

IMPACT OF MATERNAL OBESITY ON PLACENTAL FUNCTION AND OFFSPRING OUTCOMES – GIVE FISH A CHANCE

March 1st, 2023

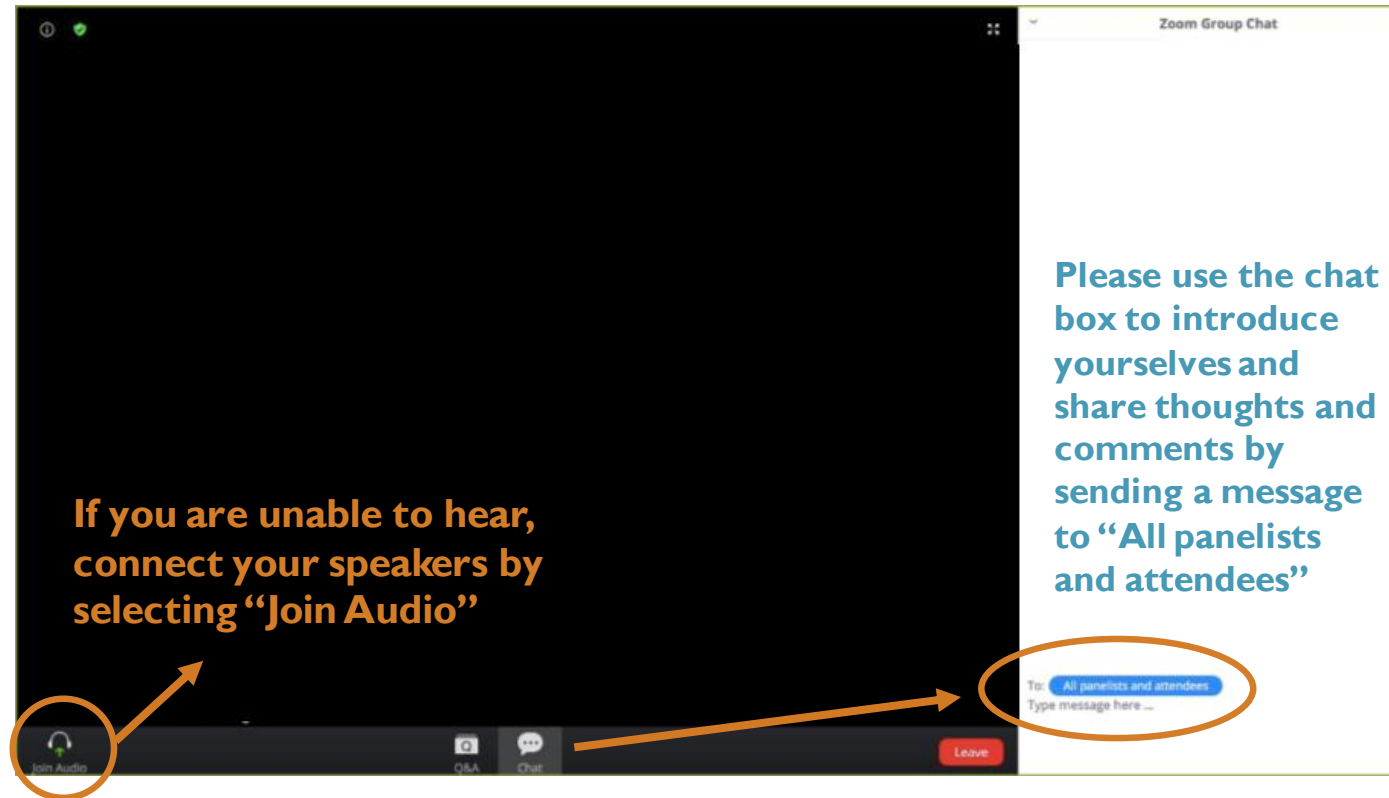
Dr. Perrie O'Tierney Ginn | Dr. Lynne Ausman



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WELCOME TO THE ZOOM WEBINAR





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Submit your questions for the panelists in the Q&A box

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The screenshot shows a Zoom meeting window with a Q&A box and a Zoom Group Chat window. The Q&A box has a "Welcome" message and a text input field labeled "Type your question here...". The Zoom Group Chat window shows a list of recipients: "All panelists" (checked) and "All panelists and attendees". The "To:" field is set to "All panelists".

Jordan Nutrition Innovation Lab Webinar

Impact of Maternal Obesity on Placental Function and Offspring Outcomes - Give Fish a Chance

Wednesday, March 1st, 2023
4:00-5:00 pm Jordan Time | 8:00-9:00 am US Eastern



LYNNE AUSMAN
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Tufts University | Tufts Medical Center



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IMPACT OF MATERNAL OBESITY ON PLACENTAL FUNCTION AND OFFSPRING OUTCOMES – GIVE FISH A CHANCE

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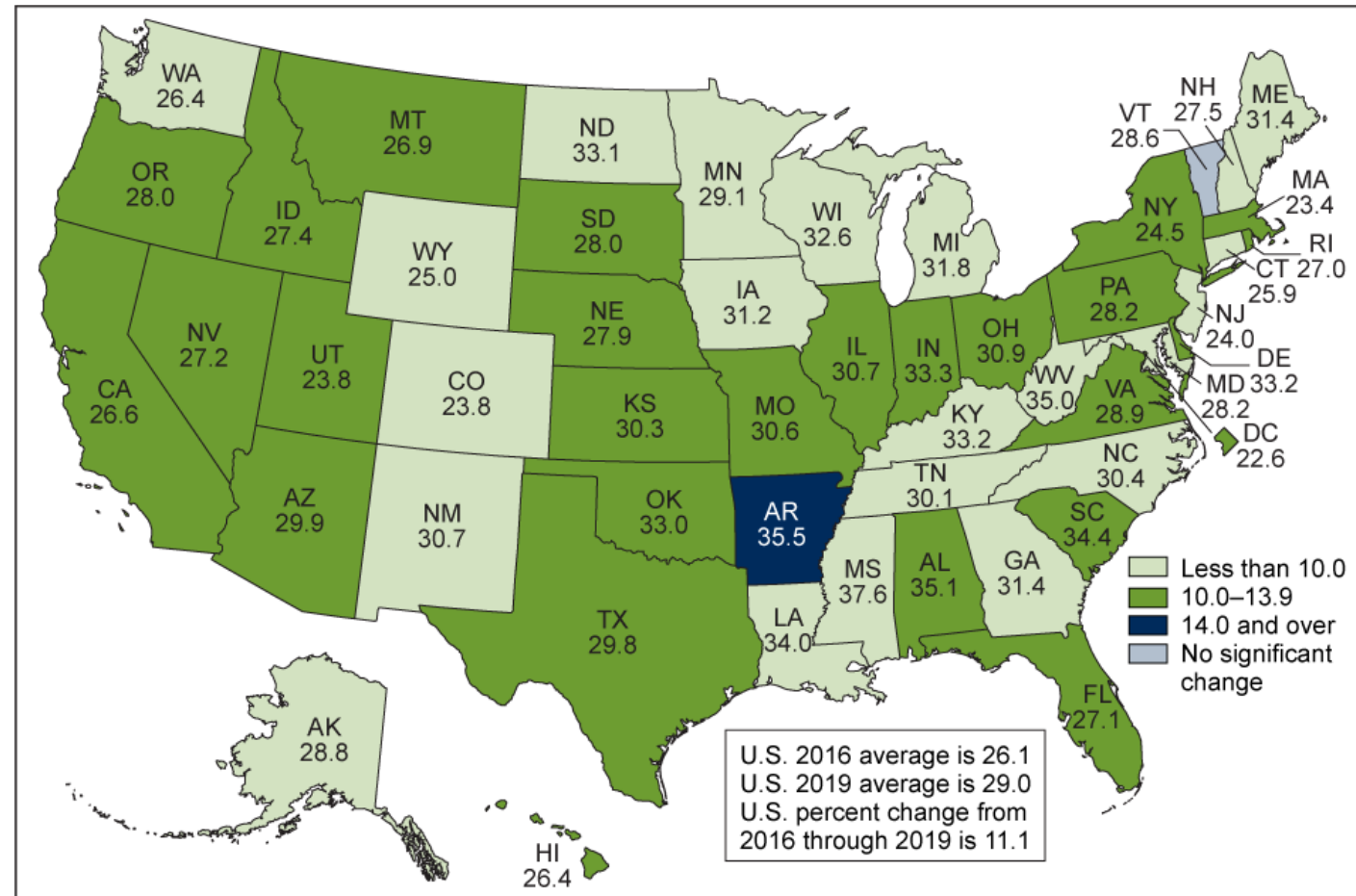
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29.0% US WOMEN ARE OBESE BEFORE PREGNANCY

Figure 4. Prepregnancy obesity, 2019 and percent change, 2016–2019: United States and each state



miscarriage

prematurity

gestational
diabetes

Cesarean birth

birth defects

preeclampsia

macrosomia

NOTES: Obesity is a body mass index of 30.0 or higher. Increases from 2016 through 2019 are significant ($p < 0.05$). Access data table for Figure 4 at: <https://www.cdc.gov/nchs/data/databriefs/db392-tables-508.pdf#4>.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Natality file.



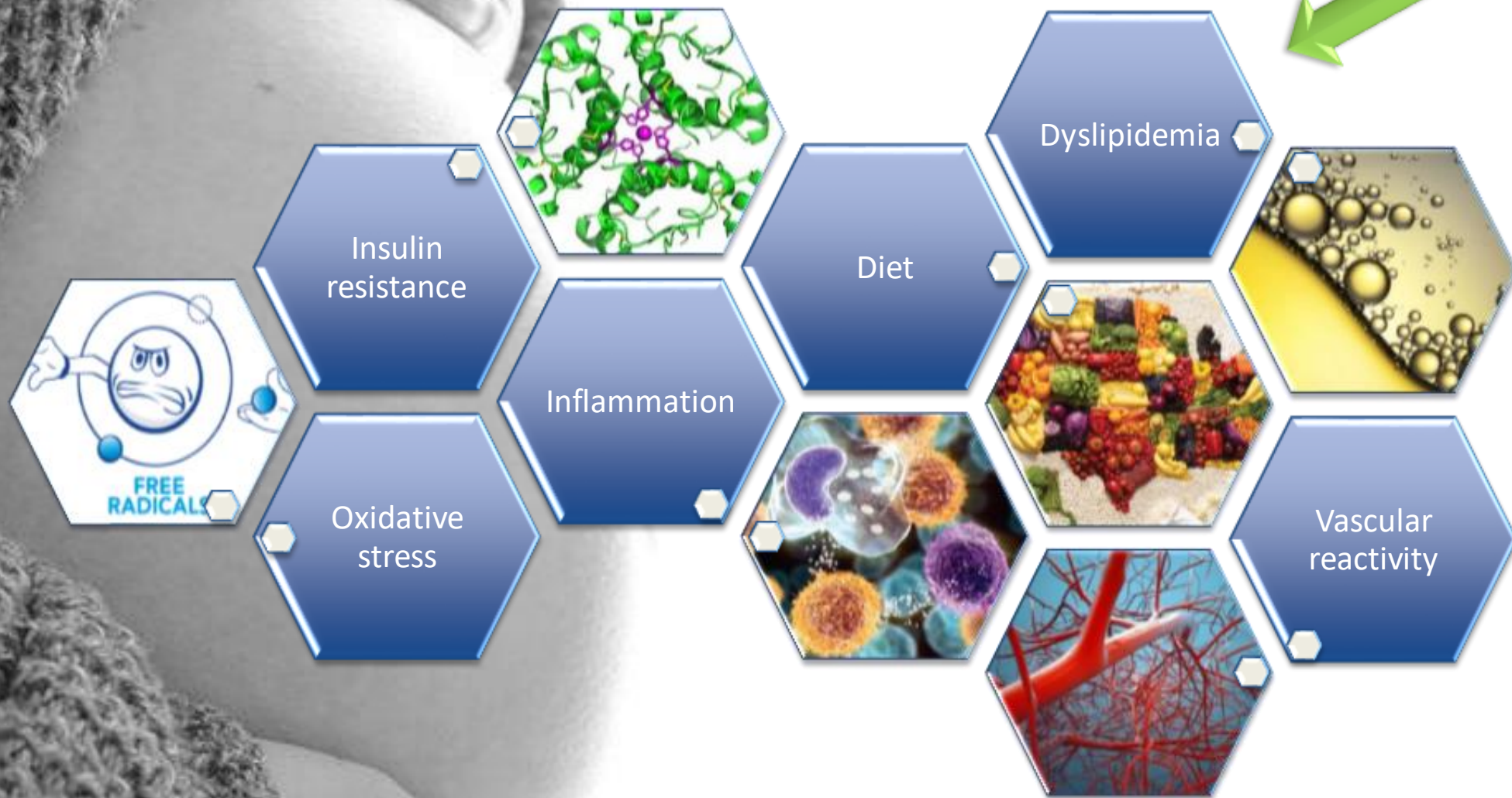
MATERNAL OBESITY INCREASES CARDIOMETABOLIC DISEASE RISK IN OFFSPRING

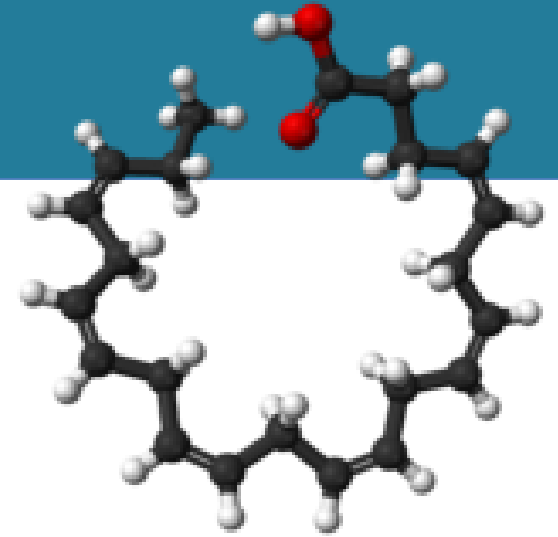


Typically, male offspring are at higher risk

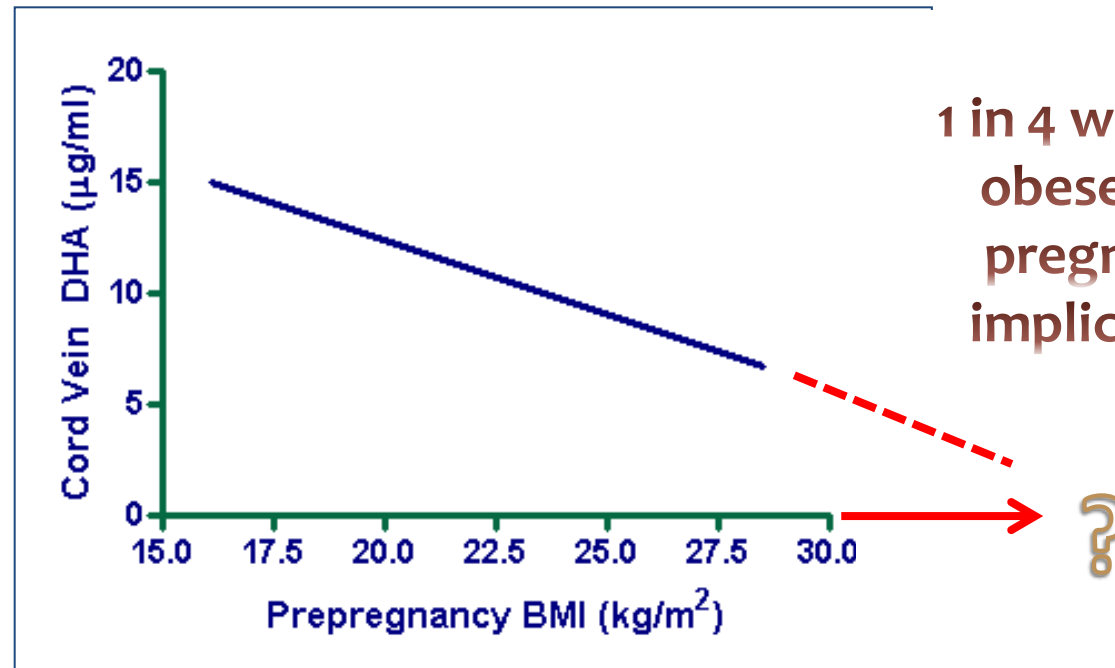
Dearden, 2018

↑ TGs
↑ FFA





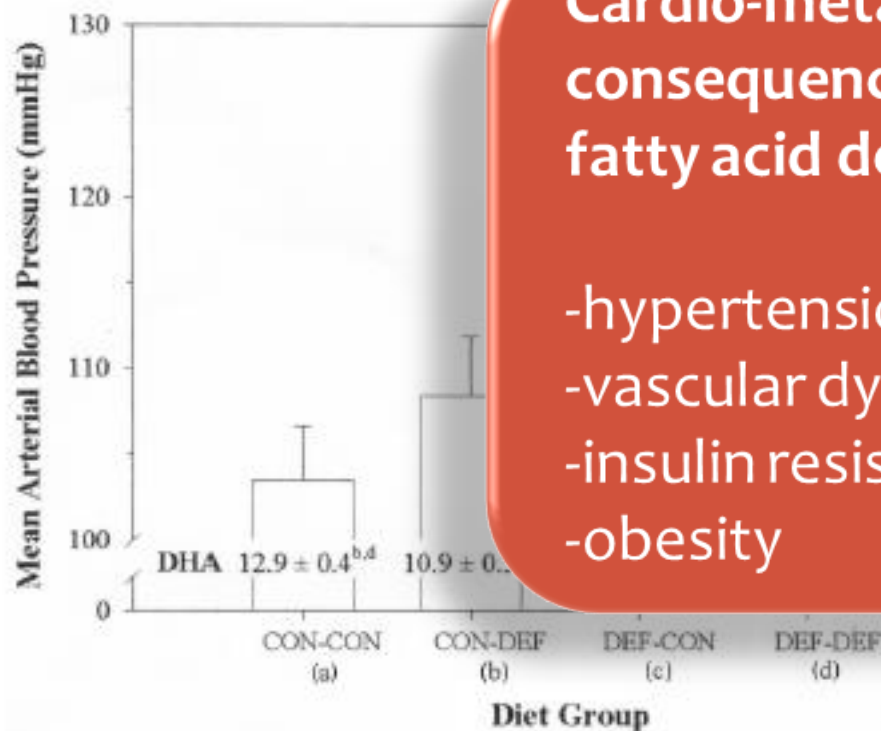
MATERNAL BMI & CORD DHA LEVELS



1 in 4 women are
obese before
pregnancy...
implications??



IMPORTANCE OF FA TO THE FETUS



Cardio-metabolic consequences of essential fatty acid deficiency:

- hypertension
- vascular dysfunction
- insulin resistance/diabetes
- obesity

Early omega-3 PUFA-deficiency, if subsequent supply, resulted in hypertension. The most marked hypertension occurred in animals raised and fed on DEF. Conversely, adequate omega-3 PUFA supply at an early age provided protection against the increase in MAP associated with omega-3 deficiency. Clearly, the early, perinatal nutritional status profoundly affects adult blood pressure. These findings implicate a critical period with regard to the functionality of neural-DHA, as it pertains to the control of blood pressure. The exact mechanisms of these early developmental changes remain to be elucidated.



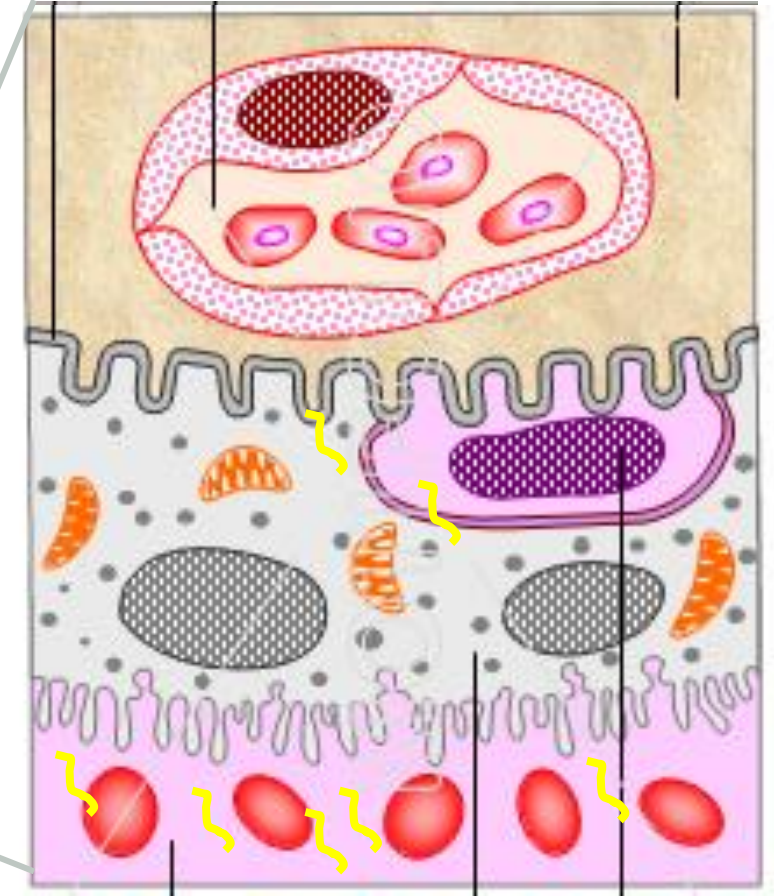
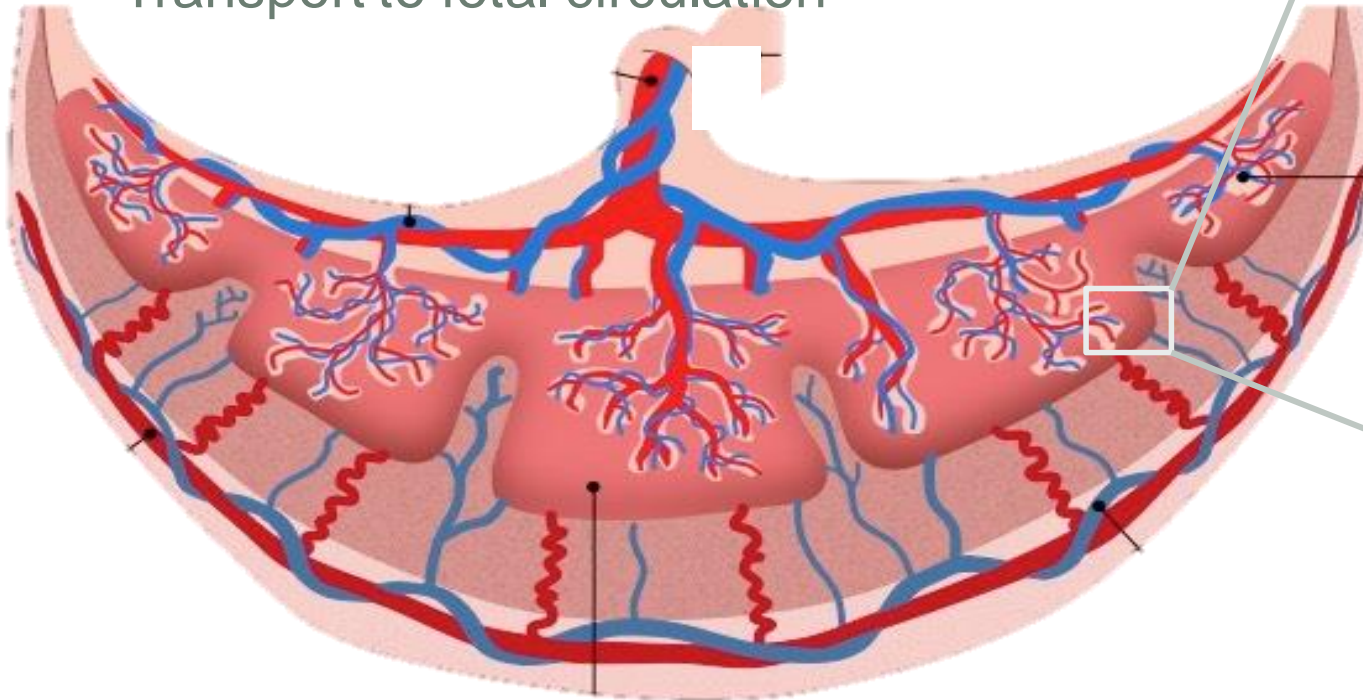
WHAT CONTROLS FETAL FA DELIVERY?

Maternal supply

Uptake

Metabolism/storage

Transport to fetal circulation

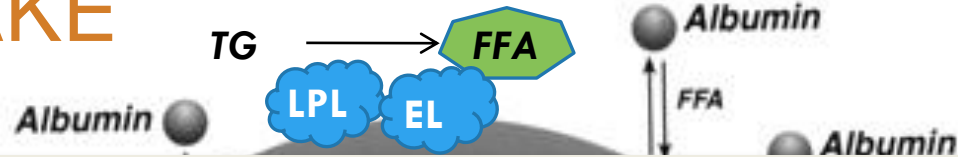




PLACENTAL FA DELIVERY

Effect of maternal obesity

PLACENTAL FA UPTAKE

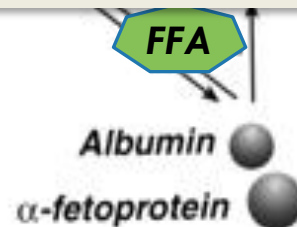


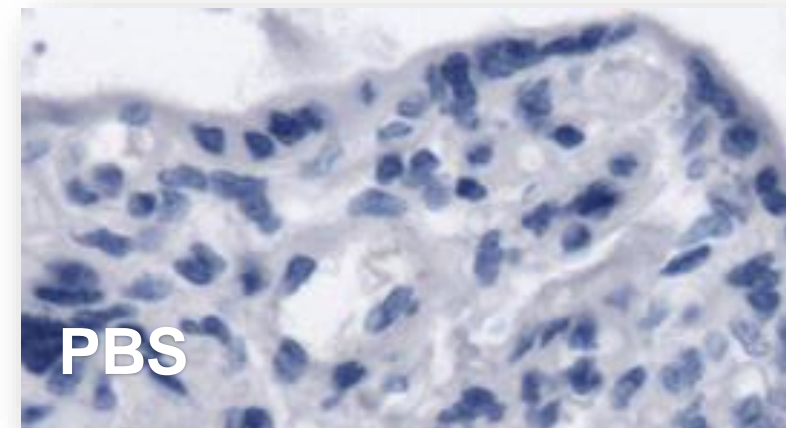
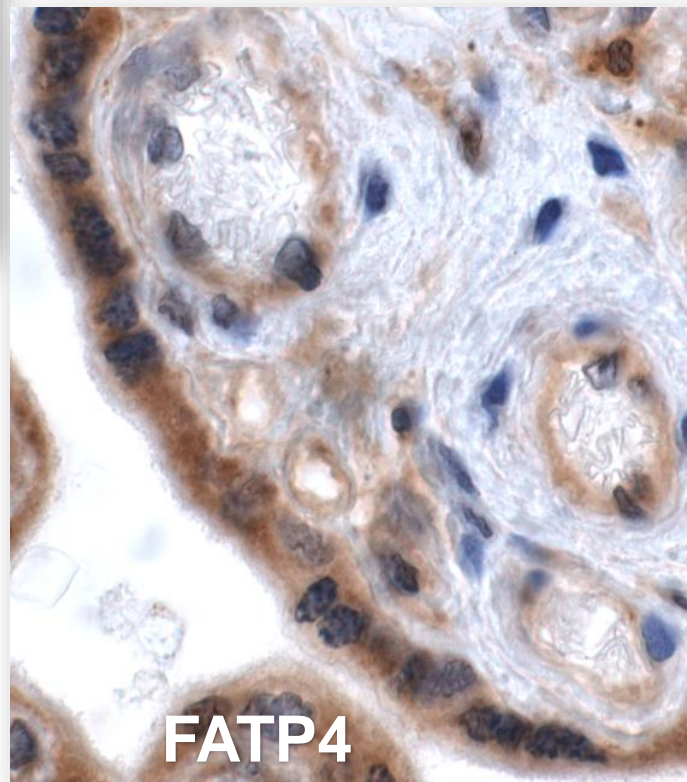
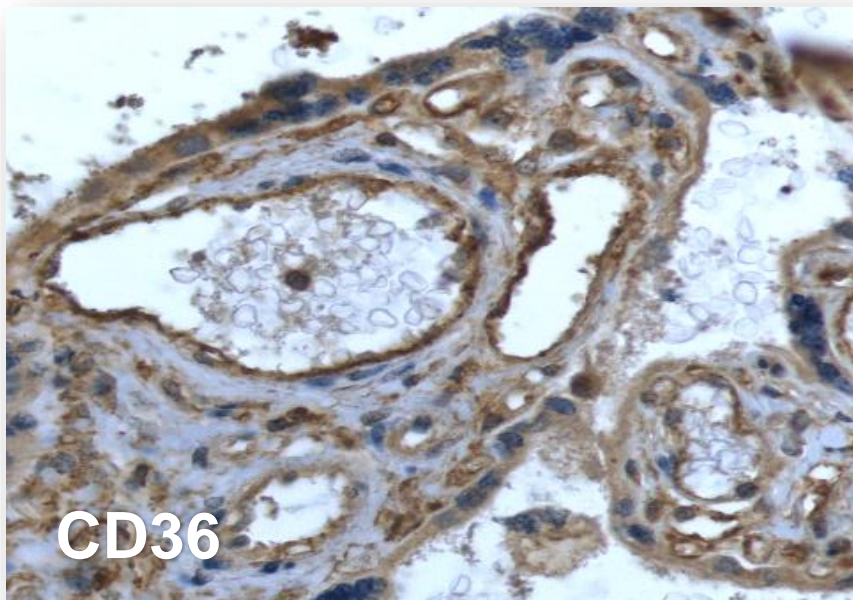
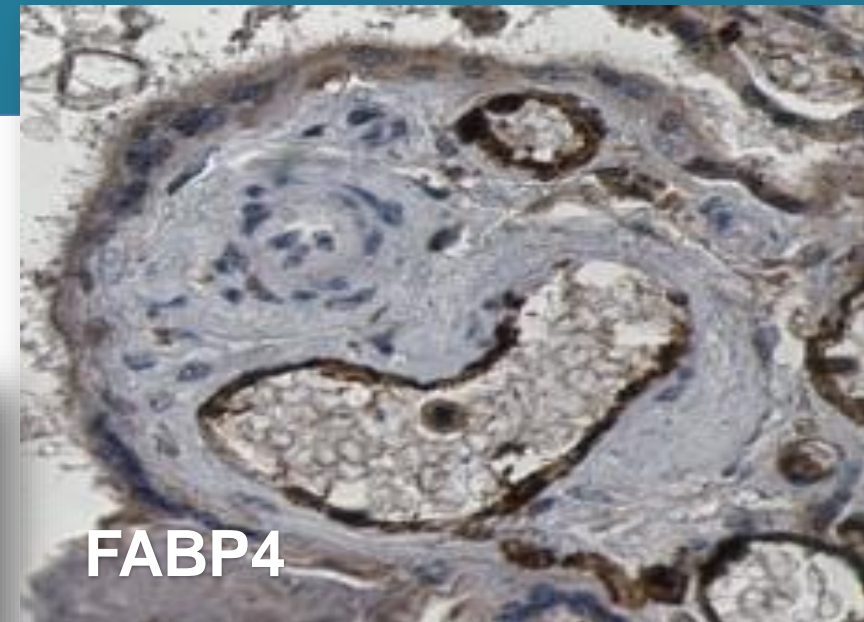
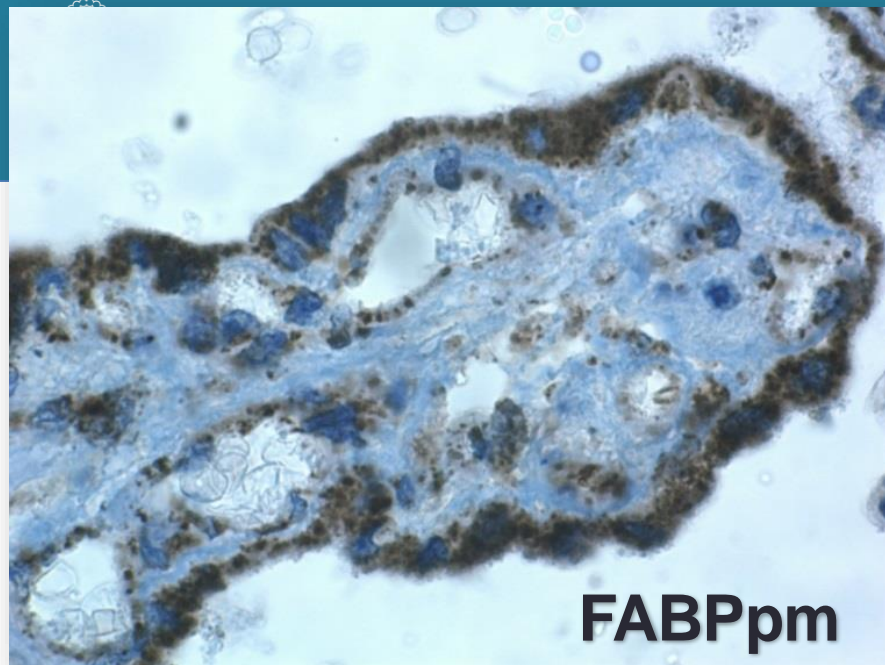
Placental FA uptake is impaired in patients with obesity and diabetes

Fatty acid transporters and binding proteins are lower in obese human term placentas (males)

- Data from [Dube 2012](#), [Brass 2013](#), [Araujo 2013](#), *(in males only) [Pagan 2013](#)

FATP4 ↓↔
CD36 ↑↓* ↓*
FABPpm ↓*
FABP1 ↓
FABP3 ↓↔
FABP5 ↓*
ACSL1 ↓







SUMMARY

- FA transporters and/or uptake is generally lower in placentas of obese patients
- FA transporter levels are very high in the trophoblast layer, suggesting that uptake regulation at this structure may be limited
- After uptake – what happens to the lipids?



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FA METABOLISM

What does the placenta do with lipids?



PLACENTA METABOLIZES FATTY ACIDS

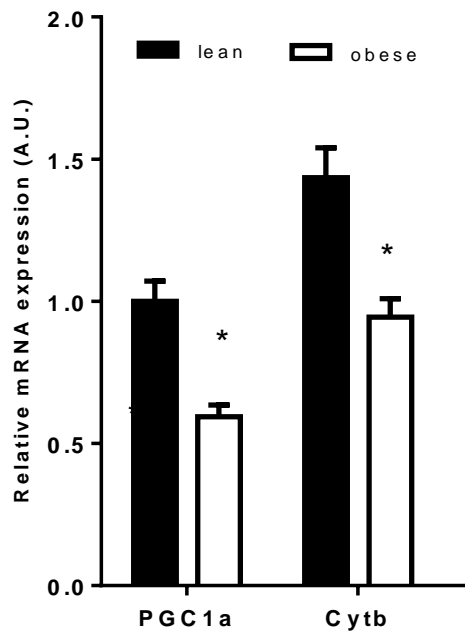
FA Oxidation

- Placenta oxidizes fatty acids even in the presence of glucose
- Drives FA uptake
- Fetuses with FAO disorders:
 - placental insufficiency due to low ATP production → fetal growth restriction, prematurity
- Placenta FAO important for proper development of the fetal-placental unit and health of the mother

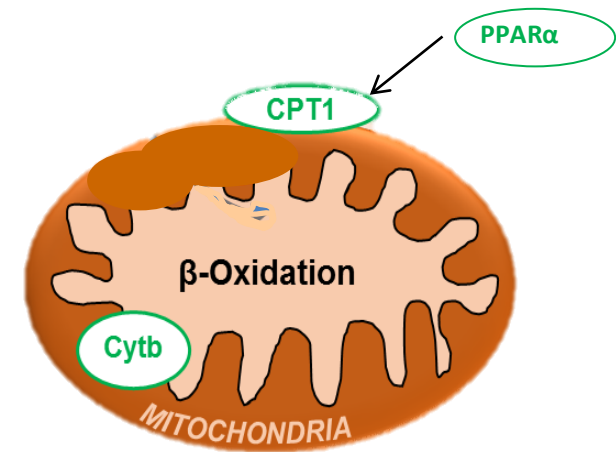
FA Esterification

- Protects trophoblast from lipotoxicity
- Leads to PL (structural lipids) and TG (storage) synthesis
- Placenta has lipid droplets that are sensitive to maternal nutrition/diet
- May be an essential intermediate step between uptake and delivery to fetus
- Placenta lipid pools are key to FA transfer dynamics

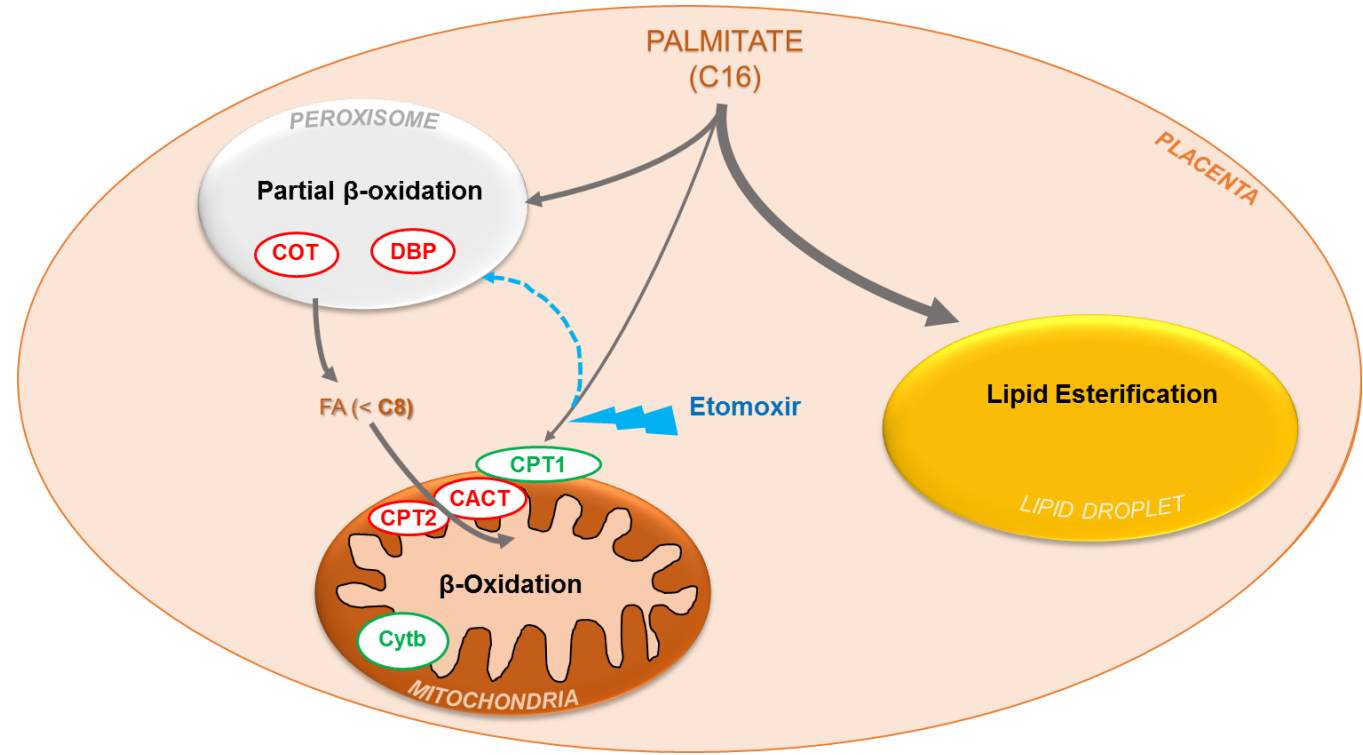
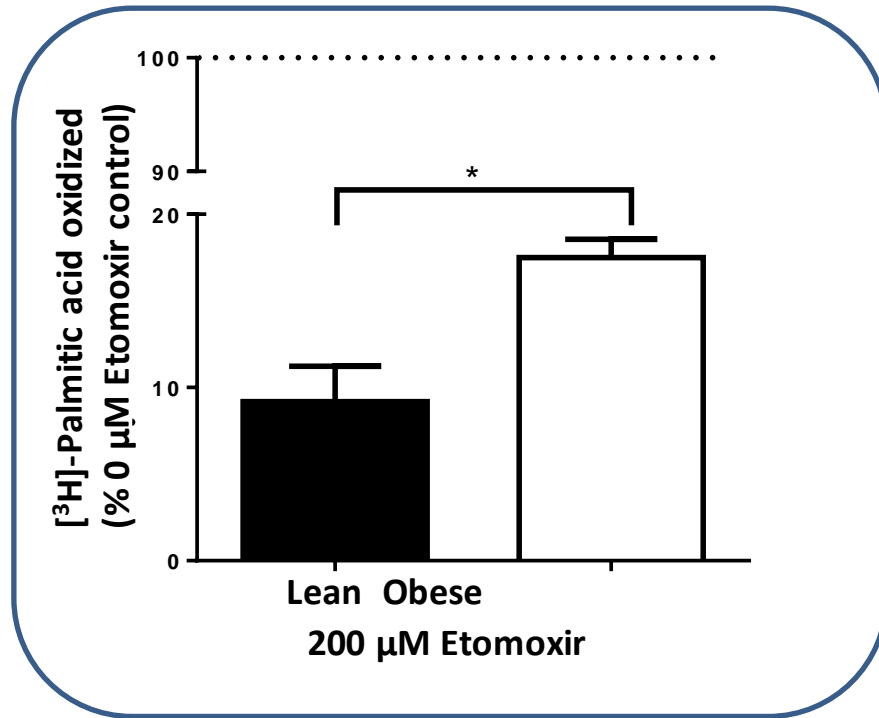
MATERNAL OBESITY ALTERS PLACENTAL LIPID METABOLISM



↓ mitochondrial
number in placentas of
patients with obesity

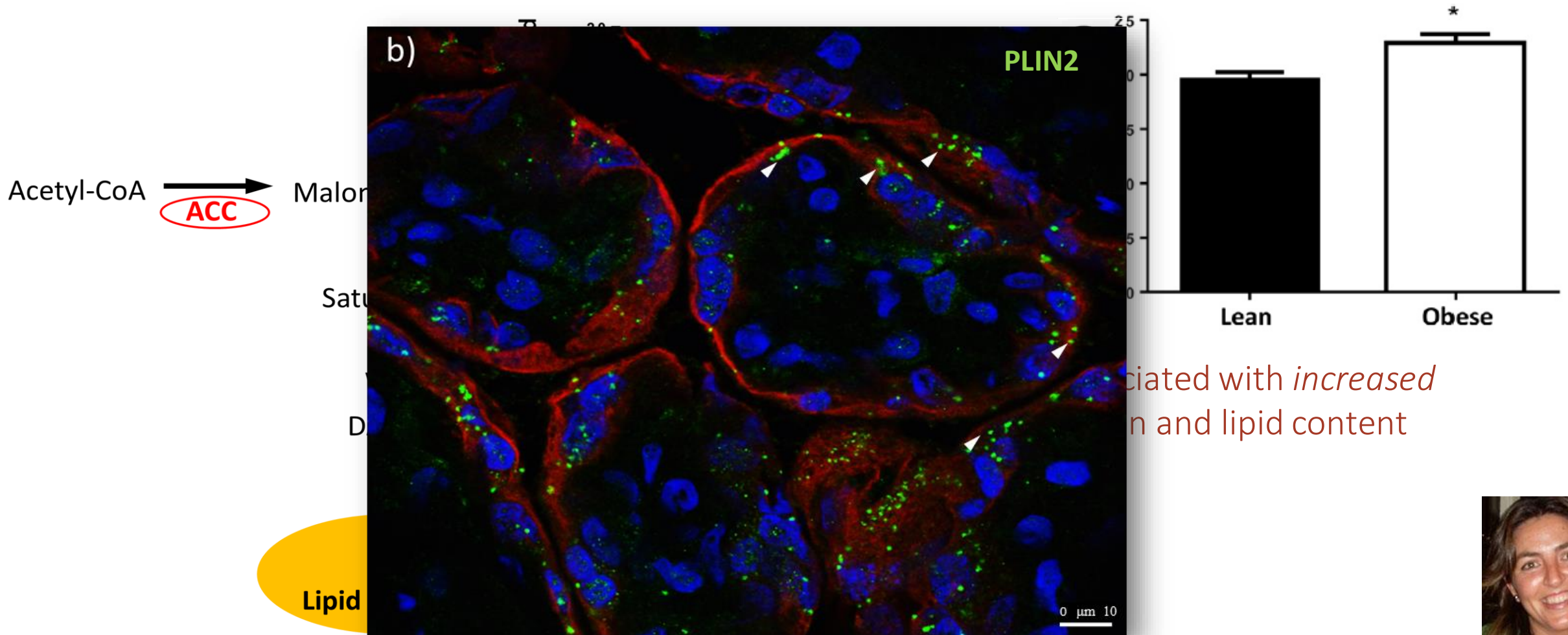


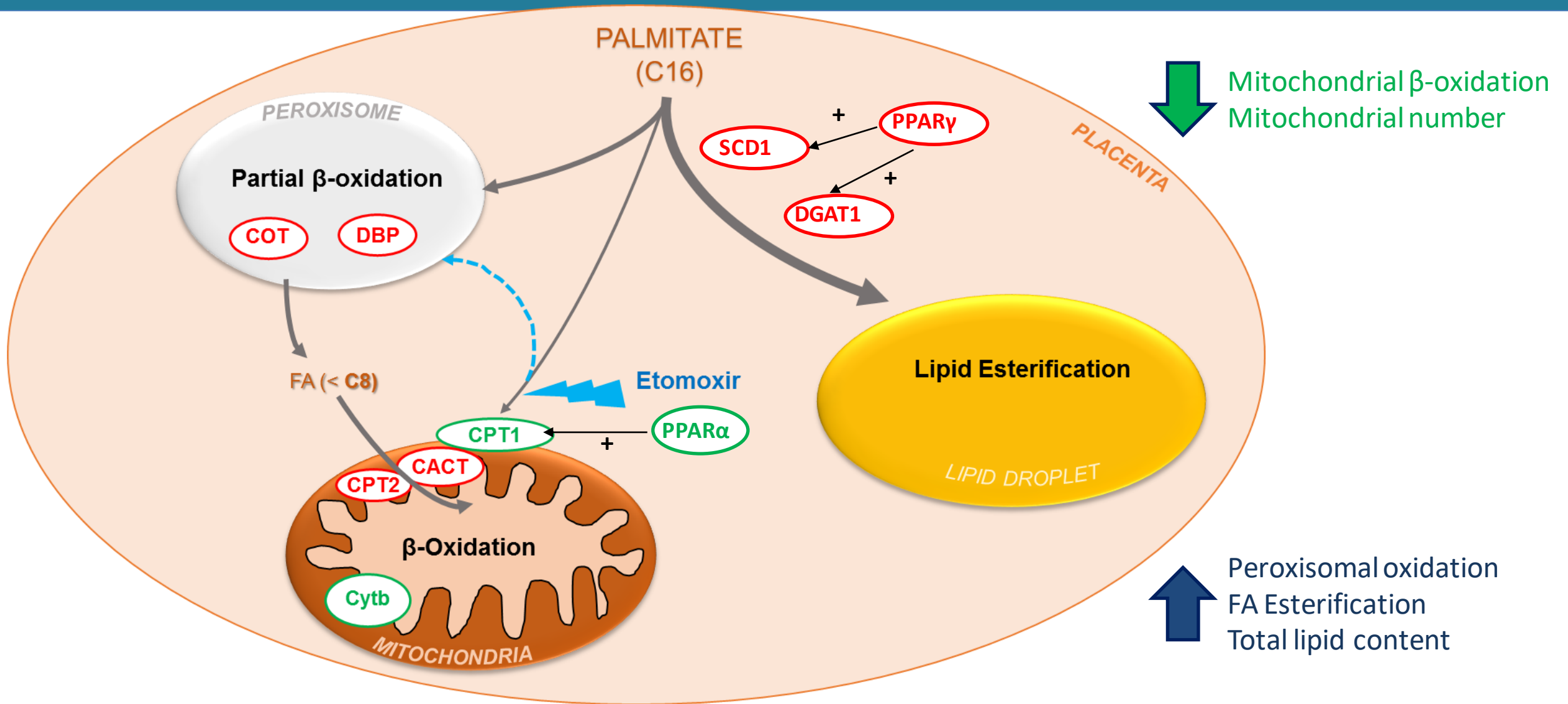
MATERNAL OBESITY ALTERS PLACENTAL LIPID METABOLISM



↑ Peroxisomal contribution in FAO in placentas of women with obesity

MATERNAL OBESITY ALTERS PLACENTAL LIPID METABOLISM







SUMMARY

- Placental FA metabolism is essential for placental function, fetal growth, and maternal health
- Mitochondrial number and β -oxidation capacity are reduced
- Peroxisomal β -oxidation capacity is greater; overall FA oxidation maintained
- FA esterification and storage pathways are increased in placentas of obese patients

ROLE OF LIPID METABOLISM IN NUTRIENT TRANSPORT TO FETUS

The influence of placental metabolism on fatty acid transfer to the fetus[§]

J Lipid Res, 2016

Simone Perazzolo
Rohan M. Lewis

Placental metabolism may drive FA uptake and modify neonatal fat accrual

Int J Obesity

Placental mobilization of
altered materno-fetal

Birgit Hirschmugl^{1,2}. Simone Perazzolo^{3,4}. Bram G. Sengers^{3,4}. Rohan M. Lewis^{4,5}. Michael Gruber^{1,2}. Gernot Desoye¹. Christian Wadsack^{1,2}

Received: 24 April 2020 / Revised: 8 January 2021 / Accepted: 1 February 2021

- The decrease in DHA mobilization from placental metabolic pool in obese women results in lower DHA levels in the fetal circulation
- Placental lipid pool is key to transfer dynamics



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CAN WE MODIFY PLACENTAL FA METABOLISM?

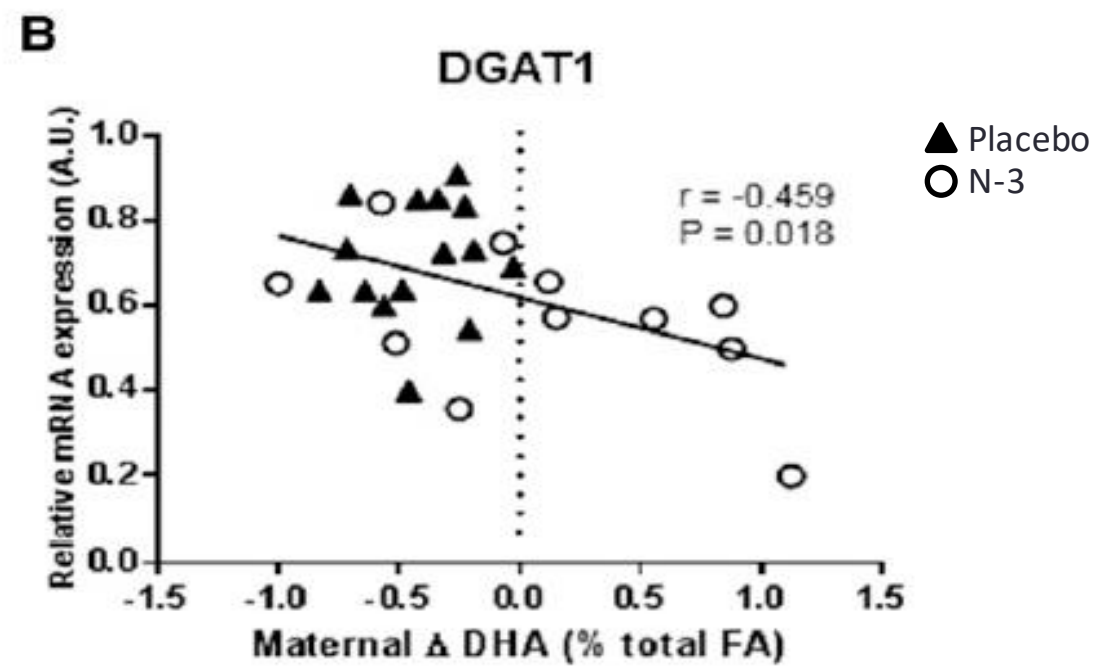
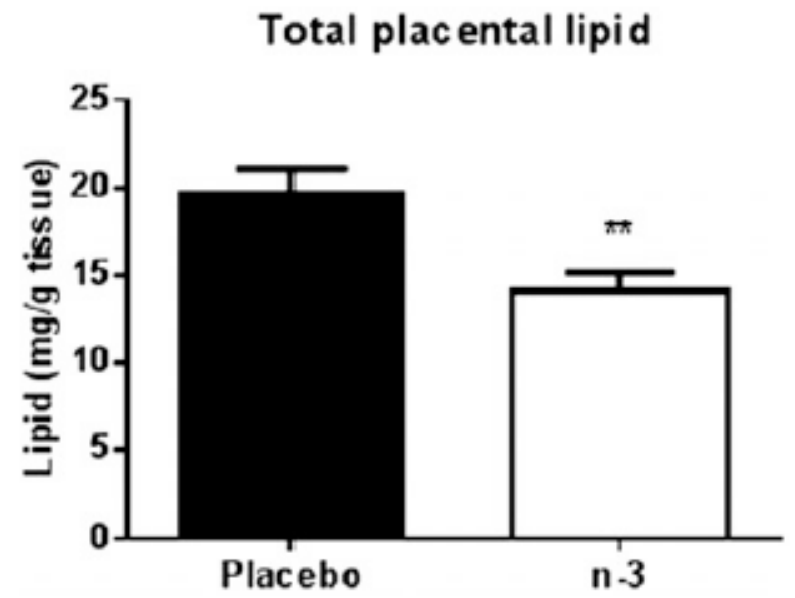
Potential for nutritional intervention

FISH OIL SUPPLEMENTATION DURING PREGNANCY



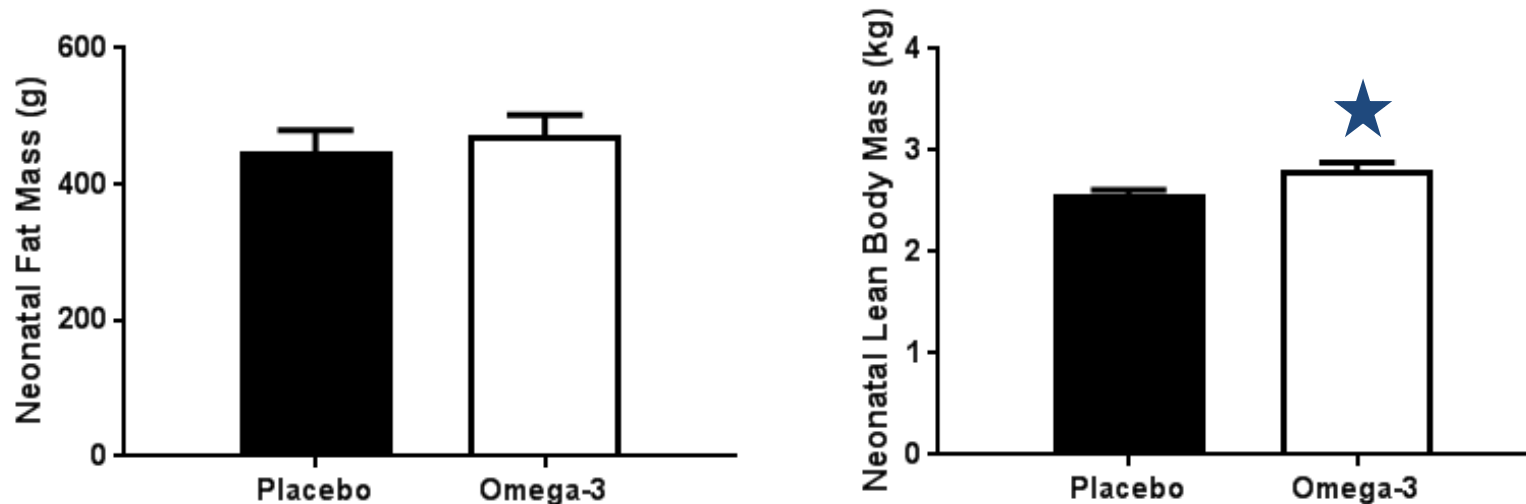
Effect of ω -3 supplementation on placental lipid metabolism in overweight and obese women^{1,2}

Virtu Calabuig-Navarro,³ Michelle Puchowicz,⁴ Patricia Glazebrook,³ Maricela Haghiac,³ Judi Minium,³ Patrick Catalano,³ Sylvie Hauguel deMouzon,³ and Perrie O'Tierney-Ginn^{3}*



No effect on FA oxidation

EFFECT ON FETAL FAT ACCRUAL



- In stratified analyses, the effect of FO on FFM was strongest in obese patients, patients with high n-6/n-3 dietary intake, and those with male offspring

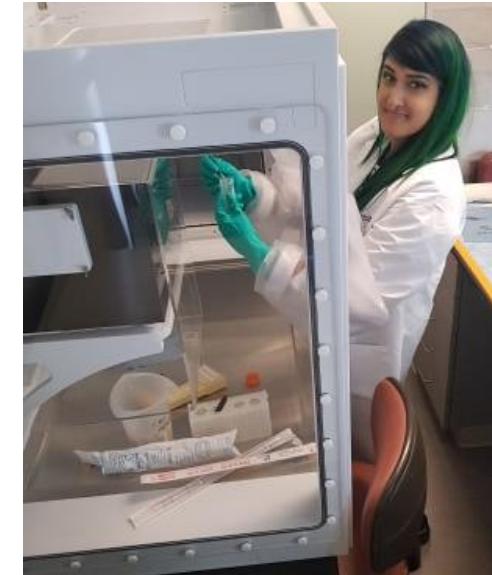
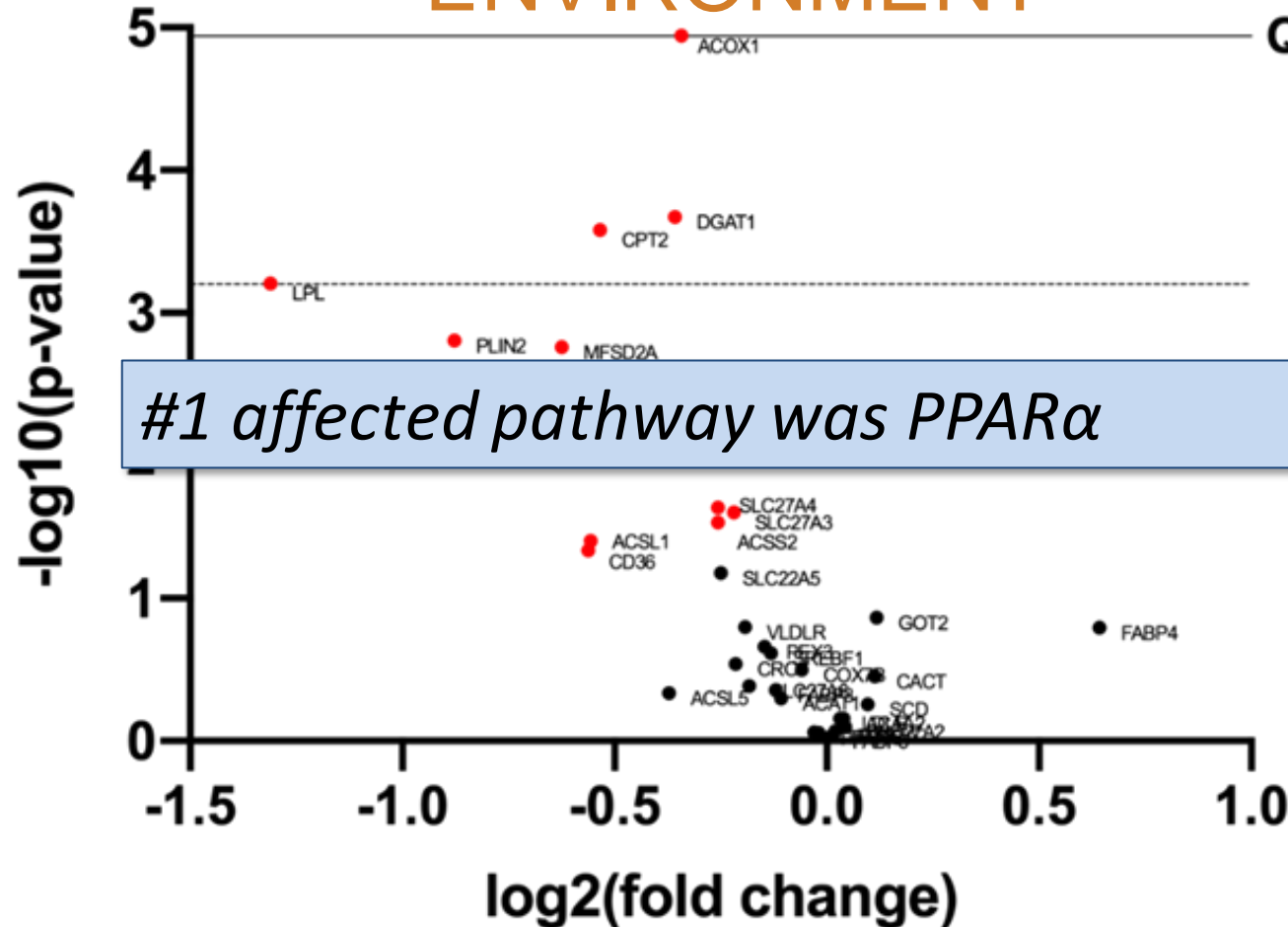
*Adjusted for fetal sex and GA; β 126g, 95% CI: 3, 249



SUMMARY

- Placental FA storage and esterification pathways are sensitive to maternal omega-3 levels
- Unclear how changes in placental lipid metabolism affect fetal fat accrual
- Supplementation did not start until 14-16 weeks of pregnancy...what if it is too late?

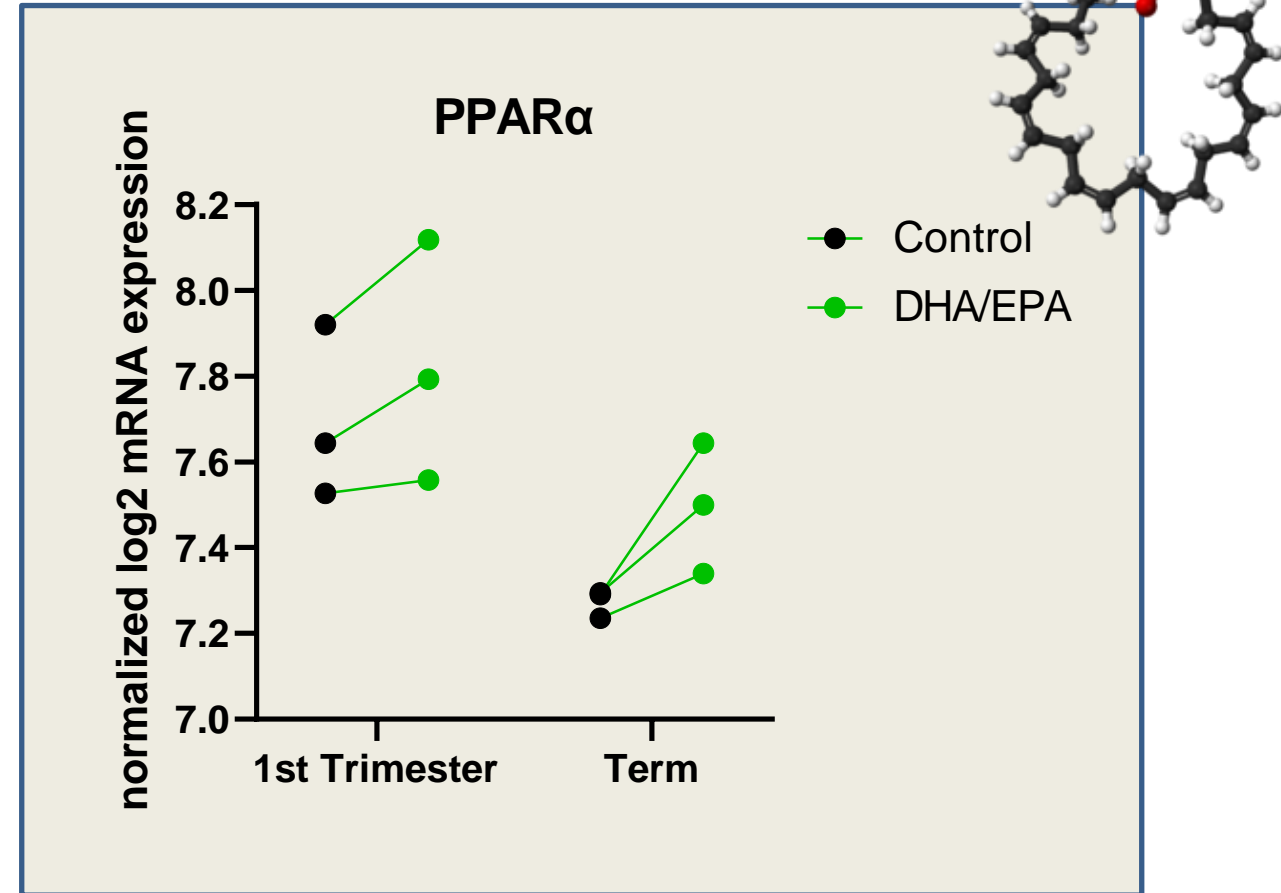
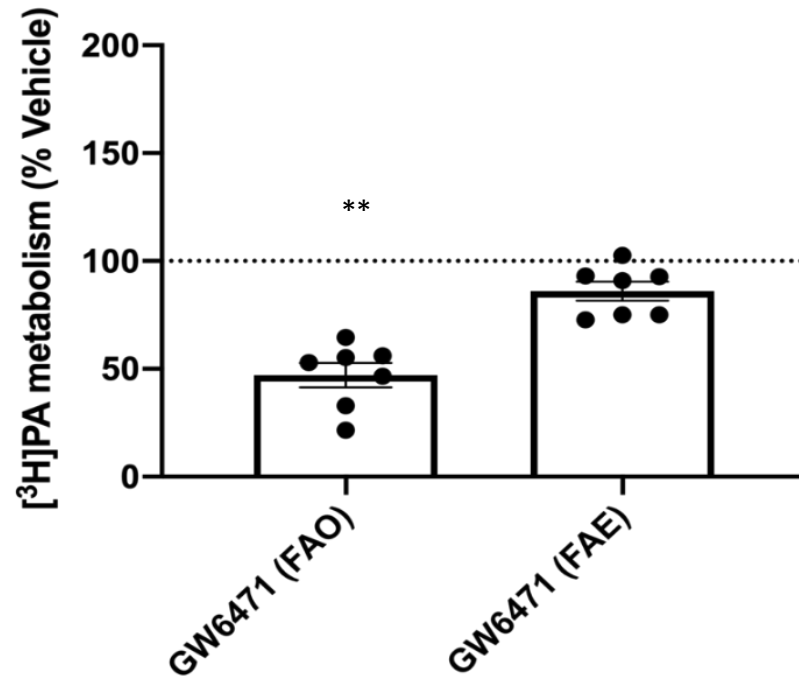
1st TRIMESTER PLACENTA IS SENSITIVE TO MATERNAL ENVIRONMENT



*Adjusted for GA: avg 10 weeks (range 6-14 w)

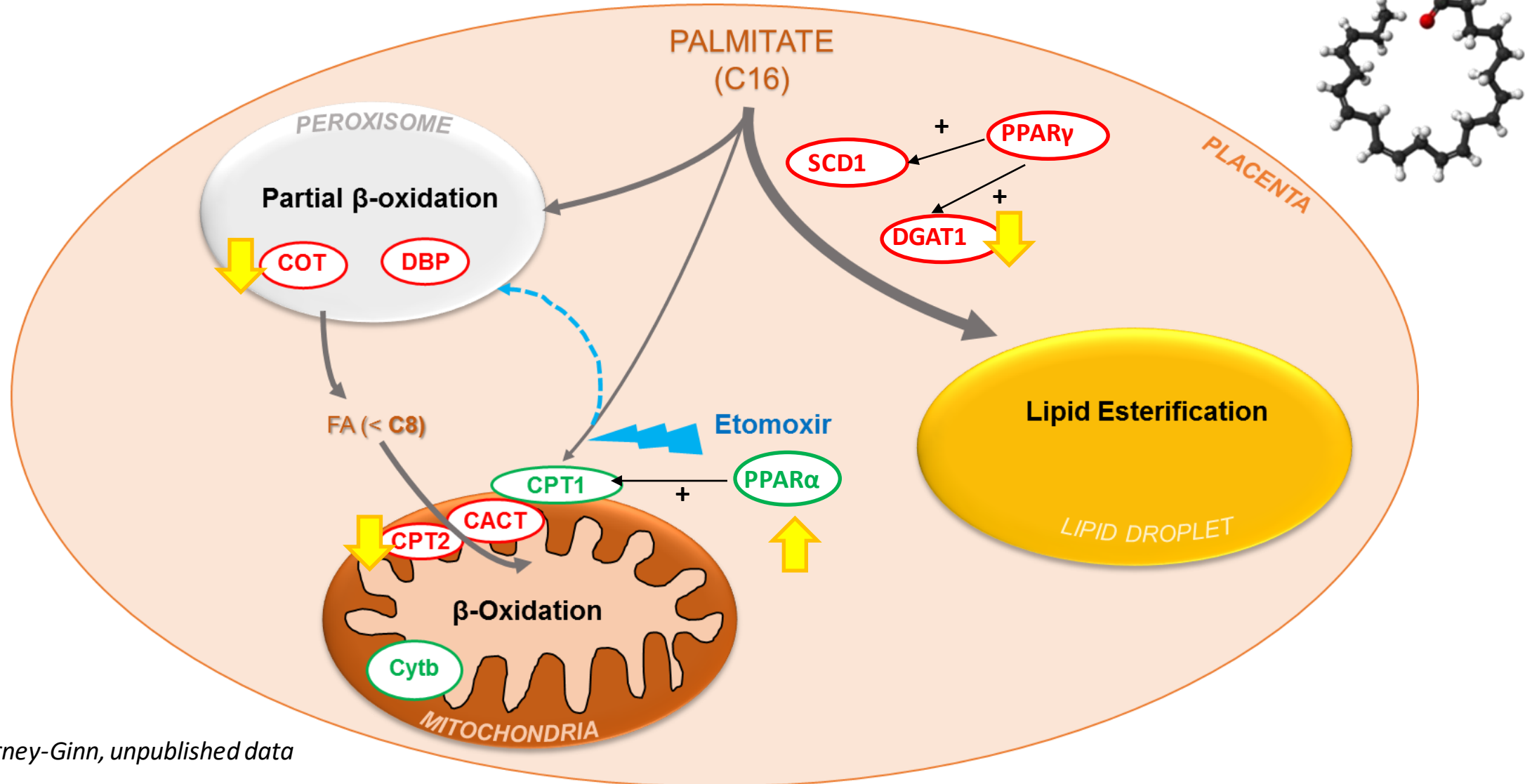
Rasool, et al. Sci Reports, 2022

PPARA IS MASTER REGULATOR OF LIPID METABOLISM





N-3 FA MODULATE PLACENTAL LIPID METABOLISM





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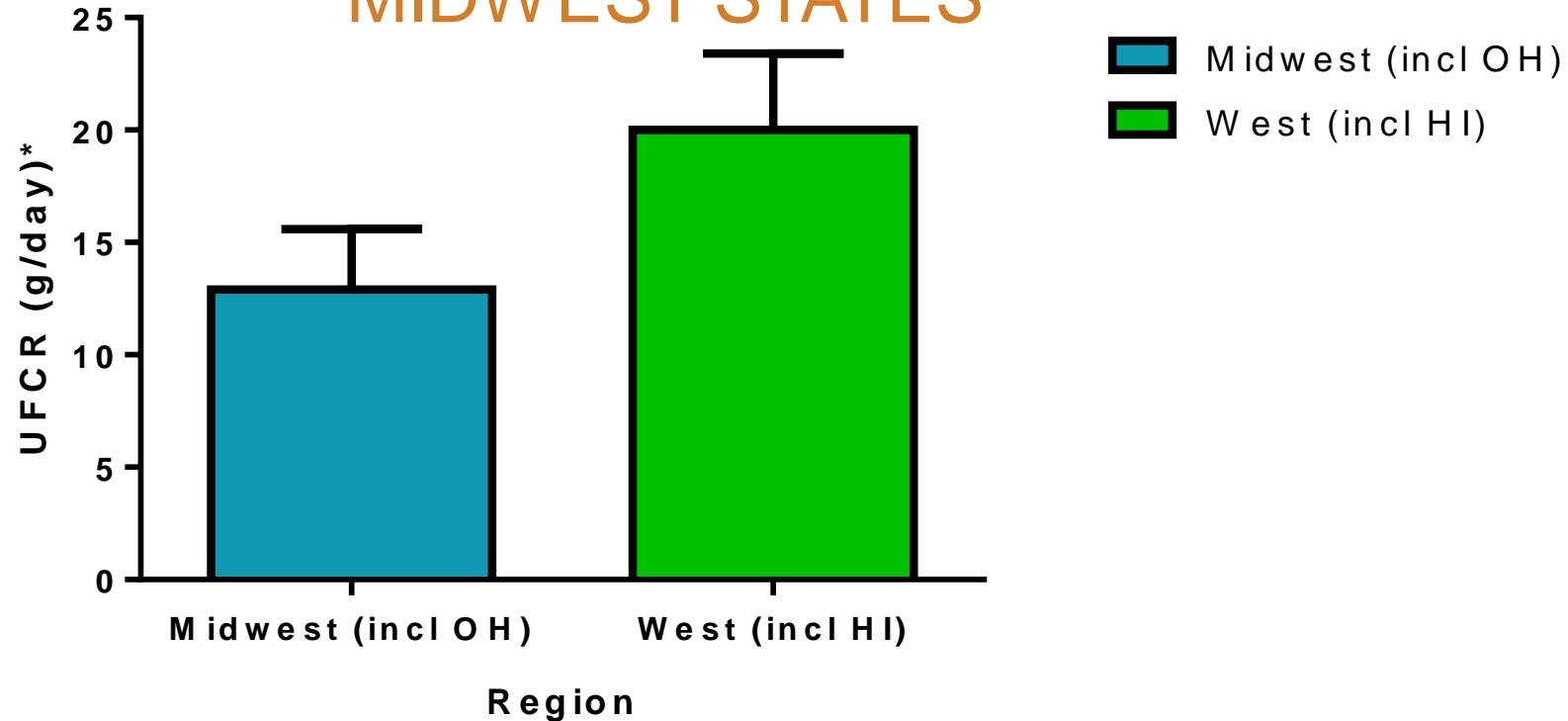


EFFECT OF A HIGH OMEGA-3 ENVIRONMENT

Preconception exposure



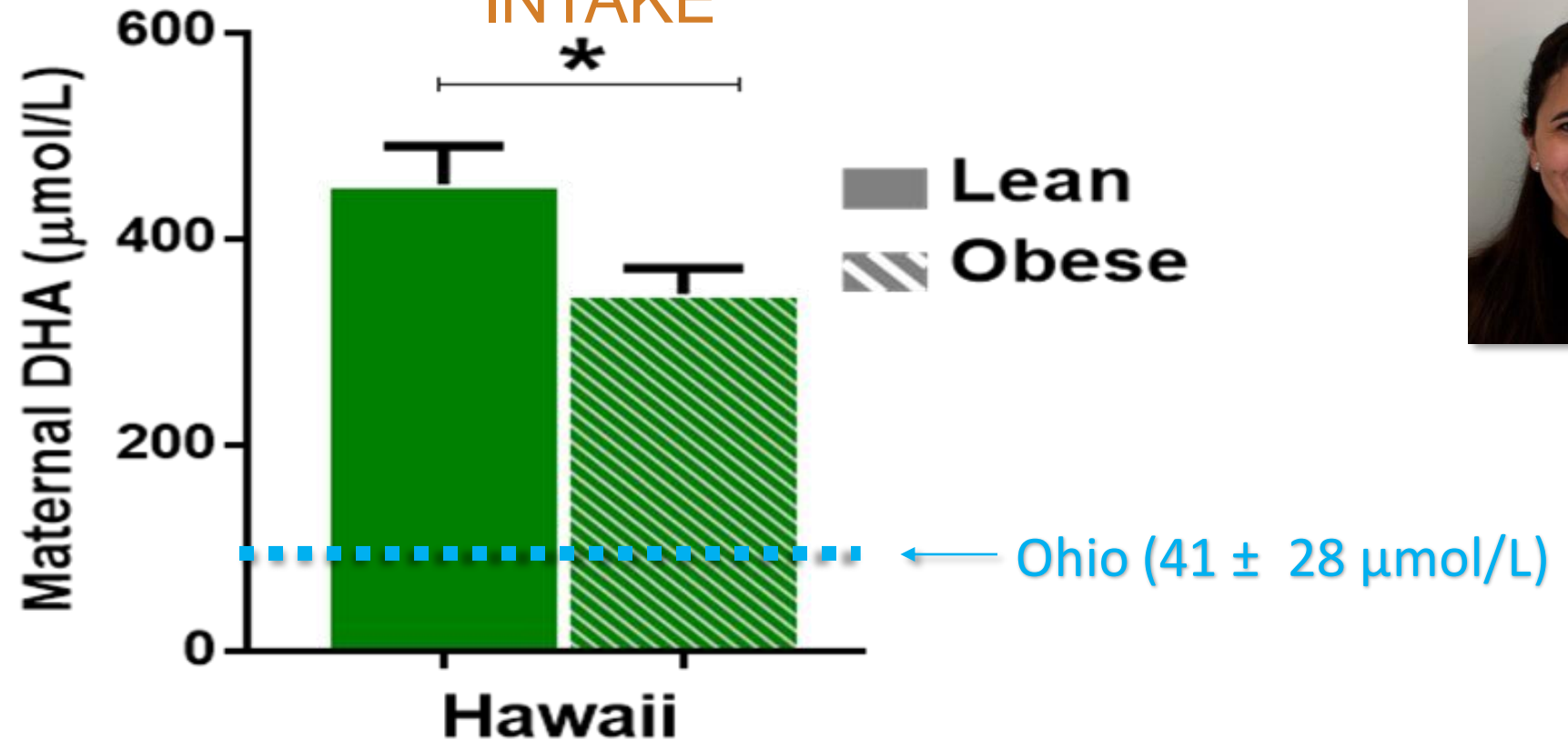
FISH CONSUMPTION IS GREATER IN WESTERN VS MIDWEST STATES



*Usual fish consumption rate estimate. Total fish; >21 years
Data is median (95% CI)

Data from NHANES 2003-2010, EPA-820-R-14-002, April 2014

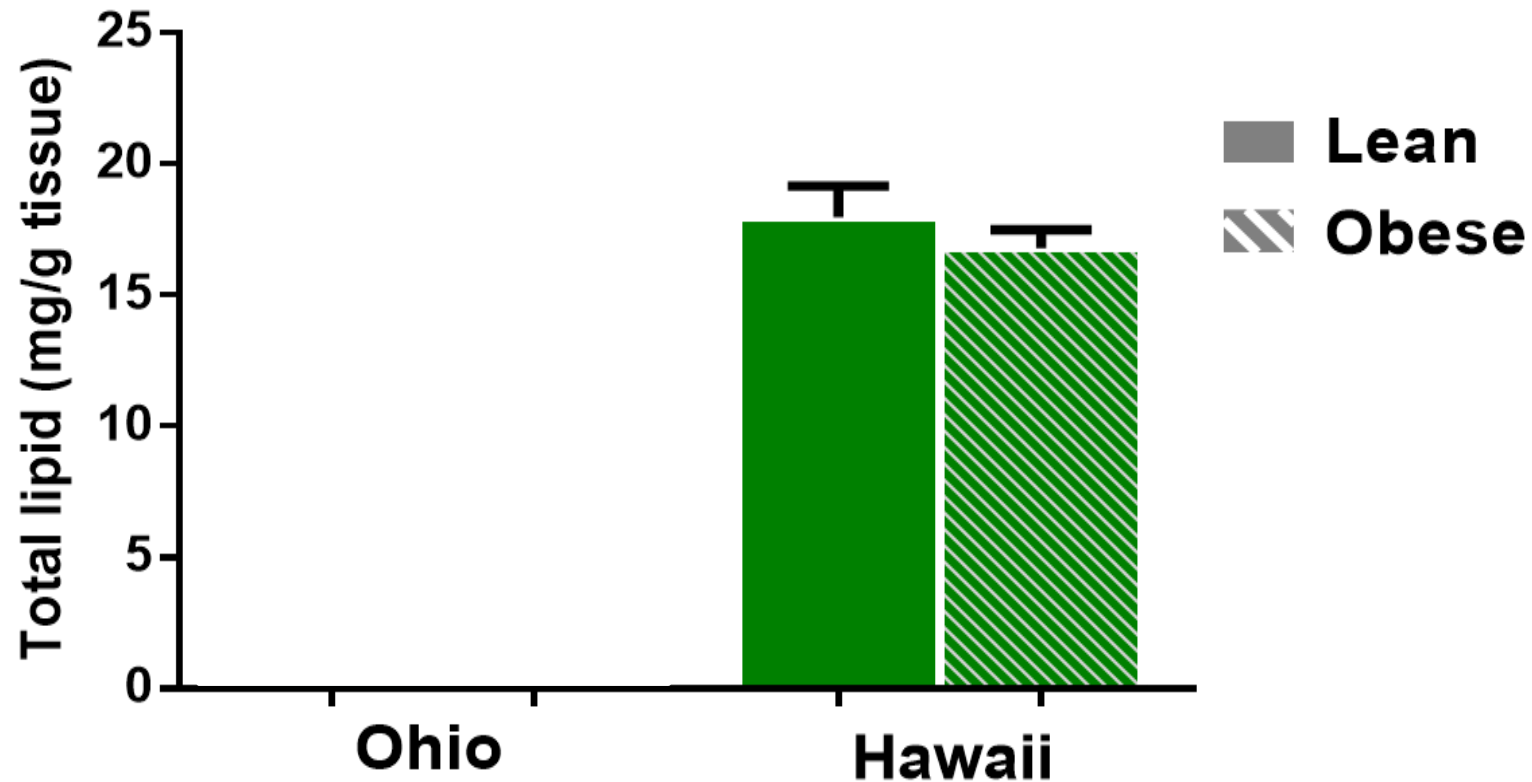
MATERNAL DHA IS HIGHER IN THE REGION OF HIGH OMEGA-3 INTAKE



Hypothesis: chronically high maternal omega-3 levels may suppress the effects of maternal obesity on placental lipid metabolism



PLACENTAL LIPID CONTENT IS NOT DIFFERENT BETWEEN LEAN AND OBESE PATIENTS IN HAWAII



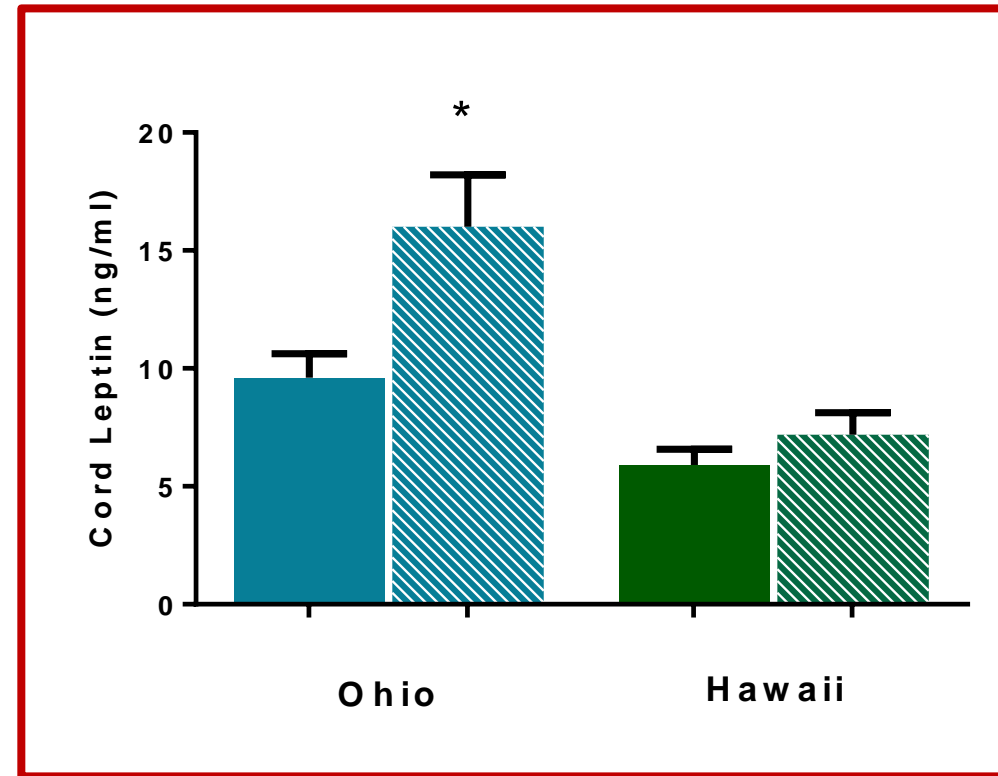
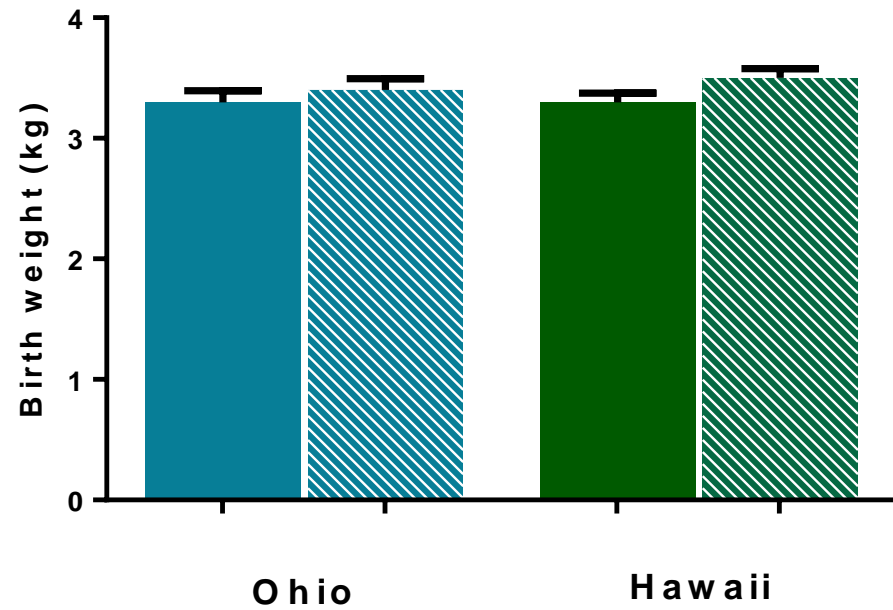
Alvarado et al., Placenta, 2018



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FETAL GROWTH IN HIGH VS LOW OMEGA-3 ENVIRONMENTS



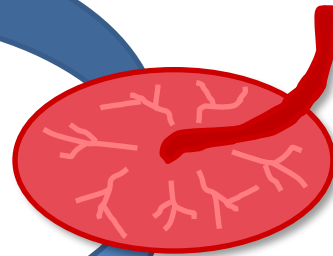
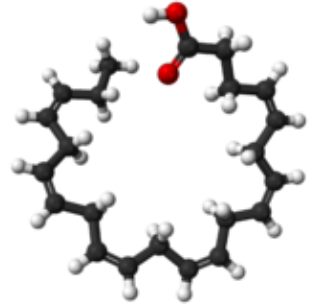
SUMMARY

- High maternal omega-3 levels may suppress effects of maternal obesity on placental lipid metabolism
- The nutritional environment is a critical consideration when studying obesity effects
- Lower neonatal leptin (a marker of fat mass) in offspring of obese patients in Hawaii compared to Ohio, suggest reduced fat accrual *in utero*.



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QUESTIONS REMAIN

- How changes in placental lipid metabolism affect placental function and fetal fat deposition
- Chronic omega-3 consumption modifies the effect of maternal obesity on metabolic pathways...how? Whole fish vs. supplements? Do all patients benefit?
- What is the role of the maternal metabolic environment in early pregnancy on these outcomes? Are interventions starting too late?



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O'Tierney-Ginn Lab BBQ, pre-COVID era

Placenta
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Thank you!

Patrick Catalano, MD; Tufts

Sylvie Hauguel deMouzon, PhD; Case Western

Hoppel, PhD; Case Western

Michelle Puchowicz, PhD; U of Tennessee

Stacy Tsai, MD; U Hawaii





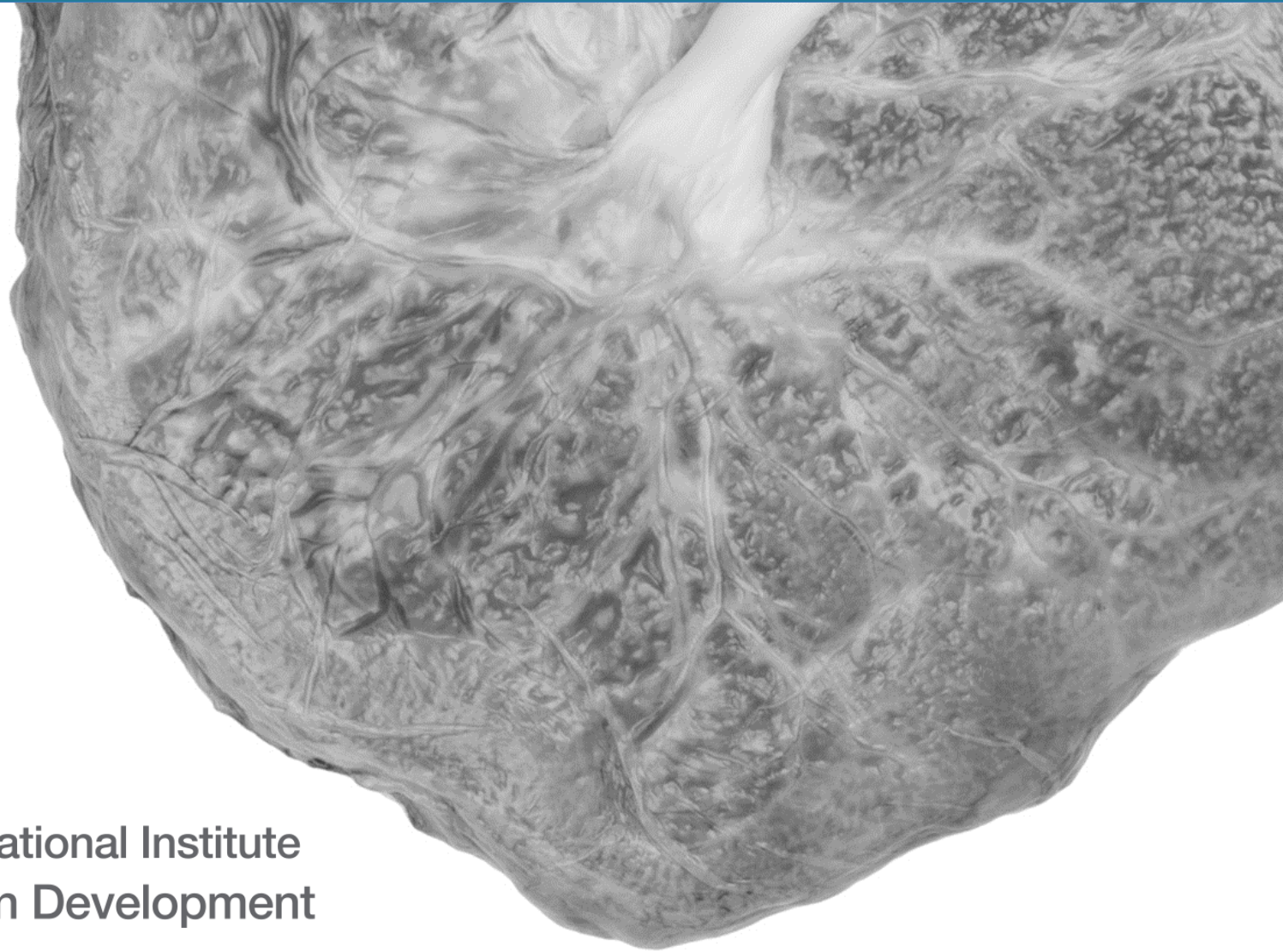
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Thank you!



Eunice Kennedy Shriver National Institute
of Child Health and Human Development





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Q&A



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