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In This Issue

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This issue of Developmental Origins of Health and Disease has one brief report and 12 original articles. Among the articles, we highlight the study of Wilson et al, in which intraplacental injection of hIGF-1 nanoparticles demonstrated efficacy in normalizing fetal hepatic responses to a maternal nutrient-restricted diet. This approach represents a potential method of *in utero* treatment to prevent adverse consequences of developmental programming resulting from an adverse pregnancy environment.

Brief Report

Oral pyrroloquinoline quinone (PQQ) during pregnancy increases cardiomyocyte endowment in spontaneous IUGR guinea pigs. Mattern et al randomly assigned guinea pig sows to receive PQQ or placebo at mid-gestation and examined fetuses identified as spontaneous IUGR or normal growth. Spontaneous IUGR cardiomyocytes demonstrated increased proliferation and apoptosis which was significantly reduced with PQQ supplementation. These data suggest that PQQ action as an antioxidant may provide a therapeutic intervention for IUGR-associated cardiomyopathy.

Original Articles

Placental nanoparticle gene therapy normalizes gene expression changes in the fetal liver associated with fetal growth restriction in a fetal sex-specific manner. Wilson and co-authors fed guinea pig dams either a controlled or maternal nutrient-restricted diet, after which dams underwent intraplacental injection of hIGF-1 nanoparticles. Maternal nutrient restriction increased hepatic expression of tumor necrosis factor and hypoxia inducible factor 1 in females, though this effect was reduced by hIGF-1 nanoparticle treatment. The authors suggest that placental treatment may normalize the disruption to fetal developmental mechanisms in a sex-specific manner.

Associations of maternal preterm birth with subsequent risk for type 2 diabetes in women from the women's health initiative. Holman-Vittone assessed the association between preterm birth and risk for subsequent type 2 diabetes using the Women's Health Initiative database. The authors report that preterm birth was associated with type 2 diabetes only prior to study enrollment, suggesting a potential causative pathway early in life.

Maternal protein restriction during lactation disrupts the ontogenetic development of behavioral traits in male Wistar rat offspring. Oliveira-Silva and colleagues examine the effect of lactational protein restriction on offspring behavior and endocrine measures. Protein-restricted offspring demonstrated a reduction in anxiety-like behaviors and better memory performance and peak exploratory activity earlier in life. The authors conclude there is considerable age-dependent variations in the expression of observed behaviors and hormonal levels as a result of lactational protein restriction.

Attenuated glucose-stimulated insulin secretion during an acute IGF-1 LR3 infusion into fetal sheep does not persist in isolated islets. White and co-authors tested the effects of IGF-1 LR3 infusion on fetal glucose-stimulated insulin secretion *in vivo* and *in vitro*. The results suggest that acute IGF-1 LR3 infusion may directly suppress insulin secretion, though the fetal beta cell *in vitro* retains the ability to recover glucose-stimulated insulin secretion. These findings have implications for treatment approaches to fetal growth restriction.

Lifetime caffeine and adolescent nicotine exposure in mice: Effects on anxiety-like behavior and reward. Dutra-Tavares et all exposed Swiss mice to lifetime caffeine and examined acute effects of nicotine in adolescents. Caffeine-induced anxiety-like behaviors were mitigated by nicotine exposure. The authors conclude that caffeine exposure could be a risk factor for nicotine use.

Prenatal dietary patterns in relation to adolescent offspring adiposity and adipokines in a Mexico City cohort. Fossee and co-authors examine the association between prenatal diet and adolescent adiposity and adipokines in the Mexico City ELEMENT cohort. The authors demonstrated differences among offspring adiposity dependent upon maternal consumption of meat and fat with the findings demonstrating sex-specific impact on offspring adiposity measures.

Moderate maternal nutrition reduction in pregnancy alters fatty acid oxidation and RNA splicing in the non-human primate fetal liver. Zimmerman and colleagues assessed fetal liver samples from offspring of maternal nutrient-reduced baboons. The results demonstrate differentially expressed transcripts for fatty acid oxidation and RNA splicing pathways as a result of maternal nutrient reduction. The authors hypothesize that the increase in spliced variants is a mechanism for adaptation to a poor *in utero* environment.

Maternal prenatal psychological distress and motor/cognitive development in 2-year-old offspring: The Japan Environment and Children's Study. Mori et al utilized the Japan

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Environment and Children's Study database to assess associations between maternal psychological distress and child motor cognitive development. The authors found that continuous maternal psychological distress from the first to second half of pregnancy was associated with lower motor and verbal development in male offspring, and lower verbal development in female. The authors discuss potential mechanisms of action.

Associations between maternal folate status and choline intake during pregnancy and neurodevelopment at 3-4 years of age in the Alberta pregnancy outcomes and nutrition study (APrON). Irvine and colleagues assessed maternal red blood cell choline in the second trimester of pregnancy in relation to childhood neurodevelopment. The results demonstrated that maternal folate status and choline intake during the second trimester of pregnancy were not associated with children's intelligence, language, memory or motor outcomes, but their interaction may influence children's executive functions.

Nicotine exposure during breastfeeding alters the expression of endocannabinoid system biomarkers in female but not in male offspring and adulthood. Miranda et al exposed lactating rats to nicotine through implanted osmotic mini-pumps. Endocannabinoid biosynthesis was impacted by nicotine exposure only in females, indicating that effects of nicotine exposure are sex- as well as tissue-dependent.

Cardiovascular and renal profiles in rat offspring that do not undergo catch-up growth after exposure to maternal protein restriction. Wood-Bradley and co-authors fed female Sprague Dawley rats a low-protein or normal-protein diet. At weaning, offspring were fed a "non-growth" diet which ensured that catch-up growth did not occur. Low-protein offspring remained smaller than normal-protein offspring and demonstrated reduced nephron number, though normal kidney function and blood pressure. The authors conclude that remaining on a slow-growth trajectory after a suboptimal intrauterine nutrition environment does not lead to offspring kidney dysfunction and hypertension.

Differential expression of genes influencing mitotic processes in cord blood mononuclear cells after a pre-conceptual micronutrient-based randomized control trial: Pune rural intervention in young adults (PRIYA). Khare et al assessed the effects of vitamin B-12 and micronutrient supplementation in a nested preconceptual controlled trial. Cord blood gene expression analysis revealed 75 differentially expressed genes between the supplement and placebo groups. The authors propose the micronutrient intervention epigenetically affected cell cycle dynamics and plan for follow up studies to examine offspring metabolic impact.

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