

Preconception Omega-3 Fatty Acid Supplementation and the Prevention of Toxicant-Associated Preterm Birth in a Mouse Model

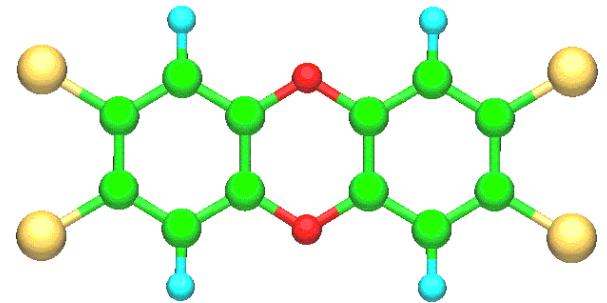
**Kaylon L. Bruner-Tran, PhD,
Kevin G. Osteen, PhD**

**Vanderbilt University Medical Center
Women's Reproductive Health Research Center
Nashville, TN USA**

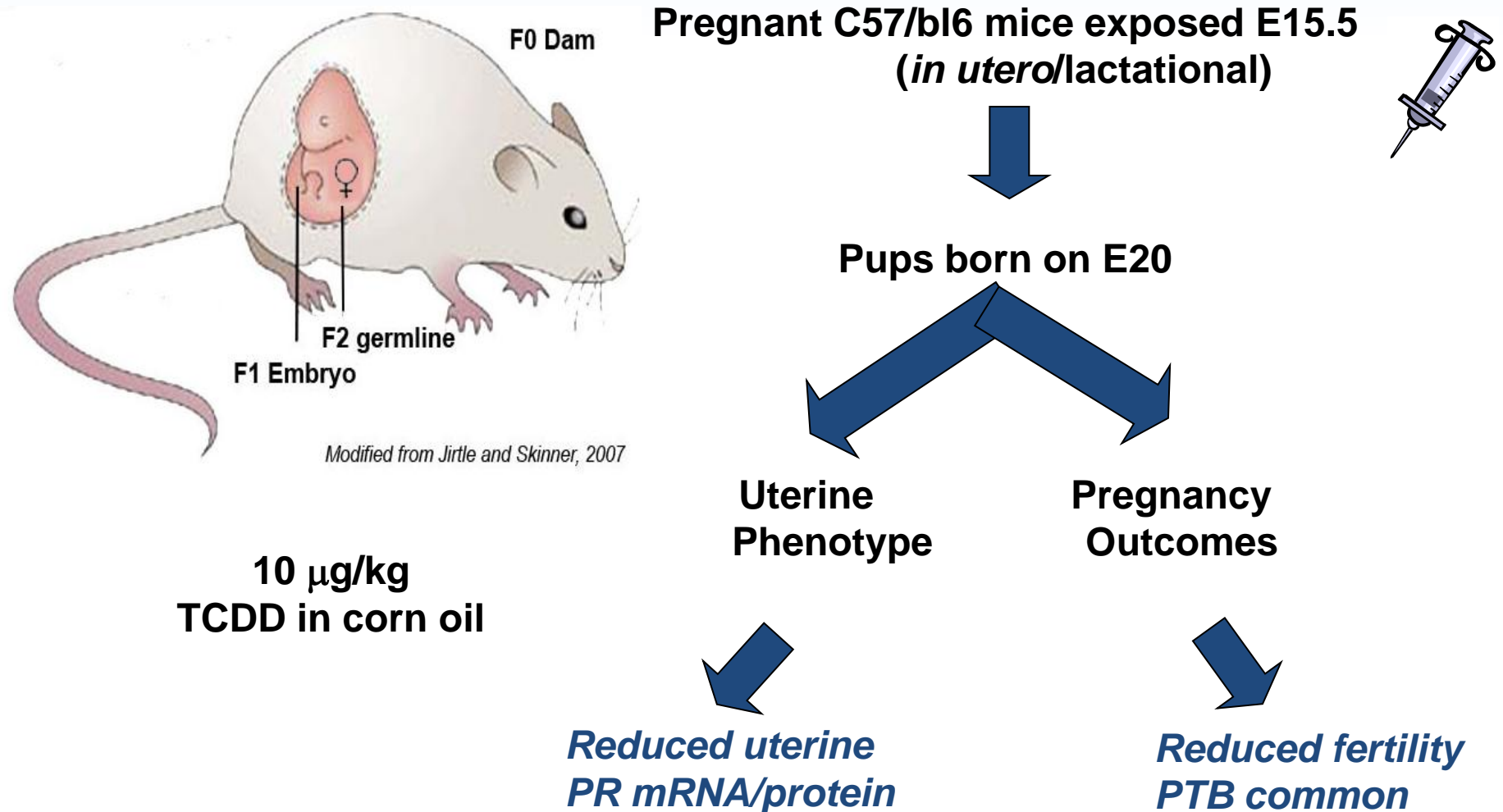
Dioxin or TCDD

(2,3,7,8-tetrachlorodibenzo-*p*-dioxin)

- By-product of industrial processes
- Known endocrine disruptor
 - Mimics estrogen; inhibits progesterone action
- “Agent Orange”—herbicide contaminated with TCDD
- Vehicle fuel combustion
- Bioaccumulates within the food chain
 - *In utero* and neonatal exposure



Impact of in utero TCDD



A History of Fetal Exposure to TCDD is Associated with Preterm Birth in a *Subsequent* Adult Pregnancy

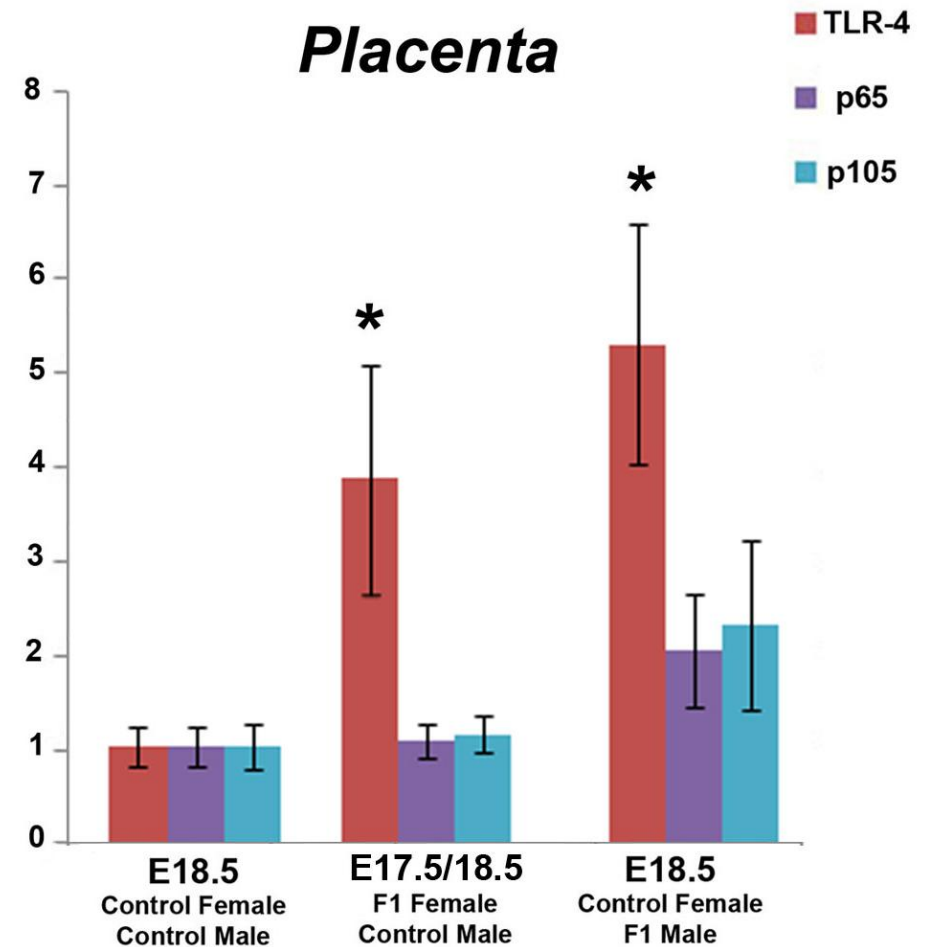
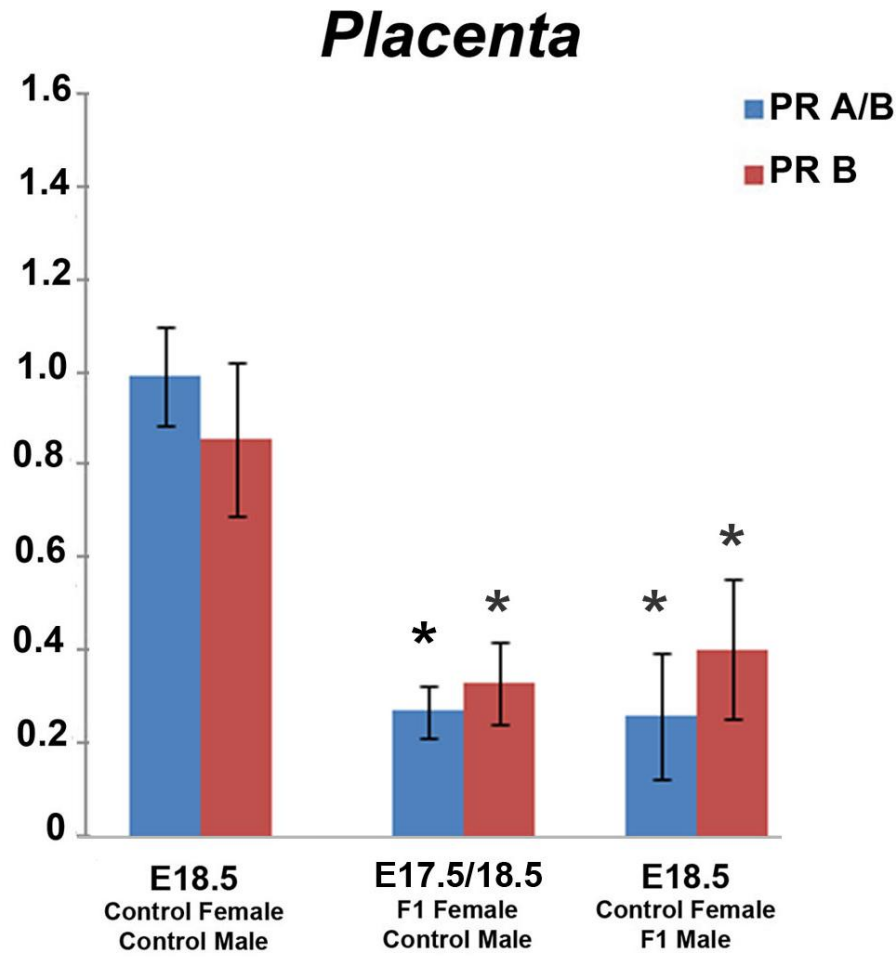
Mating Scheme	Pregnancy	Pregnancy Outcome	
		Full-term	Preterm
Control Female / Control Male	100%	100%	0%
F1 Female / Control Male	39%	64	36
Control Female / F1 Male	47%	61	39
F1 Female / F1 Male	0%		

Preterm birth was defined as spontaneous parturition >24 hrs prior to E20.

Placental Inflammation and Timing of Human Parturition

- **Placental inflammatory signals may regulate timing of parturition**
- **Placenta is largely derived from *paternal* genes**
- **Normal human placenta at end of pregnancy**
 - Increased expression of multiple TLRs
 - Decreased expression of PR

Impact of Developmental TCDD Exposure on PR Expression at the Maternal-Fetal Interface



Our data indicate that TCDD-mediated preterm birth in mice is associated with a hyper-inflammatory response within the placenta, *regardless of which parent was exposed.*

Can we reduce the inflammatory response?
Limited options for pregnant patients.

Nutritional Intervention
-*anti-inflammatory*
-*membrane fluidity*
-*brain development*

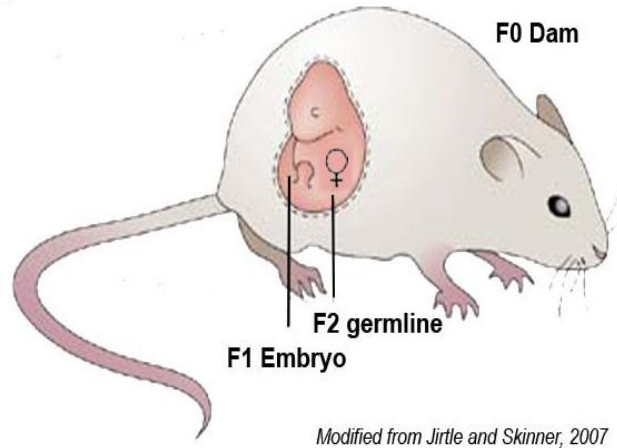


Omega-3 Fatty Acid Supplementation During Pregnancy

- **200-300 mg/day DHA/EPA recommended for all pregnant women**
- **Women “at risk” of PTB:**
 - **DHA/EPA supplementation should be initiated at 20-24 weeks**
 - **1.5-3.0 g/day/DHA/EPA**
 - **Results from studies to date are inconclusive**

Our data suggests omega-3 fatty acid supplementation prior to establishment of the maternal-fetal interface may be more effective.

Preconception Fish Oil



10 $\mu\text{g}/\text{kg}$
TCDD in corn oil

Pregnant C57/bl6 mice exposed E15.5
(*in utero/lactational*)



Pups born on E20

6-8 wk old males

Standard diet

5% Fish oil diet

*Mated at
9-10 weeks*

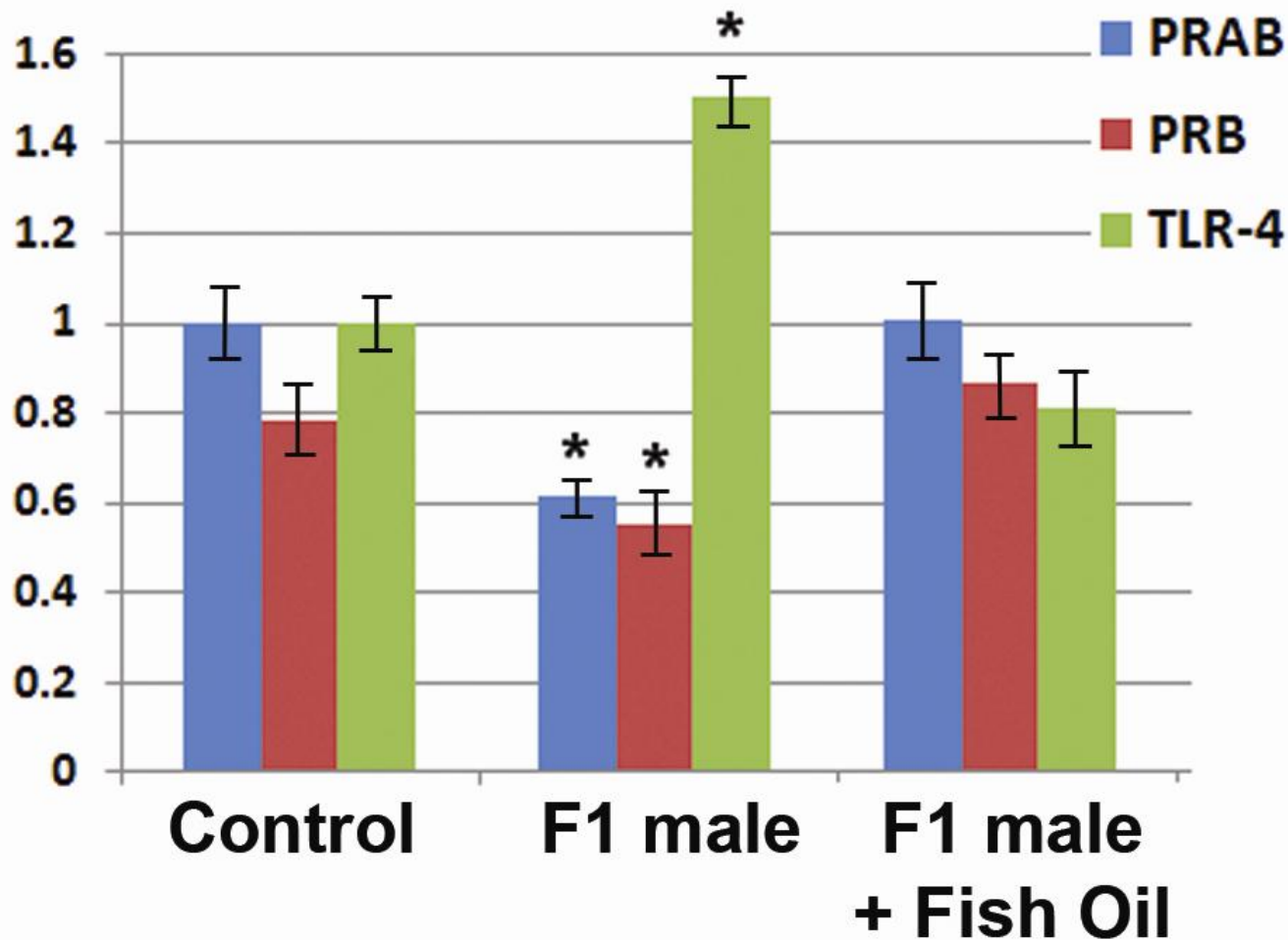
Pregnancy Outcomes

Pregnancy Outcomes

Pregnancy Outcomes following Preconception Fish Oil Supplementation of Male F1 Mice

Exposure	Pregnancy Rate	Pregnancy Outcome	
		Full-Term	Preterm
Vehicle Only	100%	100%	0%
Vehicle + Fish Oil	100	100	0
F1 male	49	61	39
F1 male + Fish Oil	80	100	0

Impact of Fish Oil Supplementation on Placental PR and TLR-4 mRNA Expression



E18.5

Conclusion

- **Dietary modification prior to the establishment of the maternal-fetal interface and which *includes both parents* should be examined for the prevention of preterm birth in women.**

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