

In This Issue

Review Articles

Evolution of DOHaD: the impact of environmental health sciences. Haugen *et al.* review the role of chemical exposures in DOHaD and the types of chemical exposures that have been studied in this context over the past 20 years.

Metabolomics in the developmental origins of obesity and its cardiometabolic consequences. This review begins by summarizing the techniques and analytical approaches used in studying metabolomics. Hivert *et al.* propose that metabolomics will identify mechanisms that may explain fetal metabolic programming. The authors argue that there are significant gaps in our knowledge of the mechanisms of fetal programming that can be elucidated using metabolomics.

Original Articles

DOHaD research with populations in transition: a case study of prenatal diet remote recall with Yup'ik Alaskan women. Despite changes in nutritional intake, there remains a low level of diabetes in some subsistence-based communities. Giordano and Benyshek propose that these communities provide an opportunity to understand mechanisms that protect from diabetes.

Themed Issue: Role of Epigenetics in Mediating Programming Effects – Part II

This issue contains invited works within the theme of the role of epigenetics in mediating programming effects from presenters at our international DOHaD meeting in Singapore.

Maternal diet as a modifier of offspring epigenetics. Lillycrop and Burdge review the literature showing that maternal diet before and during pregnancy can impact the epigenome, resulting in long-term changes in organ function that result in an increased risk of disease in adult life.

Understanding the epigenetics of neurodevelopmental disorders and DOHaD. Kubota *et al.* present data to show that mental stress during the neonatal period, just like changes in maternal nutrition during pregnancy, can result in epigenetic modifications. They highlight the fact that these epigenetic modifications may be reversible. The early identification of epigenetic changes may present windows of opportunity for intervention.

Maternal restraint stress during pregnancy in mice induces 11 β -HSD1-associated metabolic changes in the livers of the

offspring. It is well established that the stress of maternal restraint in pregnancy can affect the subsequent functioning of the offspring's hypothalamic–pituitary–adrenal axis. Maeyama *et al.* have studied the effects of stress during pregnancy in mice on the liver function of the offspring. Restraint during pregnancy altered 11 β -hydroxysteroid dehydrogenase type-1-related pathways in the offspring's liver as well as leading to lipid accumulation. These studies have shown a potential role for maternal stress in pregnancy in predisposing offspring to metabolic disease, including nonalcoholic fatty liver disease.

Association of *in vitro* fertilization with global and IGF2/H19 methylation variation in newborn twins. Loke *et al.* have used a twin cohort to study the effects of *in vitro* fertilization, and in particular intracytoplasmic sperm injection, on global DNA methylation. They have focussed on specific genes that are important in fetal growth and show lower within and between pair variation in DNA methylation.

Themed Issue: Preterm birth

Profs. John Newnham and Jeffrey Keelan organized a symposium upon which this themed content is based at the 2013 DOHaD meeting in Singapore. As a result of this symposium, they acted as guest editors for themed papers in this area. In this issue, we include reviews based on this symposium with other original articles to come in upcoming issues.

Preterm birth is the single greatest problem in human reproduction. Most children born too early will go on to lead a normal and productive life, but many are at risk of life-long disease and disability. Discovering the pathways to these problems is the key to developing clinical strategies by which they may be prevented or ameliorated.

Letters to the Editor

'Increased systemic blood pressure and arterial stiffness in young adults born prematurely'. In a letter to the Editor, Bassareo *et al.* comment on a recently published paper by Tauzin *et al.* and cite further evidence for the association between extreme preterm birth and systolic blood pressure and arterial stiffness in young adulthood. They also refer to their previous work providing a possible mechanism for this association through endogenous inhibition of nitric oxide synthesis.

Reply to letter by Bassareo regarding the article of Tauzin *et al.* 'Increased systemic blood pressure and arterial stiffness in young adults born prematurely'. In reply, Tauzin adds to the list

of possible mechanisms by which early preterm birth and low birth weight may lead to subsequent vascular disease. Other possibilities include lack of elastin owing to early birth and subsequent predisposition to left ventricular hypertrophy.

Review Articles

Antenatal glucocorticoids: where are we after forty years?

McKinlay *et al.* have provided a thorough review of 4 decades of research in the field of antenatal glucocorticoids when this treatment is used to enhance fetal maturation before preterm birth. The authors have tackled the conflicting evidence surrounding the well-known short-term benefits of treatment and the potential for long-term adverse consequences, including the use of repeated courses.

Original Articles

Premature guinea pigs: a new paradigm to investigate the late-effects of preterm birth.

DOHaD research has taught us the critical role played by early-life events in future health. Preterm birth predisposes individuals to a variety of medical problems in adult life, but detailed investigation using animal models is hampered by the difficulties associated with relative lack of maturity and confounding effects of supporting preterm newborns, and the logistics of long-term study. In this brief report, Berry *et al.* describe a novel method of inducing preterm labor in guinea pigs followed by postnatal care and nutritional support comparable with that in the care of a moderately preterm human infant. This novel paradigm opens new

opportunities for the experimental study of the short- and long-term consequences of early birth and postnatal interventions.

Stability of proposed biomarkers of prenatal androgen exposure over the menstrual cycle.

Barrett *et al.* have studied two potential biomarkers in women that aim to provide an assessment of prenatal androgen exposure, including measurement of the anogenital distance and the ratio of the second to fourth digits of the hand. The authors demonstrated that these biomarkers are stable across the menstrual cycle.

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