



Editorial Placental Related Disorders of Pregnancy

Eun D. Lee¹ and Hiten D. Mistry^{2,*}

- ¹ Department of Microbiology and Immunology, School of Medicine, Massey Cancer Center, Virginia Commonwealth University, Richmond, VA 23298, USA; eun.lee@vcuhealth.org
- ² Department of Women and Children's Health, School of Life Course Sciences, King's College London, London SE5 9NU, UK
- * Correspondence: hiten.mistry@kcl.ac.uk

We are pleased to present this Special Issue of *International Journal of Molecular Sciences*, entitled 'Placental Related Disorders of Pregnancy'. The placenta is a unique organ, produced outside the embryo and connected by a cord of vessels, and is formed as a result of various degrees of interactions between fetal and maternal tissues within the pregnant uterus. The placenta fulfils a variety of functions, which are completed by several different organs in adult life. Unlike the relatively stable mature adult organs, the placenta is programmed to complete very different functions during development. Thus, the placenta can be described as a constantly evolving organ. Its major role is the homeostasis of a protected environment for the undisturbed growth and development of an embryo/fetus.

Placental-related disorders of pregnancy are almost unique to the human species and affect around a third of human pregnancies. Many of these disorders result in increased maternal and fetal mortality and morbidity and can have life-long health implications for both the mother and her child. Recent changes in human lifestyle, such as delayed childbirth and hypercaloric diets, may have increased the global incidence of placentalrelated disorders over recent decades.

This Special Issue is a compilation of 21 research manuscripts and reviews, covering all aspects of placentation, with a particular focus on those related to placental function and disorders of pregnancy. The manuscripts cover aspects of placental physiology, biochemistry and molecular biology, and clinical and animal models are also included in this excellent Special Issue.

This collection contains some excellent reviews. The first review covers the homeostasis of the cytokine interleukin-15 (IL-15) in healthy pregnancy, providing up-to-date mechanisms of the action of IL-15 at the maternal–fetal interface [1]. A fascinating review by Anthony Carter covers why human placentation is so unique, with in-depth details on placentation in different animals to wonderfully illustrate this [2]. This is followed by a comprehensive review covering the important condition of gestational diabetes and the contribution of the placenta in the associated immunoendocrine dysregulation [3]. Finally, a very topical and informative overview highlighting the role of the placenta and the use of low-dose aspirin in the prevention of pre-eclampsia [4,5]. In addition to the reviews, our collection also contains several novel studies covering pre-eclampsia [6–8]; fetal growth restriction [7,9–11]; calcium signaling [12]; placental oxidative stress, nutrition, senescence and apoptosis [6,9,13–15]; sexual dimorphism [16–18], intrahepatic cholestasis [19]; placental vascular modelling [20]; and placental villous explant culture models [21].

This Special Issue presents placental research using a range of established and stateof-the-art techniques showcasing novel and up-to-date data to enhance and facilitate our understanding of placentation as well as mechanisms that result in associated adverse pregnancy outcomes, as well as longer-term risks of complications.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.



Citation: Lee, E.D.; Mistry, H.D. Placental Related Disorders of Pregnancy. Int. J. Mol. Sci. 2022, 23, 3519. https://doi.org/10.3390/ ijms23073519

Received: 14 March 2022 Accepted: 22 March 2022 Published: 24 March 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/).

References

- 1. Gordon, S.M. Interleukin-15 in Outcomes of Pregnancy. Int. J. Mol. Sci. 2021, 22, 11094. [CrossRef]
- 2. Carter, A.M. Unique Aspects of Human Placentation. Int. J. Mol. Sci. 2021, 22, 8099. [CrossRef]
- Olmos-Ortiz, A.; Flores-Espinosa, P.; Diaz, L.; Velazquez, P.; Ramirez-Isarraraz, C.; Zaga-Clavellina, V. Immunoendocrine Dysregulation during Gestational Diabetes Mellitus: The Central Role of the Placenta. *Int. J. Mol. Sci.* 2021, 22, 8087. [CrossRef]
- 4. Walsh, S.W.; Strauss, J.F., 3rd. The Road to Low-Dose Aspirin Therapy for the Prevention of Preeclampsia Began with the Placenta. *Int. J. Mol. Sci.* **2021**, 22, 6085. [CrossRef]
- Sun, Y.; Tan, L.; Neuman, R.I.; Broekhuizen, M.; Schoenmakers, S.; Lu, X.; Danser, A.H. Megalin, Proton Pump Inhibitors and the Renin-Angiotensin System in Healthy and Pre-Eclamptic Placentas. *Int. J. Mol. Sci.* 2021, 22, 7407. [CrossRef]
- Scaife, P.J.; Simpson, A.; Kurlak, L.O.; Briggs, L.V.; Gardner, D.S.; Broughton Pipkin, F.; Jones, C.J.; Mistry, H.D. Increased Placental Cell Senescence and Oxidative Stress in Women with Pre-Eclampsia and Normotensive Post-Term Pregnancies. *Int. J. Mol. Sci.* 2021, 22, 7295. [CrossRef]
- Mundal, S.B.; Rakner, J.J.; Silva, G.B.; Gierman, L.M.; Ausdal, M.; Basnet, P.; Elschot, M.; Bakke, S.S.; Ostrop, J.; Thomsen, L.C.V.; et al. Divergent regulation of decidual oxidative-stress response by NRF2 and KEAP1 in preeclampsia with and without fetal growth restriction. *Int. J. Mol. Sci.* 2022, 23, 1966. [CrossRef]
- 8. Sammar, M.; Siwetz, M.; Meiri, H.; Sharabi-Nov, A.; Altevogt, P.; Huppertz, B. Reduced Placental CD24 in Preterm Preeclampsia Is an Indicator for a Failure of Immune Tolerance. *Int. J. Mol. Sci.* **2021**, *22*, 8045. [CrossRef]
- Tanner, A.R.; Lynch, C.S.; Kennedy, V.C.; Ali, A.; Winger, Q.A.; Rozance, P.J.; Anthony, R.V. CSH RNA Interference Reduces Global Nutrient Uptake and Umbilical Blood Flow Resulting in Intrauterine Growth Restriction. *Int. J. Mol. Sci.* 2021, 22, 8150. [CrossRef]
- Murphy, C.N.; Walker, S.P.; MacDonald, T.M.; Keenan, E.; Hannan, N.J.; Wlodek, M.E.; Myers, J.; Briffa, J.F.; Romano, T.; Roddy Mitchell, A.; et al. Elevated Circulating and Placental SPINT2 Is Associated with Placental Dysfunction. *Int. J. Mol. Sci.* 2021, 22, 7467. [CrossRef]
- Stojanovska, V.; Shah, A.; Woidacki, K.; Fischer, F.; Bauer, M.; Lindquist, J.A.; Mertens, P.R.; Zenclussen, A.C. YB-1 Is Altered in Pregnancy-Associated Disorders and Affects Trophoblast in Vitro Properties via Alternation of Multiple Molecular Traits. *Int. J. Mol. Sci.* 2021, 22, 7226. [CrossRef]
- 12. Fecher-Trost, C.; Wolske, K.; Wesely, C.; Lohr, H.; Klawitter, D.S.; Weissgerber, P.; Gradhand, E.; Burren, C.P.; Mason, A.E.; Winter, M.; et al. Mutations That Affect the Surface Expression of TRPV6 Are Associated with the Upregulation of Serine Proteases in the Placenta of an Infant. *Int. J. Mol. Sci.* **2021**, *22*, 12694. [CrossRef]
- 13. Kohan-Ghadr, H.R.; Armistead, B.; Berg, M.; Drewlo, S. Irisin Protects the Human Placenta from Oxidative Stress and Apoptosis via Activation of the Akt Signaling Pathway. *Int. J. Mol. Sci.* 2021, 22, 11229. [CrossRef]
- Lospinoso, K.; Dozmorov, M.; El Fawal, N.; Raghu, R.; Chae, W.J.; Lee, E.D. Overexpression of ERAP2N in Human Trophoblast Cells Promotes Cell Death. *Int. J. Mol. Sci.* 2021, 22, 8585. [CrossRef]
- 15. Steinhauser, C.B.; Lambo, C.A.; Askelson, K.; Burns, G.W.; Behura, S.K.; Spencer, T.E.; Bazer, F.W.; Satterfield, M.C. Placental Transcriptome Adaptations to Maternal Nutrient Restriction in Sheep. *Int. J. Mol. Sci.* **2021**, 22, 7654. [CrossRef]
- Bucher, M.; Kadam, L.; Ahuna, K.; Myatt, L. Differences in Glycolysis and Mitochondrial Respiration between Cytotrophoblast and Syncytiotrophoblast In-Vitro: Evidence for Sexual Dimorphism. *Int. J. Mol. Sci.* 2021, 22, 10875. [CrossRef]
- Lien, Y.C.; Zhang, Z.; Cheng, Y.; Polyak, E.; Sillers, L.; Falk, M.J.; Ischiropoulos, H.; Parry, S.; Simmons, R.A. Human Placental Transcriptome Reveals Critical Alterations in Inflammation and Energy Metabolism with Fetal Sex Differences in Spontaneous Preterm Birth. *Int. J. Mol. Sci.* 2021, 22, 7899. [CrossRef]
- 18. Garcia-Martin, I.; Penketh, R.J.; Garay, S.M.; Jones, R.E.; Grimstead, J.W.; Baird, D.M.; John, R.M. Symptoms of Prenatal Depression Associated with Shorter Telomeres in Female Placenta. *Int. J. Mol. Sci.* **2021**, *22*, 7458. [CrossRef]
- 19. Ontsouka, E.; Epstein, A.; Kallol, S.; Zaugg, J.; Baumann, M.; Schneider, H.; Albrecht, C. Placental Expression of Bile Acid Transporters in Intrahepatic Cholestasis of Pregnancy. *Int. J. Mol. Sci.* **2021**, 22, 10434. [CrossRef]
- 20. Courtney, J.A.; Wilson, R.L.; Cnota, J.; Jones, H.N. Conditional Mutation of Hand1 in the Mouse Placenta Disrupts Placental Vascular Development Resulting in Fetal Loss in Both Early and Late Pregnancy. *Int. J. Mol. Sci.* **2021**, *22*, 9532. [CrossRef]
- Kupper, N.; Pritz, E.; Siwetz, M.; Guettler, J.; Huppertz, B. Placental Villous Explant Culture 2.0: Flow Culture Allows Studies Closer to the In Vivo Situation. Int. J. Mol. Sci. 2021, 22, 7464. [CrossRef]