



## OPEN ACCESS

EDITED AND REVIEWED BY  
Wei Ge,  
University of Macau, China

\*CORRESPONDENCE  
Lawrence M. Nelson  
✉ doc@conoverfoundation.org

RECEIVED 22 June 2024  
ACCEPTED 03 July 2024  
PUBLISHED 01 August 2024

CITATION  
Nelson LM, Choubey M, Kamei H and  
Rampon C (2024) Editorial: Insights in  
developmental endocrinology: 2023.  
*Front. Endocrinol.* 15:1453023.  
doi: 10.3389/fendo.2024.1453023

COPYRIGHT  
© 2024 Nelson, Choubey, Kamei and Rampon.  
This is an open-access article distributed under  
the terms of the [Creative Commons Attribution  
License \(CC BY\)](#). The use, distribution or  
reproduction in other forums is permitted,  
provided the original author(s) and the  
copyright owner(s) are credited and that the  
original publication in this journal is cited, in  
accordance with accepted academic  
practice. No use, distribution or reproduction  
is permitted which does not comply with  
these terms.

# Editorial: Insights in developmental endocrinology: 2023

Lawrence M. Nelson<sup>1\*</sup>, Mayank Choubey<sup>2</sup>, Hiroyasu Kamei<sup>3</sup>  
and Christine Rampon<sup>4,5</sup>

<sup>1</sup>Digital Women's Health, Initiative Mary Elizabeth Conover Foundation, Tysons, VA, United States, <sup>2</sup>Department of Foundations of Medicine, New York University (NYU) Grossman Long Island School of Medicine, Mineola, NY, United States, <sup>3</sup>Institute of Science and Engineering, Kanazawa University, Kanazawa, Ishikawa, Japan, <sup>4</sup>Laboratoire des Biomolécules, École Normale Supérieure, PSL University, Centre National de la Recherche Scientifique, Sorbonne Université, Paris, France, <sup>5</sup>Faculty of Sciences, Université Paris-Cité, Paris, France

## KEYWORDS

developmental endocrinology, wisdom of the body, homeostasis, integrative biology, maternal fetal interface, women's hormonal health, hormonal literacy, science advocacy

## Editorial on the Research Topic

Insights in developmental endocrinology: 2023

## Integrative developmental endocrinology

*The wisdom of the body perspective* transcends our current human understanding and is a call for more innovative biomedical research. Developmental endocrinology is integrative biology, involving the concept of homeostasis, and the elegant underpinnings of life itself (1). Developmental endocrinology involves the intricate relationship between maternal nutrition and offspring health and this has been the subject of extensive research and scientific inquiry (2). Miles et al., in a mouse model, investigate the effects of maternal caloric restriction in mid-gestation and lactation on neonatal development and adult metabolic function in response to a high-fat diet. Studies investigating the impact of maternal caloric restriction during specific stages of gestation and lactation shed light on the long-term implications for offspring health and adult metabolic function.

Exploring gene expression and developmental endocrinology in response to maternal undernutrition stresses the importance of the interplay between maternal health and offspring health outcomes (3). These findings underscore the critical importance of early developmental stages in shaping adult physiological responses. Zhang et al. review the developmental endocrinology of oxidative stress at the maternal-fetal interface (Figure 1). They suggest oxidative stress at this site is an important driver of pathology, antioxidant therapy may be the best treatment for “placental diseases”, and an antioxidant lifestyle may help prevent disease. The report thoroughly examines the physiological implications of oxidative stress on the maternal-fetal interface, highlighting the potential ramifications on nutrient transfer, immune regulation, and overall developmental processes. Moreover, it emphasizes the need for continued research endeavors and intervention strategies to mitigate the adverse effects of oxidative stress on this complex interplay, aiming to promote

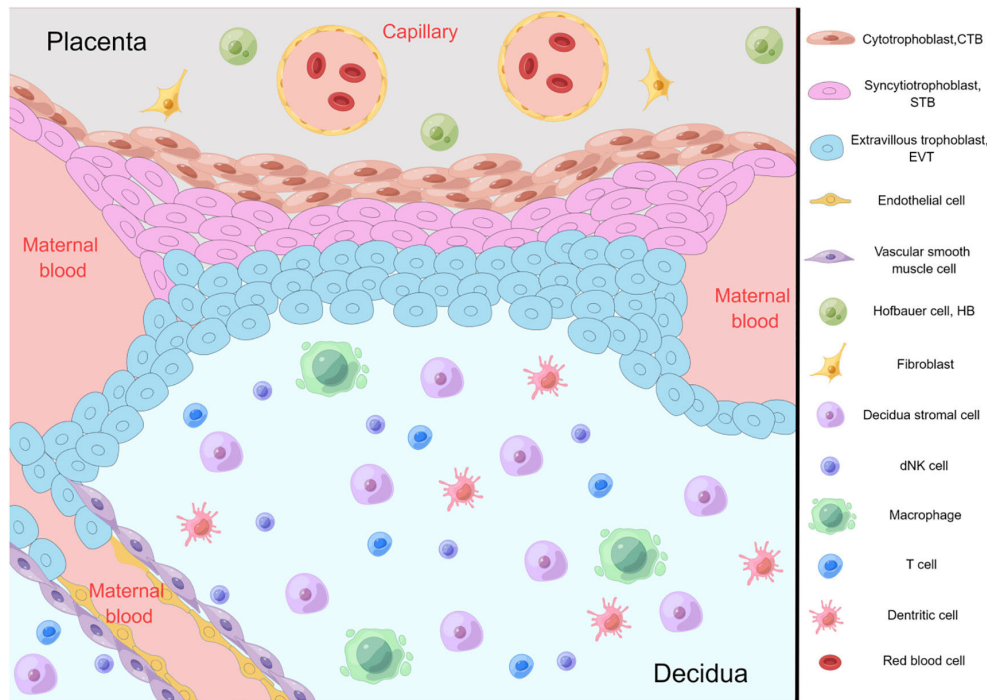


FIGURE 1

The wisdom of the body working through the cellular components at the maternal-fetal interface.

the integrated approach to establishing and maintaining the health of both the expectant mother and the developing fetus.

Thyroid autoimmunity is associated with many maternal and neonatal adverse outcomes (4). In another context of developmental endocrinology in pregnancy, Liu et al. investigate thyroid peroxidase antibodies (TPO-Ab) and their association with first-trimester miscarriage rate/live birth rate in women with unexplained recurrent spontaneous abortion (URSA), which have significant implications for understanding pregnancy outcomes. The findings highlight a higher first-trimester miscarriage rate in TPO-Ab-positive women, particularly in younger subgroups and primary URSA subgroups. While the live birth rate did not exhibit a statistically significant difference between TPO-Ab positive and negative groups, the potential impact of TPO-Ab on pregnancy outcomes, especially in the first trimester, merits further investigation. Acknowledging the study's limitations, such as its retrospective design, emphasizes the need for larger, prospective randomized studies to confirm the association between TPO-Ab and first-trimester miscarriage rate, particularly in specific subgroups of patients with URSA.

Regarding the role of  $ROR\alpha$  in developmental endocrinology, Rani reviews the fascinating “staggerer mice” story with one of its first roles materializing during embryogenesis, an intricate molecular-endocrine mediated circadian-like regulatory process. Dysfunctional  $ROR\alpha$  impairs metabolism, osteogenesis, skeletal and smooth muscles, and immunity, and makes  $ROR\alpha$  a multi-functional protein during embryogenesis. The text discusses the importance of good nutrition for effective embryonic development and the role of essential nutrients in supporting healthy transcriptional systems.  $ROR\alpha$  also functions in germ cell organization, another aspect of developmental endocrinology (5).

Adrenal development in embryonic and fetal health expands our understanding of the intricate molecular and physiological processes that shape developmental endocrinology (6). Akkuratova et al. outline a detailed single-cell atlas of chromaffin development, permitting the identification of novel cell populations and establishing nuanced transitions within subpopulations of immature chromaffin cells. The work advances the field of sympatho-adrenal developmental endocrinology. The authors report the discovery of microheterogeneity in developing chromaffin cell populations, the identification of novel markers of adrenergic and noradrenergic populations in developing adrenal glands, and the revelation of new differentiation paths leading to these populations. Additionally, the research emphasized the essential roles of chromaffin cells in fetal survival, the initiation of breathing, and the physiological response to hypoxia. The study's use of deep single-cell RNA sequencing and trajectory analysis provided valuable insights into the molecular events driving fate choices in Schwann cell precursors and the transient nature of developing chromaffin populations, leading to the identification of previously unknown transient or persisting markers of chromaffin cell subpopulations.

Hypogonadotropic hypogonadism leads to absent, partial, or arrested puberty (7). Zhang et al. provide a comprehensive characterization of Kallmann syndrome and associated genetic variations with the condition. The group provides crucial insights into the genetic and molecular mechanisms underlying this complex disorder, paving the way for precise clinical diagnosis and treatment strategies. The comprehensive study characterized the clinical phenotype and genetic variations in a 14.4-year-old male diagnosed with Kallmann syndrome (KS). Bioinformatics

analysis suggested that the IL17RD variant may disrupt fibroblast growth factor signaling by potentially affecting protein phosphorylation and modification. In contrast, the CPEB4 variant appears crucial in affecting olfactory bulb morphogenesis, potentially contributing to the patient's hyposmia. The study provides valuable insights into the genetic and molecular mechanisms underlying KS. Furthermore, the study broadens the gene expression profile of KS-related pathogenic genes, paving the way for future research in understanding KS pathogenesis. The patient received gonadorelin pump pulse therapy, improving LH, FSH, and T levels. The patient is under ongoing regular follow-up, with follow-up examinations showing noteworthy progress. This study presents significant contributions to the academic understanding of this complex genetic disorder and paves the way for further research in Kallmann syndrome.

Single-cell RNA sequencing is an emerging powerful tool to characterize cell subpopulations, circumventing the shortcomings of traditional cell population sequencing (8). Tirumalasetty et al. provide a comprehensive review of single-cell RNA-sequencing compared to the bulk RNA-seq of rodent and human patients testicular tissues. The team highlights “the cellular heterogeneity, spatial transcriptomics, dynamic gene expression, and cell-to-cell interactions with distinct cell populations within the testes”. The findings have potential implications for future clinical management of male reproductive complications. Liu et al. report a bidirectional cohort study on spermatogenesis and seminal testosterone and offer a potential method to improve the assessment of male infertility and sperm quality. The team concludes measuring testosterone in seminal fluid is more sensitive for judging the presence of local spermatogenesis in nonobstructive azoospermia patients.

These studies collectively contribute to the ongoing dialogue surrounding developmental endocrinology, maternal-fetal health, genetic disorders, and reproductive health. They underscore the importance of continued research efforts to unravel the complex

interplay between endocrinological processes, environmental factors, and genetic determinants in shaping developmental outcomes. As we navigate the intricate landscape of developmental endocrinology, this *wisdom of the body perspective* is vital in guiding future research endeavors and clinical interventions to promote maternal and offspring health and well-being.

## Author contributions

LN: Conceptualization, Investigation, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. MC: Writing – review & editing. CR: Writing – review & editing. HK: Writing – review & editing.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

## Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

## References

- Knobil E. The wisdom of the body revisited. *News Physiol Sci.* (1999) 14:1–11. doi: 10.1152/physiologyonline.1999.14.1.1
- Mitchell AJ, Dunn GA, Sullivan EL. The influence of maternal metabolic state and nutrition on offspring neurobehavioral development: A focus on preclinical models. *Biol Psychiatry Cognit Neurosci Neuroimaging.* (2022) 7:450–60. doi: 10.1016/j.bpsc.2021.11.014
- Guillaumin MCC, Peleg-Raibstein D. Maternal over- and malnutrition and increased risk for addictive and eating disorders in the offspring. *Nutrients.* (2023) 15:1095. doi: 10.3390/nu15051095
- Xu Y, Chen H, Ren M, Gao Y, Sun K, Wu H, et al. Thyroid autoimmunity and adverse pregnancy outcomes: A multiple center retrospective study. *Front Endocrinol (Lausanne).* (2023) 14:1081851. doi: 10.3389/fendo.2023.1081851
- Peer NR, Law SM, Murdoch B, Goulding EH, Eddy EM, Kim K. Germ cell-specific retinoic acid receptor  $\alpha$  Functions in germ cell organization, meiotic integrity, and spermatogonia. *Endocrinology.* (2018) 159:3403–20. doi: 10.1210/en.2018-00533
- Pignatti E, du Toit T, Flück CE. Development and function of the fetal adrenal. *Rev Endocr Metab Disord.* (2023) 24:5–21. doi: 10.1007/s11154-022-09756-3
- Alexander EC, Faruqi D, Farquhar R, Unadkat A, Ng Yin K, Hoskyns R, et al. Gonadotropins for pubertal induction in males with hypogonadotropic hypogonadism: systematic review and meta-analysis. *Eur J Endocrinol.* (2024) 190:S1–S11. doi: 10.1093/ejendo/lvad166
- Wang S, Sun ST, Zhang XY, Ding HR, Yuan Y, He JJ, et al. The evolution of single-cell RNA sequencing technology and application: progress and perspectives. *Int J Mol Sci.* (2023) 24:2943. doi: 10.3390/ijms24032943