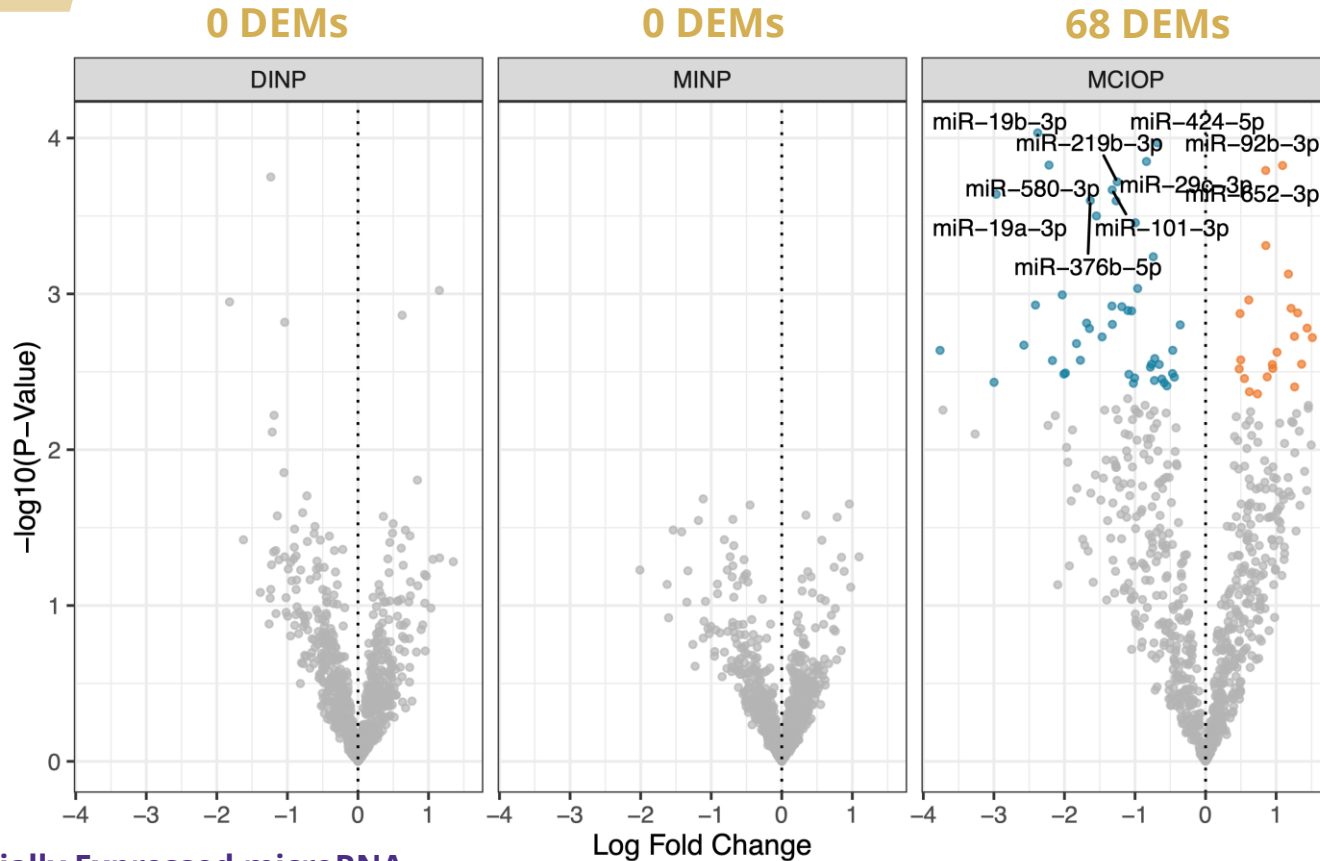


FDR < 0.05



DEG = Differentially Expressed Gene

Differential Expression Analysis - microRNA

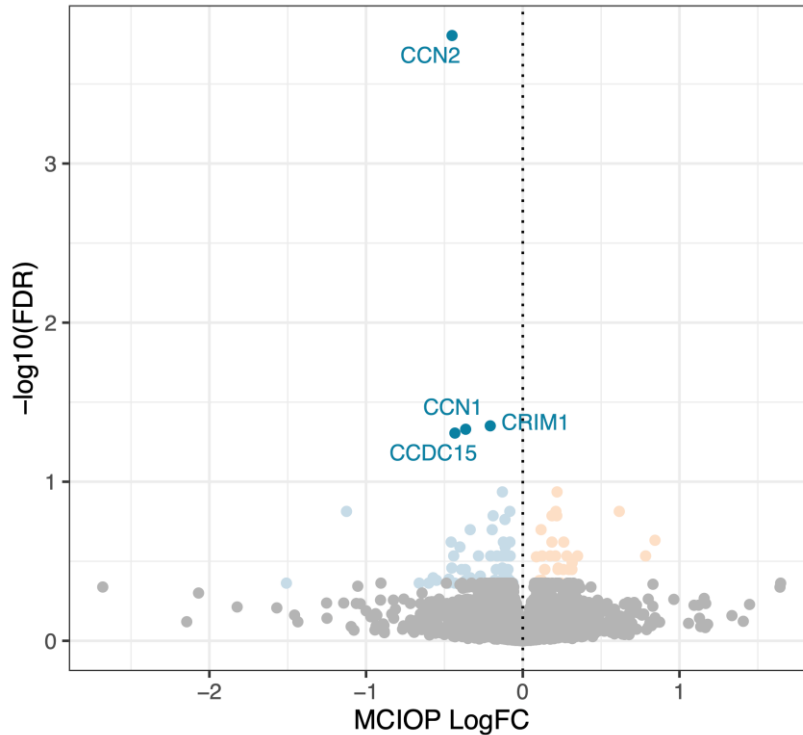


DEM = Differentially Expressed microRNA



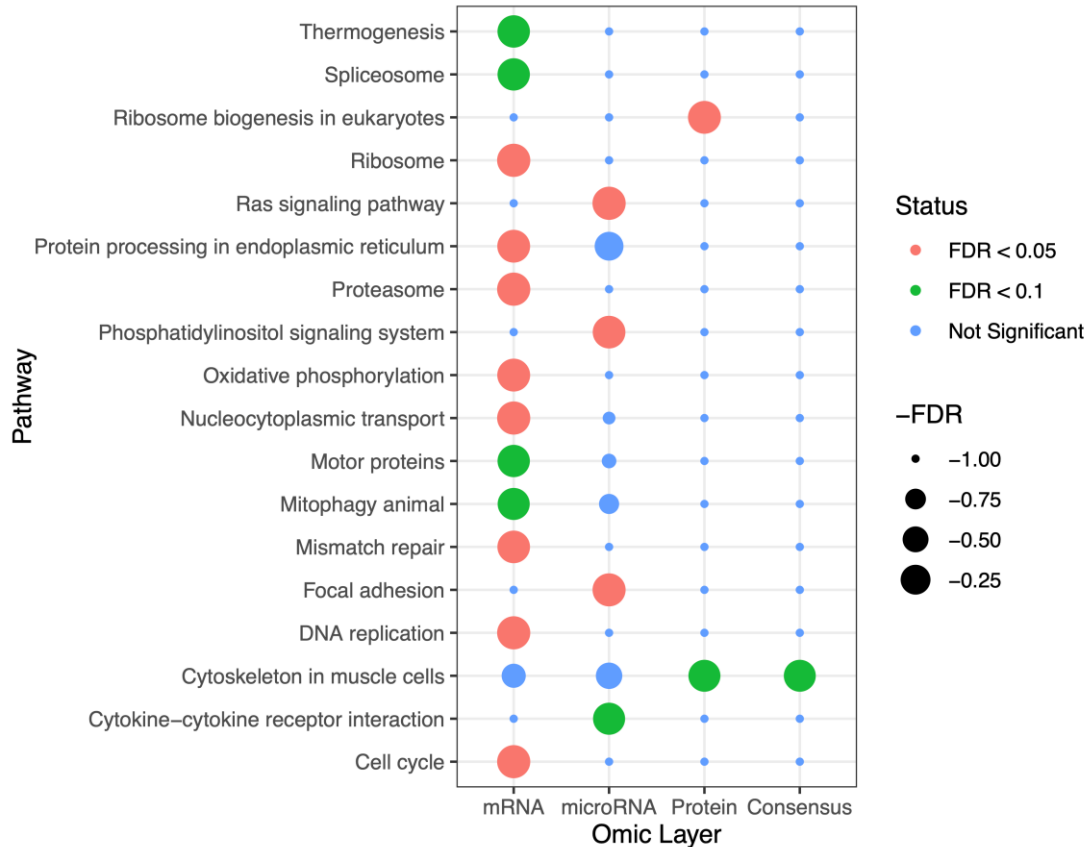
Differential Protein Abundance

MCIOP

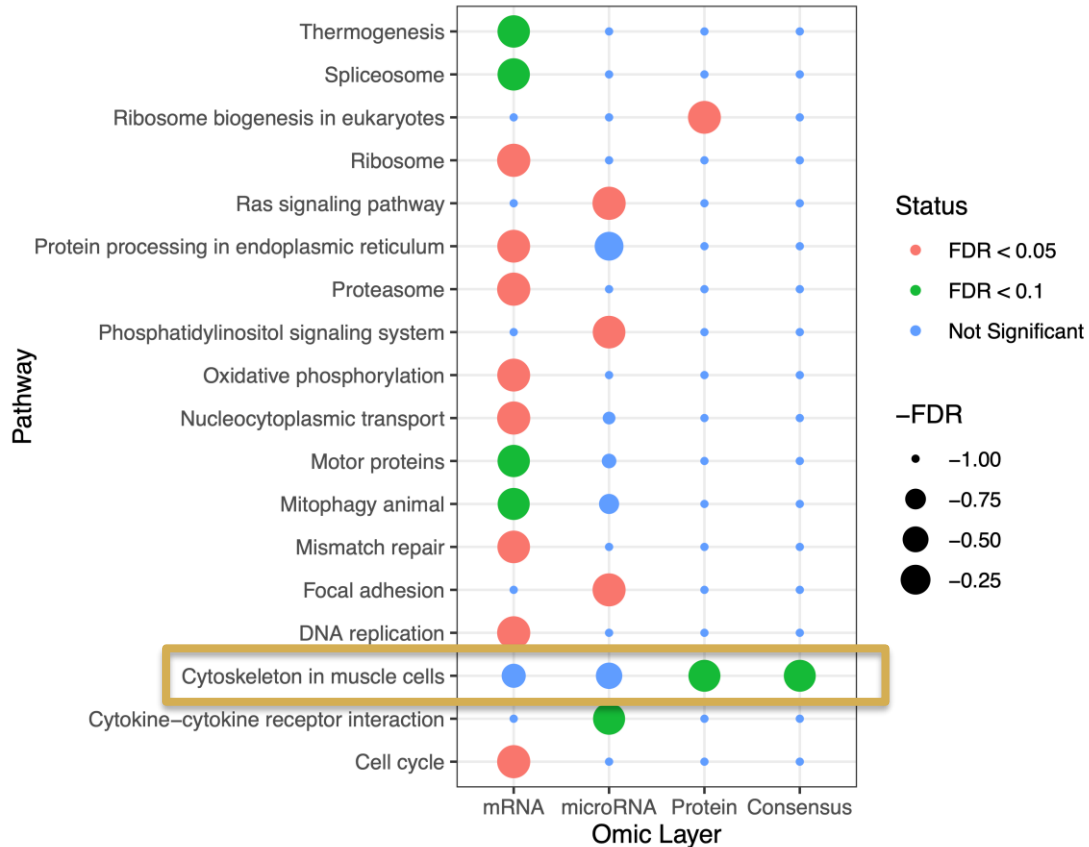


4 Proteins ($\text{FDR} < 0.05$)
116 Proteins ($p < 0.005$)

Multi-omic Pathway Integration

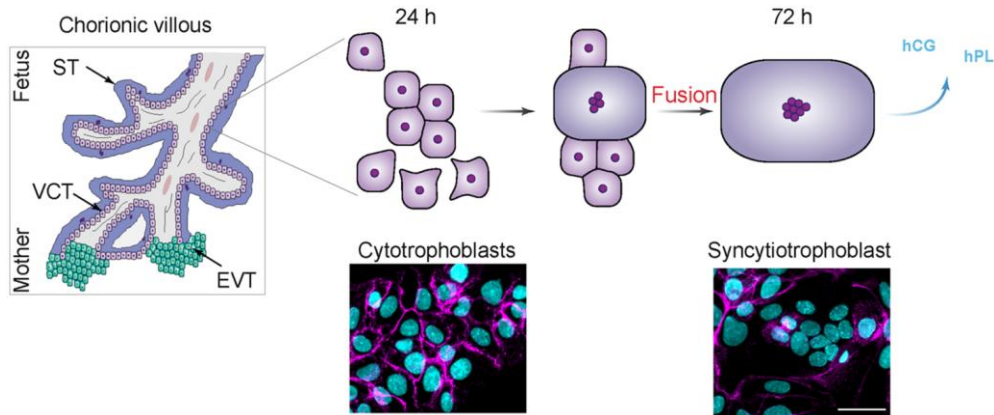


Multi-omic Pathway Integration

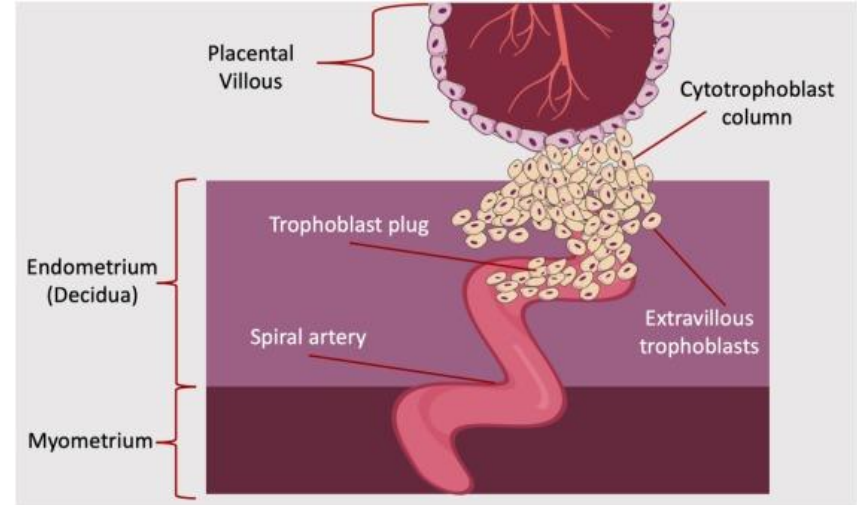


Cytoskeletal Roles in the Placenta

Trophoblast fusion



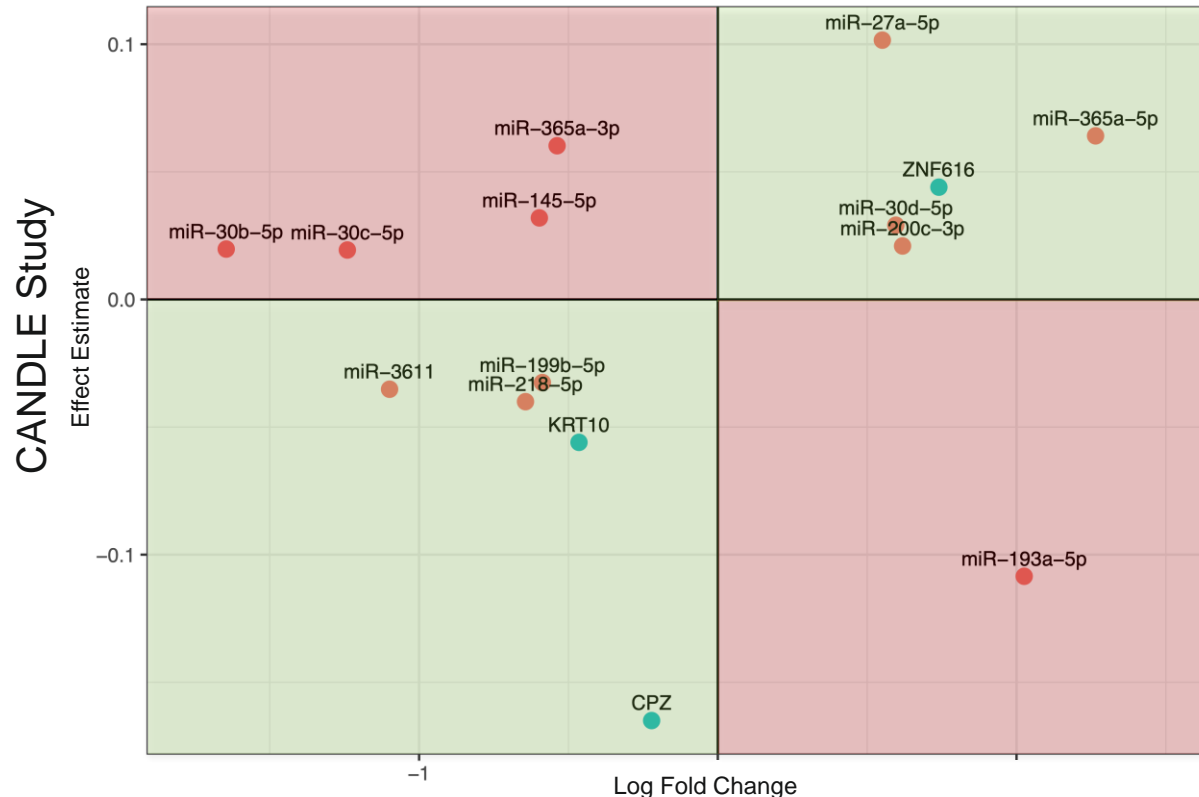
Trophoblast invasion and endovascular remodeling



Gerbaud, Tasken, Pidoux 2015

Meakin, Barrett, and Aleksunes 2022

Validation of Human Studies



- microRNA (58.3% Concordant)
- mRNA (100% Concordant)

Conclusions and Future Directions

Conclusions

- Placental mRNA is more sensitive than microRNA or proteins to EDC exposures.
- MCIOP, but not its precursors, affected all three omic layers.
- Multi-omic integration revealed cytoskeletal components as a potential target of MCIOP.

Future Directions

- Lower physiological concentrations
- EDC mixtures
- Other placental models

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Questions?

Paquette Lab

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