Project Exploring Hepatitis and Maternal Galectins in Pregnancy: A Path to Better Care

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Background and preliminary data:

Metabolic Adaptations in Pregnancy During Chronic Viral Infections

Hepatitis B (HBV), C (HCV), and D (HDV) are major global health threats, particularly for pregnant women, where they present significant risks to both maternal and fetal health. Chronic infections with these viruses contribute to liver disease, with HBV and HCV being among the leading causes of morbidity and mortality worldwide. Hepatitis D, which only occurs in co-infection with HBV, worsens liver pathology and complicates the clinical course.

Pregnancy induces a unique physiological state characterized by significant metabolic and immune system changes, which can interact with viral infections such as those caused by hepatitis viruses. These alterations affect the function of various organs, particularly the liver. Hepatic adaptations during pregnancy, including changes in protein synthesis, glucose metabolism, and bile acid production, are essential to support fetal development but can also exacerbate pre-existing liver conditions, including chronic viral infections. These interactions may worsen liver function, increase viral replication, and accelerate liver fibrosis progression. Moreover, immune system modulation during pregnancy may alter the course of chronic viral infections, potentially leading to viral flare-ups or persistent viral replication. The risk of maternal-fetal transmission, particularly with HBV, remains a critical concern, as it may result in chronic infections and long-term liver-related complications in the neonate.

Galectins (gal), a family of β-galactoside-binding proteins, are critical regulators of immune responses, inflammation, and fibrosis in the liver. Among them, gal-1, gal-3, and gal-9 are particularly relevant to liver pathology. During pregnancy, these galectins are upregulated, contributing to the immune tolerance necessary for fetal development while simultaneously modulating maternal immune responses and metabolic functions. In the context of chronic viral infections, galectins are implicated in promoting immune evasion and fibrosis. The interplay between pregnancy-induced metabolic changes, galectin-mediated immune regulation, and viral hepatitis may exacerbate liver damage, increase the risk of viral persistence, and heighten the likelihood of vertical transmission.

Preliminary data from our laboratory and other studies suggest that galectin levels are significantly elevated in pregnant women with chronic viral infections, including HBV and HCV, and may contribute to immune dysregulation and liver fibrosis. However, the role of galectins in the specific context of viral hepatitis during pregnancy is poorly understood. Investigating how galectins influence liver pathology, immune responses, and viral dynamics in pregnant women is crucial for identifying potential biomarkers and therapeutic targets to improve maternal and fetal outcomes.

Hypothesis: We hypothesize that galectins play a pivotal role in modulating immune responses and liver pathology during pregnancy in women infected with Hepatitis B, C, and D. Specifically, we propose that galectins contribute to immune tolerance, viral persistence, and liver damage, thereby affecting both maternal and fetal outcomes. We aim to explore galectin expression and function throughout pregnancy to better understand their role in disease progression, immune modulation, and the potential for vertical

transmission. Additionally, we hypothesize that elevated galectin levels in pregnant women with chronic viral hepatitis are associated with worse maternal outcomes, such as liver fibrosis progression, and an increased risk of mother-to-child transmission.

Aims and Work Programme

Aim 1: Assess the maternal galectin signature in pregnant women with Hepatitis B, C, and D infections. This aim will provide insights into the upregulation of galectins in response to viral infection during pregnancy. We will investigate whether galectin levels correlate with key clinical parameters such as viral load, liver function (e.g., FIB-4 score, FibroScan), and pregnancy outcomes. These findings will help elucidate the role of galectins in viral pathogenesis during pregnancy and their potential as biomarkers of disease severity.

Aim 2: Correlate maternal and neonatal galectin levels with clinical outcomes. In a cohort of pregnant women with Hepatitis B, C, and D, we will assess the correlation between maternal and neonatal galectin expression levels and outcomes, including liver fibrosis, viral persistence, and mother-to-child transmission. This will allow us to identify how galectin expression influences both maternal health and neonatal outcomes, such as viral transmission and liver health in the offspring.

Impact on Researcher Development and Public Health: The clinical researcher working on this project will gain comprehensive expertise in both infectious disease and pregnancy care, including the postpartum period. This project has the potential to enhance our understanding of the molecular mechanisms underlying viral hepatitis during pregnancy. By investigating how galectins influence immune responses, viral replication, and liver damage, we aim to provide novel insights that could inform therapeutic strategies to improve maternal and fetal health outcomes. This research will lay the groundwork for the development of targeted interventions that may mitigate the effects of chronic viral hepatitis during pregnancy, ultimately reducing the burden of disease on both mothers and their children.

Project-related publications: (max. 5)

1. Jiménez Cruz J, … **Verlohren S**,.. Ongoing outbreak of maternal parvovirus B19 infections in Germany since end of 2023: consequence of COVID-19 pandemic? Ultrasound Obstet Gynecol. 2025 Apr;65(4):456-461. doi: 10.1002/uog.29197. PMID: 40051033 2.

2. **Blois SM**, … Garcia MG, Mazzolini G. Dendritic cells regulate angiogenesis associated with liver fibrogenesis. Angiogenesis. 2014 Jan;17(1):119-28. doi: 10.1007/s10456-013-9382-5. PMID: 24068342

3. Atorrasagasti C, … **Blois SM**, Garcia MG. Acceleration of TAA-Induced Liver Fibrosis by Stress Exposure Is Associated with Upregulation of Nerve Growth Factor and Glycopattern Deviations. Int J Mol Sci. 2021 May 11;22(10):5055. doi: 10.3390/ijms22105055. PMID: 34064584

4. Xie Y, … **Blois SM.** Fetal growth restriction induced by maternal gal-3 deficiency is associated with altered gut-placenta axis. Cell Death Dis. 2024 Aug 8;15(8):575. PMID: 39117607.

5. Zhao F, … **Blois SM**. A unique maternal and placental galectin signature upon SARS-CoV-2 infection suggests galectin-1 as a key alarmin at the maternal-fetal interface. Front Immunol. 2023 Jul 5;14:1196395. PMID: 37475853.