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## In This Issue

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This issue of the Journal of Developmental Origins or Health and Disease contains one review article, one brief report and 12 original research articles. Among these are three articles reporting on diverse developmental epigenetic effects including methylation and microRNA, illustrating the depth of DOHaD scientific studies.

#### **Review Article**

The impact of smoking and nicotine exposure during pregnancy on fetal nephrogenesis: A systematic review. Popham and Kandasamy review the impact of smoking and nicotine exposure on fetal renal development. Evidence from human studies identify a reduction in fetal kidney size and weight in offspring exposed to cigarette smoking during pregnancy, while animal studies demonstrate kidney injury and microscopic changes in response to nicotine exposure. In view of the increased recreational use of nicotine, further studies into the adverse effects on renal development are warranted.

# **Brief report**

Building strong health and career trajectories through translational research. O'Leary et al report the workshop from the DOHaD World Congress of 2022 exploring career pathways with trainees. In view of the challenges for translational research career pathways, the authors provide recommendations for the development of translational research specific programs, opportunities and funding.

## **Original Articles**

Association of maternal psychosocial stress with newborn body composition in the Healthy Start study. Buck et al assessed 604 mother-newborn pairs from the Healthy Start study. Using established depression and perceived stress scales, the authors demonstrate that increased depression scores correspond with lower offspring fat mass and shorter length. These results add to the continuing evidence regarding the effects of maternal stress on fetal growth.

Factors associated with low birthweight among late preterm singletons in Japan using pregnancy birth registry data. Kasuga and co-authors assess the Japanese successive pregnancy birth registry system, analyzing over 56,000 late preterm singleton births. Among the infants, low birth weight occurred in 62.5%, being associated with modifiable maternal factors including pre-pregnancy underweight, inadequate gestational weight gain and smoking, as well as nonmodifiable factors including younger maternal age, nulliparity and preeclampsia. These findings suggest an opportunity for preventative interventions focusing on modifiable risk factors.

Maternal childhood maltreatment: Associations to offspring brain volume and white matter connectivity. Lugo-Candelas and co-authors examine 92 mother-infant dyads including mothers with and without childhood maltreatment. Male offspring among the maltreatment group, demonstrated greater interhemispheric fronto-limbic connectivity which was related to somatic complaints. These findings suggest that childhood maltreatment may have intergenerational associations for offspring brain development.

Alteration of the embryonic microenvironment and sex-specific responses of the preimplantation embryo related to a maternal high-fat diet in the rabbit model. Calderari and co-authors examine the effect of maternal high-fat diet on the embryo. The authors demonstrate significant metabolite alterations in response to high-fat diet within uterine fluid, blastocoelic fluid, and the blastocyst transcript. The findings identify an early sex-specific response from the blastocyst stage to maternal high-fat diets.

Puberty as a DOHaD programming window: High-fat diet induces long-term hepatic **dysfunction in male rats.** dos Santos and co-authors assess the effect of a high-fat diet during puberty on adult life hepatic function. High-fat offspring demonstrated pancreatic islet cell hypertrophy, increased blood glucose levels and altered hepatic morphology consistent with increased lipid inclusion. These findings indicate that high-fat diet during puberty results in an obese phenotype with evidence of nonalcoholic fatty liver disease.

Preterm birth, birth weight, and subsequent risk for depression. Rahalkar and co-authors utilize data from the Women's Health Initiative to assess association between preterm birth status and risk for depression during adulthood. The authors demonstrate that individuals weighing less than 6 pounds and greater than 10 pounds, as were infants born preterm, had significantly high depression scores. The authors suggest that infants born at low or high birth weights and those

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born preterm may benefit from early evaluation and followup for prevention and treatment of mental health disorders.

Developmental origins of health and disease knowledge is associated with diet quality in preconception young adult men and women. Salvesen et al utilize data from 1,362 preconception young adults to assess DOHaD-related knowledge and diet quality. The authors found a potential for diet quality improvements including sugary foods and processed meats. The results indicate that knowledge of DOHaD implications is positively associated with diet quality in preconception young men and women.

Neonatal nicotine exposure affects adult rat hepatic pathways involved in endoplasmic reticulum stress and macroautophagy in a sex-dependent manner. Souza and colleagues assess the effect of nicotine exposure during early postnatal life. Male offspring exposed to nicotine demonstrated evidence of triglyceride esterification and oxidative stress. These findings highlight potential adverse effects of maternal smoking during breastfeeding.

Associations between early infections and childhood cognition in the Newcastle Thousand Families Study birth cohort. Pennock and co-authors assess the relationship between early-life infections and childhood cognition among 741 subjects. Although total number of infections during the first five years of life was not significantly associated with IQ, there were negative impacts of lower respiratory tract infection and *H. pylori* seropositivity. These findings suggest that lower respiratory tract infections and gastrointestinal infections may impact cognitive development.

Associations between epigenome-wide DNA methylation and height-related traits among sub-Saharan Africans: The

**RODAM Study.** Swart et al performed an epigenome-wide DNA methylation association analysis of 704 Ghanaians. The results suggest DNA methylation associations with select differentially methylated positions and regions in genes related to bone cell regulation and development in relation to height. These findings provide insight into the role of DNA methylation in skeletal development.

Upregulation of miR-21-5p rescues the inhibition of cardiomyocyte proliferation induced by high glucose through negative regulation of *Rhob*. Wu and co-authors examine the process by which maternal hyperglycemia inhibits cardiomyocyte proliferation and promotes cell apoptosis. The authors demonstrate that miR-21-5p regulates *Rhob* to rescue the inhibition of cardiomyocyte proliferation induced by high glucose. These results indicate a potential clinical therapeutic target for prevention of fetal cardiac abnormalities in mothers with high glucose.

Stress response abnormalities transgenerationally inherited via miR-23 downregulation are restored by a methyl modulator during the lactation period. Nemoto utilizes a fetal undernourished model identifying factors that regulate noncoding RNA GAS-5 which acts as a glucocorticoid receptor decoy. The expression of miR-23 was significantly lower in low birth weight compared with control rats, while the methyl modulator intervention in lactating maternal rats restored expression in multiple generations. These findings emphasize the importance of glucocorticoid levels on brain development and psychiatric disorders.

Michael G. Ross, MD, MPH Editor-in-Chief