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Editorial

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My full name is Elena Zambrano González because in Mexico we use both our paternal and maternal last names, which may explain my interests in maternal and paternal factors in DOHaD. However, my scientific name is Elena Zambrano because in countries where the two surnames are not used, the first surname is sometimes thought to be the middle name. To avoid problems in science, I use only one last name. I completed a BSc degree in chemistry pharmacobiology, master's degree in science (biology), and PhD in science (biology) at the Universidad Nacional Autónoma de México (UNAM), Mexico City, Mexico. I have been interested in reproductive biology since my PhD years, in which I focused on studying hypothalamic gonadotropins. During my 2 years of postdoc with Dr. Peter W. Nathanielsz at Cornell University, I developed an interest in fetal programming and its life-course consequences. After Cornell, I returned to Mexico to develop several powerful rat models of developmental programming. These were the first studies I undertook as an independent investigator. They were published as first author papers in the prestigious *Journal of Physiology*.^{1–4}

When I came back to Mexico from my postdoctoral training at Cornell, it was very challenging to set up my own research program as an independent researcher. I was very frustrated because I had many ideas that I wanted to develop, but as a young scientist there was no money or resource to support me. At the beginning of the century, the DOHaD field was not a research priority in Mexico, so it was a very difficult concept to sell to granting bodies. One day I was very depressed and decided to visit one of my PhD mentors, Dr. Fernando Larrea Gallo. He told me that in order to do good scientific research I needed to have a great tolerance and resilience to endure setbacks. This advice matched perfectly with a typical phrase of Dr. Peter Nathanielsz (my mentor for my postdoctoral training, and still my counselor): “pain is inevitable, but stress is controllable.” He also taught me the need to never give up and always respond politely when one feels that a wrong decision has been made on a grant or paper. He reminded me that when the great American Frontier was opened up by the pioneers it was not the arrows in the front they feared but the bullets in the back. There is always a price for proposing an innovative idea. In addition to Peter Nathanielsz, the late Dr. Thomas J. McDonald was an important influence in my career; he taught me to do pure science just for the pleasure of fulfilling my innate human curiosity. He also taught me the value of friendship and going the extra mile for each other.

Advice from my mentors helped me to be patient, which was eventually rewarded with the success of my first funded grant. Here, I have been supported in my passion to contribute to answering questions in controversial areas. Developmental programming was controversial in Mexico when I started research in the field in 2000. Now programming is clearly seen as a major area of human health in almost all the countries of Latin America. In 2013, I was invited to participate in the 3rd International Symposium on Metabolic Programming and Stress, held in Morretes, Brazil under the leadership of Prof. Paulo Mathias from the Universidade Estadual de Maringá. At that meeting, he shared with me his vision of a Brazilian DOHaD Society, and I suggested that we should start a wider Latin American group, which was finally established during the 8th DOHaD World Congress, in Singapore, as the Ibero-American DOHaD Chapter under the presidency of Prof. Francisco Mardones. Following which Prof. Mathias organized the 1st Meeting of the Ibero-American DOHaD Chapter in November 2014 in Ponta Grossa, Brazil, to be held every 2 years. During the second meeting in São Luís – Brazil, Paulo Mathias was elected as president with myself as vice president. The third meeting was in November 2018 in Cancún, México and it was at this meeting that we established that our Society should be named as the Latin American DOHaD Chapter. We have published a themed issue in *Journal of Developmental Origins of Health and Disease* to raise awareness of the work of our Chapter members.⁵ In this sense, it has been very rewarding to know that I am a part of the history of DOHaD in Mexico, to be a pioneer in the area and a person that worked in the consolidation of a DOHaD Society in Latin America.

Since I have been asked to address the issue of “Promoting DOHaD in Latin America,” it gives me pleasure to note that my country Mexico and others as Brazil, Chile, and Argentina are increasingly paying more attention to the importance of DOHaD. Our Latin American DOHaD Chapter is committed to enrolling investigators from the other smaller Latin American countries. We need a plan/vision of the long-term sustainability and involvement of researchers, students, and government officials in the field of DOHaD in order to maximize public health benefits.

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Working in a country with relatively few economic resources creates challenges for researchers. For example, there are many layers of bureaucracy and reagents cost more and take longer to be delivered. The availability of fewer resources means we must optimize and strengthen our existing resources. In our case, our limited resources prevented us from buying commercial diets from companies. This prompted us to prepare our own diets, allowing us better control of the ingredients and to make variations according to our research question. Importantly, the human population we have is ideal for DOHaD studies. Unfortunately in Mexico and other Latin American countries, there are fewer resources for the majority of the population. As a result, malnutrition and poor diets that generate problems of undernutrition, overweight, and obesity are common among the population. Thus, the people of Mexico are most likely to benefit from the knowledge gained in my research.

I am excited by the biology of programming at the molecular to the whole animal phenotype. I have contributed toward uncovering molecular mechanisms underlying changes in phenotype in response to programming challenges. I have conducted studies on maternal nutrient restriction,^{1-4,6-9} obesity,¹⁰⁻¹³ and more recent studies on aging-related issues.^{4,14-16} We are currently working on programming changes related to microbiome and probiotics. Our studies use protocols that permit identification of the period of exposure- and sex-dependent outcomes resulting from decreased and increased maternal nutrition during important windows of development (fetal and neonatal). My group was one of the first groups to address gender-related differences in the programming field.^{2,3}

There is now much interest in the passage of programming outcomes across generations. The paper on the intergenerational passage of insulin resistance from mother to second-generation offspring² was cited as a meritorious study by *The Physiologist*, the official magazine of the American Physiological Society. It was also highlighted by the *Wall Street Journal* and appeared on the web page of several international news organizations such as the British Broadcasting Corporation.

Our group was among the first to evaluate maternal interventions to prevent offspring outcomes and to explore mechanisms of negative programming by maternal undernutrition and obesity. We have developed three different models of maternal interventions to prevent adverse offspring outcomes: (1) dietary intervention prior to pregnancy,^{10,11} wherein we demonstrated that the metabolic abnormalities seen in offspring of obese rats can, to some extent, be prevented by dietary intervention prior to pregnancy. For this paper,¹⁰ I received the Funsalud Award (best nutrition paper in Mexico in 2010) and an award from the largest food retailer in the whole of Latin America (Bimbo Co, 2010); (2) both maternal and offspring exercise interventions^{17,18} and recently (3) maternal antioxidant interventions.¹⁹ However, if interventions cannot be applied in obese pregnant women, it is necessary to determine whether interventions in offspring are beneficial, since it is becoming evident that paternal obesity induces paternal programming through changes in spermatozoa, we have recently published data on how maternal obesity impairs male rat offspring reproductive capacity.²⁰ We showed that regular physical voluntary exercise even in old male offspring of obese mothers improves sperm quality, reduces oxidative stress biomarkers in both the testes and the sperm, and improves fertility. The study highlights the fact that it is never too late for exercise to be beneficial.

In November 2019, during the Meeting of the National Institutes of Health of Mexico, our group was acknowledged as published the best article in the biomedical area in 2018.¹³ This paper was the first to undertake transcriptomics in offspring of obese mothers. The first author, Consuelo Lomas, was one of my first postdoctoral students and we still work together. This recognition shows the importance that the concept of development programming has acquired in Mexico in terms of public health. As I write this commentary even this week, *Journal of Physiology* published a paper in which another postdoctoral student, Guadalupe Rodríguez, was the first author on a paper¹⁶ on the interaction of programming and aging – another new frontier.

Science is my passion. To work in science is a privilege, we get paid to play. My work is a kind of lifestyle; I cannot take it away from my mind. The small details in my life can be applied to simple experiments. We, as scientists, get excited very easily with results hot off the bench or when our papers and grants are accepted, often after much clarification and debate with reviewers. This critical appraisal of work improves us all and must be encouraged in ourselves and our students. I love to give public presentations showing our results to our peers and the general public. I also love teaching and advising students. An advantage of doing science in Mexico is that many students want to pursue an experimental thesis at undergraduate, bachelor's, master's, and doctoral levels. I have acted as mentor for 23 undergraduate thesis students, 5 masters and 8 PhD students, 7 of them currently work in self-funded research in permanent positions, and some with grants of their own, at different Mexican National Institutes of Health and at the UNAM. Some of them are continuing their research in the programming field – an example of intergenerational passage of research involvement. Their studies have been very productive. Teaching to me is so special because it is like planting seeds that you may never see grow, but you know that one day they will flourish.

Besides being a scientist, I am a mother of two children, Andrea and Ricardo. A big difficulty as a women scientist is being a mom at the same time. In my experience, motherhood has been more challenging than being a scientist. However, experiencing pregnancy and lactation gave me new tools to understand maternal physiology and modify according to my personal experience, the experiments I was designing. Children when they are young demand a lot of time and many unforeseen events arise. While the priority in my life is my children, which does not make me irresponsible in my work, it just makes me much more efficient with my time. In my case, the first articles I published as an independent researcher and corresponding author came out right after the birth of my two children. Their births marked the beginning of my productivity as an independent researcher. My kids and my husband Eduardo are the most important part of my life. I love my work, but I definitely think that family is the core of one's personal life. My parents, Mario and Angeles, have been the living example of this close family love and support for me. They have supported me throughout my entire life. I am the proof that being raised within a loving family helps to find happiness in a well-balanced life or "positive programming." I also need other activities to feel fulfilled as a person. I like to take pictures and have published one book of pictures and stories titled "Luz y Tinta, fotos para leer," which means "Light and Ink, pictures to be read." I also like running and always bring my trainers to conferences. Maybe we can talk science during an early morning run at the next DOHaD conference.

References

1. Zambrano E, Rodriguez-Gonzalez G, Guzman C, *et al.* A maternal low protein diet during pregnancy and lactation in the rat impairs male reproductive development. *J Physiol.* 2005; 563, 275–284.
2. Zambrano E, Martinez-Samayoa P, Bautista C, *et al.* Sex differences in transgenerational alterations of growth and metabolism in progeny (F2) of female offspring (F1) of rats fed a low protein diet during pregnancy and lactation. *J Physiol.* 2005; 566, 225–236.
3. Zambrano E, Bautista C, Deas M, *et al.* A low maternal protein diet during pregnancy and lactation has sex- and window of exposure-specific effects on offspring growth and food intake, glucose metabolism and serum leptin in the rat. *J Physiol.* 2006; 571, 221–230.
4. Guzman C, Cabrera R, Cardenas M, *et al.* Protein restriction during fetal and neonatal development in the rat alters reproductive function and accelerates reproductive ageing in female progeny. *J Physiol.* 2006; 572, 97–108.
5. Mathias P. The Ibero-American Chapter of DoHaD. *J Develop Orig Health Dis.* 2016; 7, 221.
6. Bautista CJ, Boeck L, Larrea F, *et al.* Effects of a maternal low protein isocaloric diet on milk leptin and progeny serum leptin concentration and appetitive behavior in the first 21 days of neonatal life in the rat. *Pediatr Res.* 2008; 63, 358.
7. Reyes-Castro L, Rodriguez J, Rodriguez-Gonzalez G, *et al.* Pre- and/or postnatal protein restriction in rats impairs learning and motivation in male offspring. *Int J Develop Neurosci.* 2011; 29, 177–182.
8. Morimoto S, Calzada L, Sosa T, *et al.* Emergence of ageing-related changes in insulin secretion by pancreatic islets of male rat offspring of mothers fed a low-protein diet. *Br J Nutr.* 2012; 107, 1562–1565.
9. Reyes-Castro L, Padilla-Gómez E, Parga-Martínez N, *et al.* Hippocampal mechanisms in impaired spatial learning and memory in male offspring of rats fed a low-protein isocaloric diet in pregnancy and/or lactation. *Hippocampus* 2018; 28, 18–30.
10. Zambrano E, Martínez-Samayoa P, Rodríguez-González G, *et al.* Rapid report: dietary intervention prior to pregnancy reverses metabolic programming in male offspring of obese rats. *J Physiol.* 2010; 588, 1791–1799.
11. Rodriguez J, Rodriguez-Gonzalez G, Reyes-Castro L, *et al.* Maternal obesity in the rat programs male offspring exploratory, learning and motivation behavior: prevention by dietary intervention pre-gestation or in gestation. *Int J Develop Neurosci.* 2012; 30, 75–81.
12. Bautista C, Montaña S, Ramirez V, *et al.* Changes in milk composition in obese rats consuming a high-fat diet. *Br J Nutr.* 2016; 115, 538–546.
13. Lomas-Soria C, Reyes-Castro LA, Rodríguez-González GL, *et al.* Maternal obesity has sex-dependent effects on insulin, glucose and lipid metabolism and the liver transcriptome in young adult rat offspring. *J Physiol.* 2018; 596, 4611–4628.
14. Rodríguez-González GL, Reyes-Castro LA, Vega CC, *et al.* Accelerated aging of reproductive capacity in male rat offspring of protein-restricted mothers is associated with increased testicular and sperm oxidative stress. *Age* 2014; 36, 9721.
15. Rodríguez-González G, Vega C, Boeck L, *et al.* Maternal obesity and over-nutrition increase oxidative stress in male rat offspring reproductive system and decrease fertility. *Int J Obes.* 2015; 39, 549.
16. Rodríguez-González GL, Reyes-Castro LA, Bautista CJ, *et al.* Maternal obesity accelerates rat offspring metabolic aging in a sex dependent manner. *J Physiol.* 2019; 597, 5549–5563.
17. Vega CC, Reyes-Castro LA, Bautista CJ, *et al.* Exercise in obese female rats has beneficial effects on maternal and male and female offspring metabolism. *Int J Obes.* 2015; 39, 712.
18. Ibáñez CA, Vázquez-Martínez M, León-Contreras JC, *et al.* Different statistical approaches to characterization of adipocyte size in offspring of obese rats: effects of maternal or offspring exercise intervention. *Front Physiol.* 2018; 9, 1571.
19. Vega CC, Reyes-Castro LA, Rodríguez-González GL, *et al.* Resveratrol partially prevents oxidative stress and metabolic dysfunction in pregnant rats fed a low protein diet and their offspring. *J Physiol.* 2016; 594, 1483–1499.
20. Santos M, Rodríguez-González GL, Ibáñez C, *et al.* Adult exercise effects on oxidative stress and reproductive programming in male offspring of obese rats. *Am J Physiol Regul Integr Compar Physiol.* 2014; 308, R219–R225.