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**Placental Immunity Against Viral Infections: Defensive
Mechanisms and Impact on Preterm Birth**

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Abstract

The placenta serves as a critical organ during pregnancy, not only facilitating nutrient and oxygen exchange between mother and fetus but also acting as an immunological barrier to protect the developing fetus from pathogens. This article explores the placenta's defensive mechanisms against viral infections, including cellular, molecular, and immunological strategies. It further examines how certain viruses, such as cytomegalovirus (CMV), Zika virus (ZIKV), and SARS-CoV-2, can evade these defenses, leading to placental inflammation and complications like preterm birth. Recent studies highlight the importance of understanding these interactions to develop preventive strategies and improve pregnancy outcomes.

Keywords: Pregnancy- Viral Infections- Immunological- Preterm Birth

Introduction

The placenta is a transient yet vital organ in mammalian pregnancy, responsible for nutrient transfer, gas exchange, and hormonal regulation while providing immune protection to the fetus. Viral infections pose a significant threat during pregnancy, potentially causing congenital anomalies, fetal growth restriction, or preterm birth—defined as delivery before 37 weeks of gestation, a leading cause of neonatal morbidity and mortality.

This review examines the placenta's multi-layered defenses against viruses and the pathways by which pathogens overcome them, ultimately contributing to preterm birth. Insights are drawn from recent research on placental immunology and infections by viruses like CMV, ZIKV, and SARS-CoV-2.

Defensive Mechanisms of the Placenta Against Viral Infections

The placenta employs a combination of physical, molecular, and immunological barriers to restrict viral entry and replication. These can be categorized into cellular, molecular, and immunological components.

Cellular Mechanisms

The syncytiotrophoblast layer, forming the outer surface of placental villi, acts as the primary physical barrier. This multinucleated structure, continuously renewed through fusion of underlying cytotrophoblasts, lacks lateral cell junctions, limiting persistent viral infections. Hofbauer cells—fetal-

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derived macrophages in the villous stroma—phagocytose pathogens but can also serve as viral reservoirs in infections like HIV, CMV, or ZIKV.

Extravillous trophoblasts, invading the maternal decidua, express non-classical HLA-G to modulate maternal immune cells, such as uterine natural killer (uNK) cells, preventing fetal rejection while potentially creating entry points for viruses.

Molecular Mechanisms

Viral entry receptors, including ACE2 (for SARS-CoV-2), AXL (for ZIKV), and integrins (for CMV), are differentially expressed across gestation. For instance, higher AXL expression in mid-gestation increases ZIKV susceptibility, while declining ACE2 later in pregnancy may reduce SARS-CoV-2 risk. Hormones like estrogen and progesterone regulate these receptors.

Placental microRNAs, such as those in the C19MC cluster, inhibit viral replication by inducing type III interferons (e.g., IFN- λ 1 against ZIKV). Viral transmission may occur via transcytosis (e.g., FcRn-mediated for antibody-virus complexes), paracellular routes (disrupted tight junctions, as with SARS-CoV-2 spike protein), or cell-to-cell spread.

Immunological Mechanisms

Placental immunity relies heavily on innate responses. Pattern recognition receptors (PRRs), including Toll-like receptors (TLR3 for double-stranded RNA, TLR7/8 for single-stranded RNA) and RIG-I-like receptors, detect viruses and trigger type I and III interferons. These activate interferon-stimulated genes (ISGs) like ISG20 (degrading ZIKV RNA), OAS (activating RNase L), and MxA (blocking nuclear transport).

Adaptive elements include uNK cells exerting cytotoxicity via perforin and granzyme, and CD8+ T cells eliminating infected cells through MHC class I. Maternal antibodies transfer via FcRn, but viruses evade by suppressing interferons (e.g., ZIKV NS5 degrading STAT2) or downregulating MHC-I (e.g., CMV US2/US11 proteins).

How Viruses Overcome Placental Defenses

Despite robust barriers, viruses like CMV, ZIKV, HSV, and parvovirus B19 exploit hematogenous routes. They utilize receptors such as CD46 (CMV) or lipid rafts (coxsackievirus). ZIKV enhances trophoblast permeability at specific gestational ages and employs antibody-dependent enhancement (ADE) via cross-reactive antibodies (e.g., from dengue).

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SARS-CoV-2 induces intervillitis and villitis, while CMV causes trophoblast apoptosis via TNF- α and villous immaturity. Viremia and early-gestation timing increase risks, as the syncytiotrophoblast is less mature.

Impact of Viral Infections on Preterm Birth

Viral infections trigger placental inflammation, promoting preterm birth through cytokine storms (e.g., TNF- α , IL-1 β , IL-6, IL-8). This leads to trophoblast apoptosis, oxidative stress, and barrier disruption. Inflammasome activation (NLRP3) releases IL-1 β and IL-18, causing vascular malperfusion, villous immaturity, and impaired spiral artery remodeling.

Pathologies mimic preeclampsia or fetal growth restriction, inducing prostaglandins and uterine contractions. ZIKV causes villitis, CMV villous immaturity, and SARS-CoV-2 malperfusion. Early infections heighten risks of premature rupture of membranes and chorioamnionitis. Viruses may also sensitize the placenta to bacterial products, exacerbating preterm birth. Gestational timing matters: early infections pose higher congenital risks, while late ones cause acute inflammation.

Conclusion

The placenta's immunity against viruses is a dynamic, multifaceted system integrating cellular barriers, molecular inhibitors, and innate-dominant responses. However, evasion strategies allow viruses to induce inflammation and preterm birth. Ongoing initiatives, such as the Human Placenta Project, focus on biomarkers and interventions like antivirals or immune modulators.

Preventive measures—including maternal vaccination, infection screening, and further molecular research—are essential to mitigate preterm birth risks and enhance maternal-fetal health.

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References

- Bayer, A., Lennemann, N. J., Ouyang, Y., Bramley, J. C., Morosky, S., Marques, E. T. A., Jr., & Sadovsky, Y. (2016). Type III interferons produced by human placental trophoblasts confer protection against Zika virus infection. *Cell Host & Microbe*, 19(5), 705–712. <https://doi.org/10.1016/j.chom.2016.03.008>
- Delorme-Axford, E., Donker, R. B., Mouillet, J. F., Chu, T., Bayer, A., Ouyang, Y., Wang, T., Stolz, D. B., Sarkar, S. N., Morelli, A. E., Sadovsky, Y., & Coyne, C. B. (2013). Human placental trophoblasts confer viral resistance to recipient cells. *Proceedings of the National Academy of Sciences of the United States of America*, 110(29), 12048–12053. <https://doi.org/10.1073/pnas.1304718110>
- Hamilton, S. T., van Zuylen, W., Shand, A., Scott, G. M., Naing, Z., Hall, B., Craig, M. E., & Rawlinson, W. D. (2012). Human cytomegalovirus-induces cytokine changes in the placenta with implications for adverse pregnancy outcomes. *PLoS ONE*, 7(12), e52899. <https://doi.org/10.1371/journal.pone.0052899>
- Megli, C. J., & Coyne, C. B. (2022). Infections at the maternal–fetal interface: An overview of pathogenesis and defence. *Nature Reviews Microbiology*, 20(2), 67–82. <https://doi.org/10.1038/s41579-021-00610-y>
- Ouyang, Y., Bayer, A., Chu, T., Tyurin, V. A., Sadovsky, Y., & Coyne, C. B. (2018). Chromosome 19 microRNAs exert antiviral activity independent from type III interferon signaling. *Placenta*, 66, 1–7. <https://doi.org/10.1016/j.placenta.2018.04.008>
- Pereira, L., Maidji, E., McDonagh, S., & Tabata, T. (2003). Human cytomegalovirus transmission from the uterus to the placenta correlates with placental villitis and focal infection of cytotrophoblasts. *Journal of Pathology*, 208(4), 509–518. <https://doi.org/10.1002/path.1524>
- Racicot, K., Kwon, J. Y., Aldo, P., Silasi, M., & Mor, G. (2014). Understanding the complexity of the immune system during pregnancy. *American Journal of Reproductive Immunology*, 72(2), 107–116. <https://doi.org/10.1111/aji.12289>
- Robbins, J. R., & Bakardjiev, A. I. (2012). Pathogens and the placental villus: A barrier to maternal-fetal transmission. *Current Opinion in Microbiology*, 15(1), 32–39. <https://doi.org/10.1016/j.mib.2011.11.004>
- Tabata, T., Petitt, M., Puerta-Guardo, H., Harris, E., Pereira, L., & Coyne, C. B. (2025). Zika virus and the fetal-maternal interface: Deciphering the mechanisms of placental infection and implications for pregnancy outcomes. *Emerging Microbes & Infections*, 14(1), 2532681. <https://doi.org/10.1080/22221751.2025.2532681>
- Vilchez, G., Sokol, R. J., & Coyne, C. B. (2025). Recent updates on research models and tools to study virus–host interactions at the placenta. *Viruses*, 12(1), 5. <https://doi.org/10.3390/v12010005>