

## Editorial

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# The challenge of spreading DOHaD concept throughout Latin America

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Latin America has a primordial importance for studies on the developmental origins of health and disease (DOHaD) because of its ethnical, cultural, and geopolitical diversities. Latin American people have experienced intermittent periods of famine, undernourishment, or over-nutrition,<sup>1</sup> likewise other societies around the world, which have concurred for the current dual burden of malnutrition perceived throughout its countries.<sup>2,3</sup> Thus, to promote network between DOHaD researchers and translate scientific data into societal welfare, the Latin American DOHaD Chapter (LA-DOHaD) has organized biennial meetings to bring together scientists, clinical researchers, obstetricians, pediatricians, public health professionals, and policymakers to discuss and share exciting and cutting-edge knowledge. In particular, LA-DOHaD has made consistent efforts to support the enrollment of undergraduate and graduate students, as a way to nurture the next generation of LA-DOHaD researchers.

Hence, this themed issue of the *Journal of Developmental Origins of Health and Disease* brings representative studies presented during the 6<sup>th</sup> International Symposium on Metabolic Programming and Microbiome & 3<sup>rd</sup> Meeting of Latin American DOHaD Chapter, held on November 7–10, 2018, in Cancun, Mexico. Under the chairmanship of Dr. Arturo Cardona, director of the Mexican National Institute of Perinatology, this meeting brought about 250 attendees, from 13 different countries, to present 217 studies distributed into 3 categories: basic science (70%), clinical science (17%), and epidemiology (13%). Noteworthy, 71% of attendees were women and 47% were between 20 and 30 years old. Such numbers rejoice for the massive attendance of women and youth but unveil the challenge of attracting more Latin clinicians and epidemiologists to our trenches. The collection herein presented is composed of 10 articles, being 2 reviews on important animal disease models, and 8 original researches, mostly from basic science approaches, which covers the 4 main aspects of DOHaD research: challenges, mechanisms of disease, outcomes, and interventions. In accordance with the LA-DOHaD commitment to enroll students, most of the first authors of the current issue are students.

Early postnatal nutrition, exclusive breastfeeding, and adequate perinatal health have proven to be protective factors for latter cardiometabolic disorders. Having this into account, Souza *et al.*<sup>4</sup> provide a comprehensive review of diverse animal models of early weaning and programming that can result in the development of metabolic syndrome. The authors discuss novel aspects, such as sex-specific responses and the mechanisms involved, which can generate new insights into therapeutic strategies for obesity management, improving health outcomes. Likewise, González-Candia *et al.*<sup>5</sup> reviewed diverse studies from their own and other groups to propose the newborn sheep as a translational animal model to study mechanistic aspects of neonatal pulmonary arterial hypertension at high altitude, a recurrent perinatal concern in Andean countries. Still on perinatal health, Ortiz-Dosal *et al.*<sup>6</sup> assessed the expression of microRNAs, related to adult metabolic outcomes, in dried blood spots from newborns with low or high birth weight, which were compared to normal weighed babies. The authors found out a set of microRNAs targeting carbohydrate metabolism-related genes which were increased in macro-somic but not low birth weighted ones. This is an interesting finding that opens up the perspective of using microRNA assessment in dried blood spots from newborn screening cards as a predictive tool for late-in-life metabolic disorders.

Nutritional challenges are virtually the most used tool to get insight into the mechanisms underlying DOHaD studies. In this themed issue, Pedrana *et al.*<sup>7</sup> explored the effects of maternal protein restriction during pregnancy and/or lactation on adult rat offspring testis. The authors concluded that pre- and postnatal undernutrition have window-dependent effects on testicular development, functional changes in spermatogenesis with long-term consequences in male fertility mediated by insulin growth factor –1 and its receptor. Similarly, Mathias *et al.*<sup>8</sup> showed in weaned rats that maternal malnutrition during lactation, induced by diet with low protein supply, resulted in programming of pancreatic islet dysfunction. In this regard, maternal malnutrition impaired the vagal nerve-mediated autonomic control of pancreatic  $\beta$ -cells leading to inadequate insulin secretion at a very young age. On the other hand, Chavaglia-Calavet *et al.*<sup>9</sup>

showed that rats postnatally overfed through litter reduction presented obese phenotype and cardiac remodeling at adulthood, outcomes not prevented by food restriction during adolescence.

Focusing on liver physiology, Bertasso *et al.*<sup>10</sup> assessed *de novo* lipogenesis, as well as VLDL assembly and secretory pathways, to compare the impact of pharmacological and non-pharmacological early weaning on hepatic lipid metabolism at adulthood. Male rats submitted to precocious non-pharmacological weaning presented higher levels of both acetyl-CoA carboxylase-1 and stearoyl-CoA desaturase-1 than rats whose mothers were injected with bromocriptine during lactation. Interestingly, female offspring did not show those changes but rather presented higher levels of microsomal triglyceride transfer protein, which may confer protection against hepatocyte lipid accumulation and hepatic steatosis onset. França *et al.*<sup>11</sup> evaluated metabolic factors involved in the onset and progression of non-alcoholic fatty liver disease (NAFLD) in post-weaning Swiss mice fed a high-sucrose diet. This study addressed an important aspect of the development of NAFLD by examining the crosstalk between liver and white adipose tissue (WAT). The authors showed triggering of insulin resistance in the WAT as a major factor for dysfunctional release of free fatty acids toward portal circulation and consequent upregulation of lipogenic genes and hepatic inflammatory response onset.

From an interventional perspective, Klein *et al.*<sup>12</sup> showed the healthy impact of maternal swimming during pregnancy on programming fetal brain with adaptations that persist into adulthood. Moreover, the authors demonstrated that such adaptations attenuated several neurotoxic outcomes induced by later *i.c.v.* injection of amyloid- $\beta$  oligomers in the offspring's male rat cerebellum. This elegant study brings the perspective of maternal exercise as a preventive intervention against late-in-life neurodegenerative diseases. Finally, Castro-Rodríguez *et al.*<sup>13</sup> used a probiotic intervention on obese rats during gestation and lactation to show its potential to reverse unwanted metabolic outcomes in offspring. The authors administered *Leuconostoc mesenteroides* SD23, a probiotic isolated from aguamiel (edible sweet sap obtained from Agave salmiana, a traditional Mexican drink) and observed beneficial effects on maternal metabolism, which might help to prevent adverse metabolic programming in the offspring due to maternal obesity.

The above-mentioned studies are just a small frame of all the exciting DOHaD research conducted in Latin America. However, first authors of these studies come from only 4 different countries, while the region comprises 53 countries and territories. This observation imposes an obvious challenge to be overcome: how to support DOHaD research in the region, particularly in the under-represented countries, making it trustful, robust, and visible. In this regard, LA-DOHaD executive board has decided to maintain the 4th Meeting of Latin American DOHaD Chapter, to be

held on the web next October 13–16, 2020, under the motto “One World, One Health”. The main goal is to reach a broader audience, with greater attendance of DOHaD interested researchers from all over Latin America, shortening distances and expanding horizons.

**Conflicts of interest.** The authors declare no conflict of interest to be disclosed.

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