

Adaptive Responses in Uteroplacental Metabolism and Fetoplacental Nutrient Shuttling and Sensing During Placental Insufficiency

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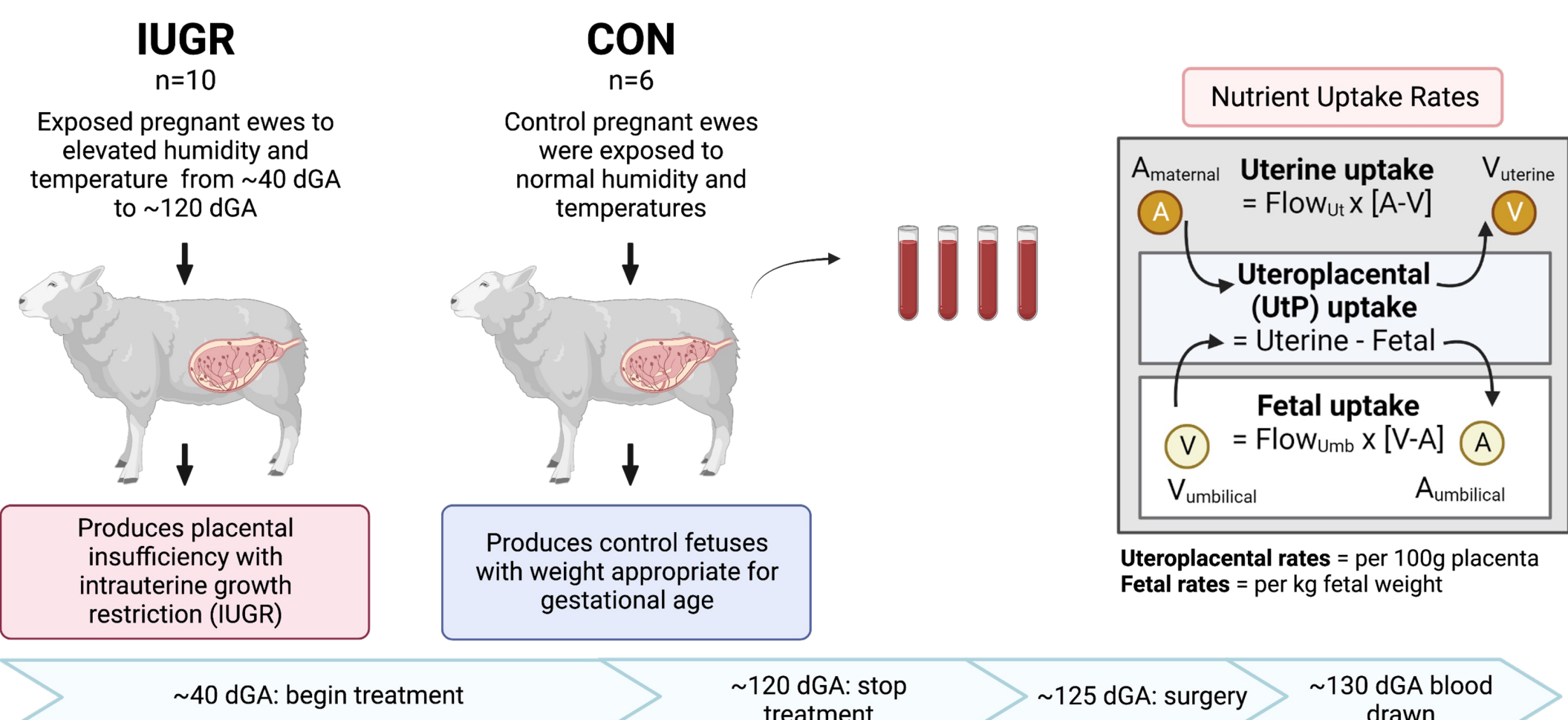
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Background

- Intrauterine growth restriction (IUGR) is a significant cause of fetal morbidity and mortality resulting from uteroplacental vascular insufficiency.
- In response to reduced oxygen and nutrient supply in IUGR, placental and fetal tissues optimize the allocation and utilization of substrates to maintain oxidative metabolism.
- Our prior data in sheep pregnancies with sustained hypoxemia found increased fetal pyruvate output and increased placental lactate production from pyruvate, supporting the idea of an accelerated fetoplacental lactate-pyruvate shuttle.
- Little is known about the effect of placental insufficiency-induced intrauterine growth restriction (PI-IUGR) on lactate-pyruvate shuttling.

Hypothesis: Uteroplacental metabolism adapts to PI-IUGR by altering the fetoplacental lactate-pyruvate shuttle, whereby there is increased pyruvate flux to the placenta and increased placental utilization of pyruvate to produce lactate for the fetus.

Methods



Results

Table 1: Uteroplacental and Fetal Growth and Blood Flow

	CON	PI-IUGR
Male-to-female ratio†	1:4:1	7:3
Gestational age, days	133.5 ± 1.2	133.6 ± 1.1
Placentome number	82.2 ± 4.7	64.9 ± 4.3*
Placentome total weight, g	340.2 ± 39.1	192.0 ± 29.1*
Fetal weight, kg	3.2 ± 0.1	2.1 ± 0.2*
Uterine blood flow, mL/min	1,667 ± 183.2	1,101 ± 143*
Umbilical blood flow, mL/min	565.3 ± 69.4	292.5 ± 36.8*
Umbilical blood flow, mL/min/kg	172.8 ± 13.8	135.2 ± 9.7*

Values are mean ± SE. *P < 0.05 in PI-IUGR vs. CON by t test.

Figure 1: Uteroplacental Nutrient Flux in CON vs. IUGR

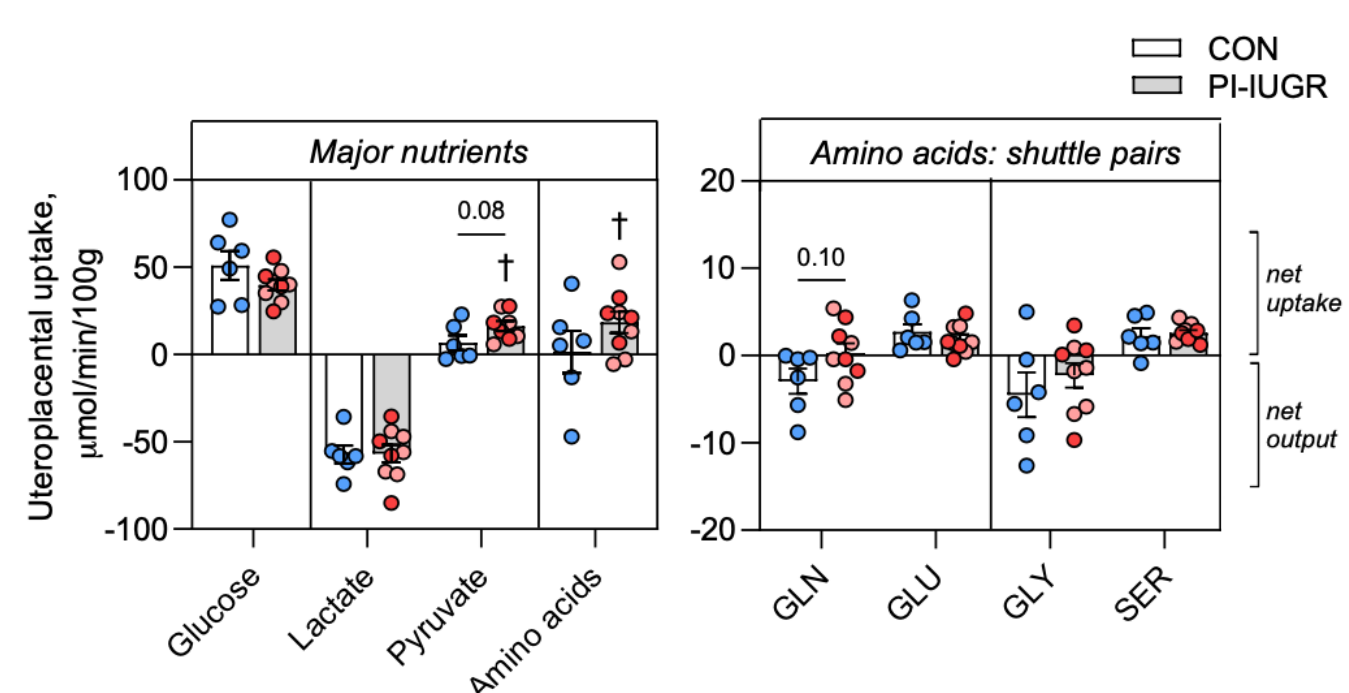


Figure 2: Fetal Nutrient Flux in CON vs. IUGR

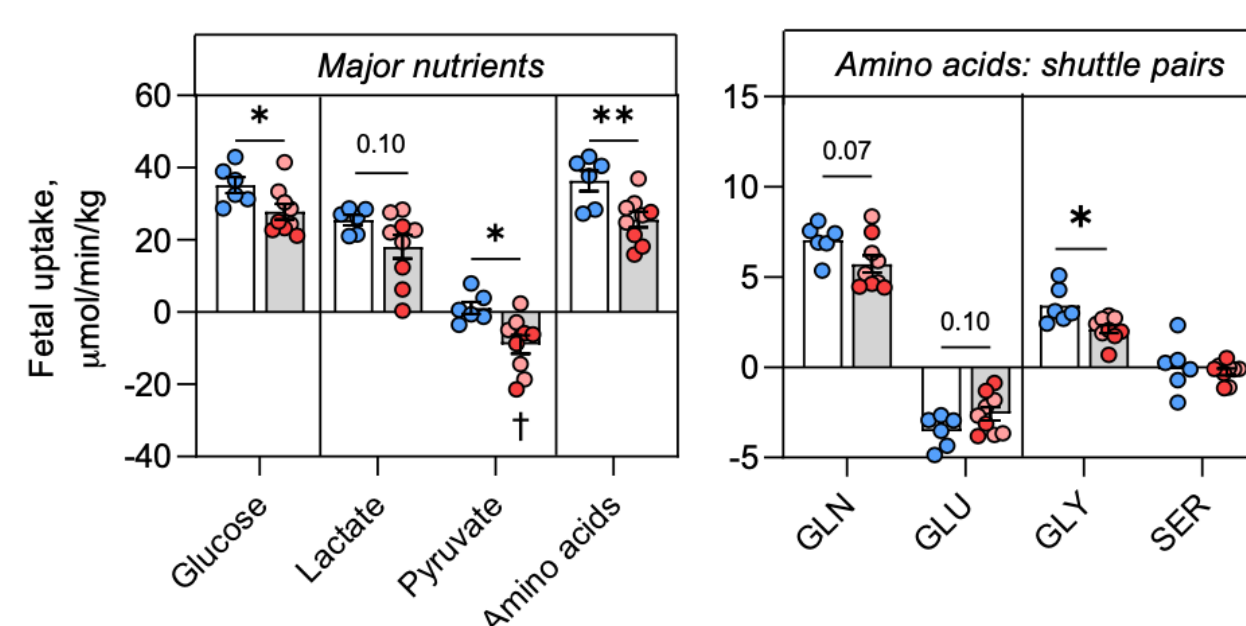
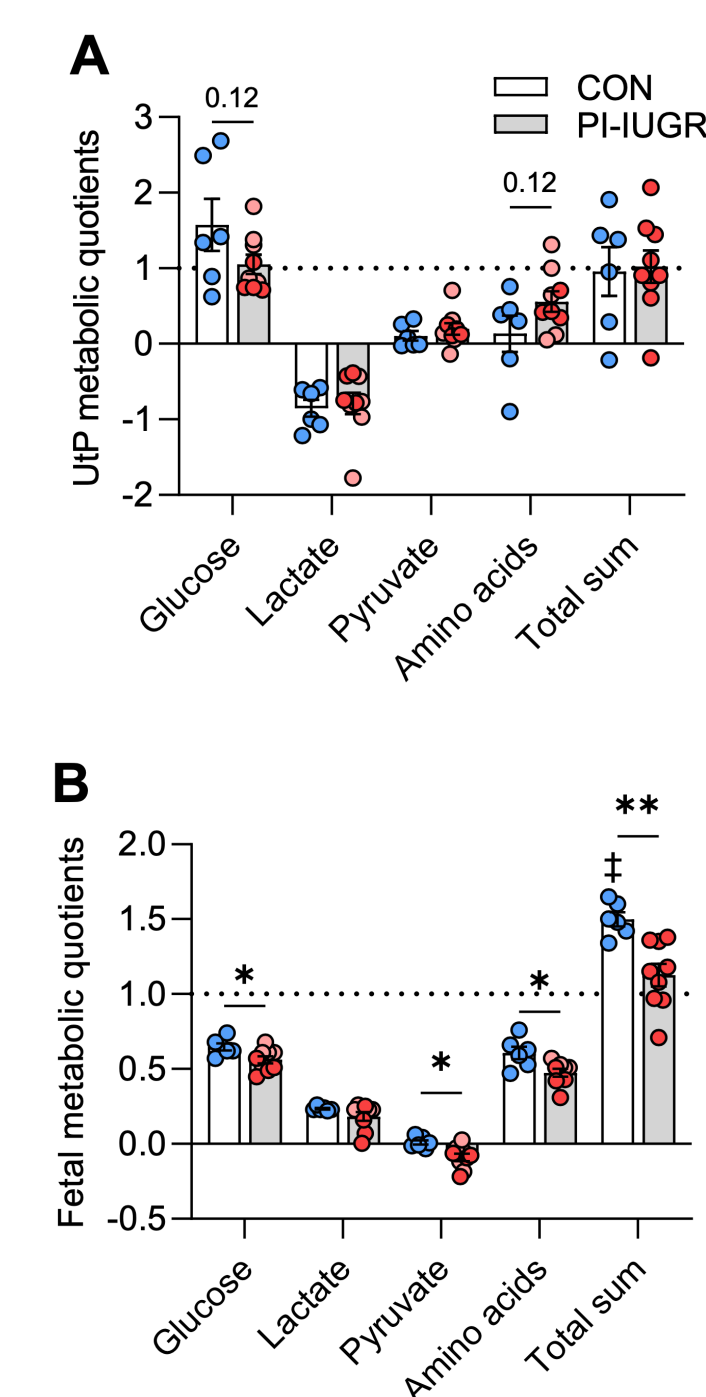
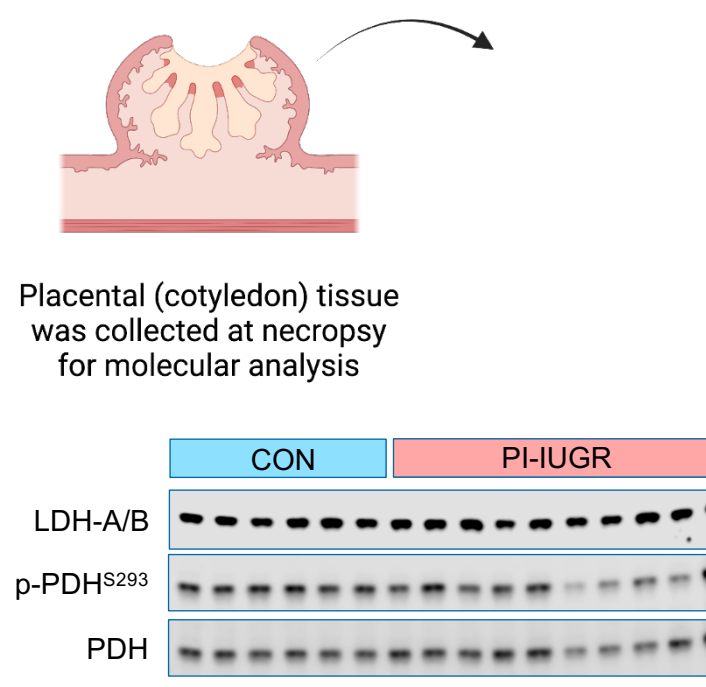
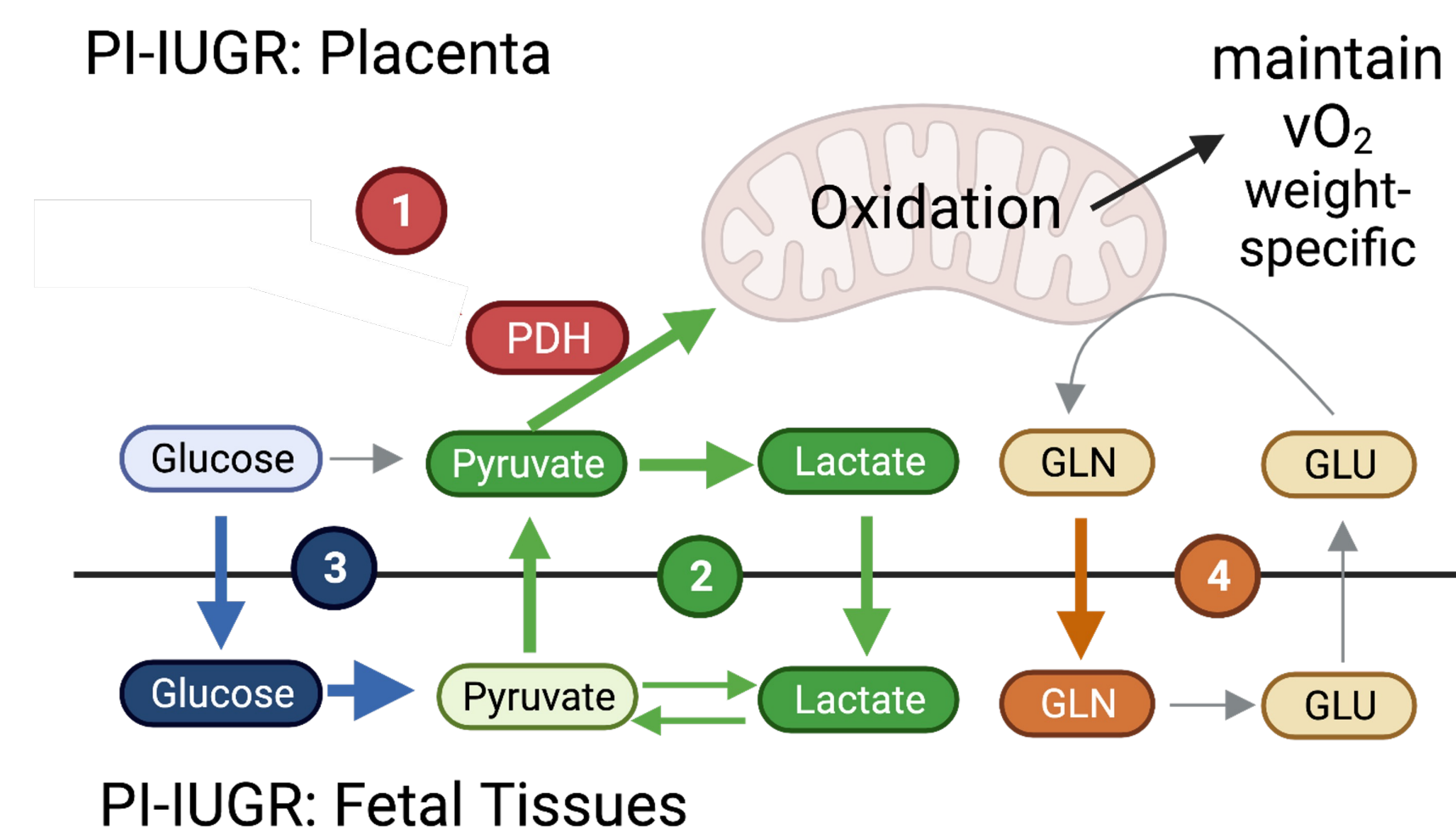


Figure 3: Metabolic Quotients



Conclusions

- PI-IUGR pregnancies have increased fetal to placental pyruvate flux and placental PDH activation, supporting increased placental capacity to oxidize pyruvate.
- We did not detect increased placental to fetal lactate flux in PI-IUGR. Placental expression of *LDHA* trended higher in PI-IUGR, while protein abundance and activity of LDH did not differ.
- Future studies using metabolic tracers are needed to further elucidate fetoplacental lactate flux given that both the fetus and placenta simultaneously produce and utilize lactate.
- Our results demonstrate shifts in placental and fetal nutrient shuttling in association with metabolic responses in the placenta during placental insufficiency, which may represent adaptive strategies that enable the placenta to maintain oxidative metabolism.



Disclosures

We have no disclosures or conflicts of interest to report.