DOHaD 2026 ABSTRACT

Transgenerational Inheritance Of Growth Restriction Phenotypes: Molecular and Physiological Insights From The Paternal Line

Thu Ngoc Anh Doan[1,2], Lisa K. Akison[3], James M. Cowley[1], Aaron L. Phillips[1], Jessica F. Briffa[4], Tania Romano[5], Helle Bielefeldt-Ohmann[6], Mary E. Wlodek[4,7], Tina Bianco-Miotto[1,2]

[1]School of Agriculture, Food and Wine, & Waite Research Institute, Adelaide University, Adelaide, Australia
[2]Robinson Research Institute, Adelaide University, Adelaide, Australia
[3]School of Biomedical Sciences, University of Queensland, Brisbane, Australia
[4]Department of Anatomy and Physiology, University of Melbourne, Parkville, Australia
[5]Department of Physiology, Anatomy and Microbiology, La Trobe University, Bundoora, Australia
[6]School of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, Australia.
[7]Departmeny of Obstetrics and Gynaecology, University of Melbourne, Parkville, Australia

Email: tina.bianco@adelaide.edu.au

Background: Intrauterine growth restriction (IUGR) results in poor fetal growth and babies being born too small for gestational age. Uteroplacental insufficiency (UPI) is a common cause of IUGR, with IUGR offspring having a higher risk of chronic diseases later in life.
Methods: Using a rat model of UPI we investigated the impact on offspring physiological and metabolic measures across multiple generations from the paternal line. Gene expression was also investigated by RNA sequencing in the kidneys of offspring across multiple generations.
Results: Accelerated growth was observed in male and female offspring in the F2 and F3 generations. Postmortem organ weights were altered at weaning and adulthood of both F2 and F3 offspring. Additionally, F3 males and females had impaired insulin secretions at 12 months of age, with a decrease of 40% in first-phase insulin secretion in IUGR males, and a 20% decrease in second-phase insulin secretion of IUGR females, compared to same-sex controls. However, in contrast to the maternal line, there were no significant changes in blood pressure in IUGR F2 or F3 offspring, compared to sham controls. Molecular changes in the kidneys of F1, F2 and F3 offspring were seen, including imprinted genes.
Conclusions: UPI is associated with changes in postmortem organ weights, reduced vascular and metabolic functions, and aberrant renal functions in IUGR offspring from both maternal and paternal lines, regardless of birth weight. Alterations to offspring postmortem organ weights were seen in the paternal line, while vascular and metabolic dysfunctions were more severe in the maternal line.