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PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Improving Pregnancy Outcomes Among Racially and Ethnically Diverse Communities Impacted by Autoantibody Diseases

Katie Abouzahr, M.D.
Vice President, Portfolio Development Leader, Autoantibody,
The Janssen Pharmaceutical Companies of Johnson & Johnson (Janssen)

Globally, autoantibody-driven diseases represent an immense unmet patient need. There are more than 80 auto- and allo-antibody driven conditions,[1-4] and most have few or no safe, effective, and approved therapies. Autoantibody diseases are driven by pathogenic antibodies - autoantibodies - that are made by one's own body and attack important organs and tissues, resulting in a range of inflammatory conditions, such as systemic lupus erythematosus and myasthenia gravis. During pregnancy, the pathogenic antibodies are termed alloantibodies and can attack the developing fetus in utero resulting in severe diseases, such as hemolytic disease of the fetus and newborn (HDFN). Critically, minority populations are more likely to experience poorer outcomes, including greater disease severity and faster progression.[5] These diseases also disproportionately affect women and birthing people and can increase the risk of serious pregnancy complications and potential disease flares.[6-9]

New insights, research, and treatments for transplacental immune pathways are helping unlock opportunities that could help revolutionize the way we treat autoantibody diseases.

Developing New Treatments for Antibody-Driven Diseases

Janssen is taking an innovative development approach to treating antibody-driven diseases that occur during pregnancy to minimize and prevent negative outcomes using a pathway-centric development strategy. A specific target of this research is HDFN. In HDFN, the mother's immune system recognizes the fetal red blood cells as "foreign" and produces maternal immunoglobulin G (IgG) alloantibodies which are targeted against them. These alloantibodies are transported across the placenta by FcRn, the neonatal Fc-receptor.[10] Once in the fetal circulation, the maternal IgG alloantibodies attack fetal red blood cells, causing them to break down quickly, resulting in fetal anemia.[10,11] Fetal anemia can produce hydrops – a condition in which large amounts of fluid collect in a baby's tissues and organs and can cause extensive swelling, organ damage, heart failure, or death.[11,12]

FcRn naturally regulates antibody levels. During pregnancy, FcRn transports IgG antibodies across the placenta from the mother's circulation to the fetal circulation. After birth, FcRn rescues IgG antibodies from rapid destruction by pulling them out of a degradation pathway in tissue and "recycling" them back into circulation.[13-15] Targeting the antibody binding site of FcRn is an attractive mechanism to investigate for the treatment of HDFN as it both reduces levels of harmful alloantibodies in the mother's circulation (by blocking the IgG recycling pathway) and prevents the alloantibodies from crossing to the fetal circulation (by blocking the placental transport pathway).[16] This pathway strategy has potential to provide significant therapeutic benefit for women and birthing people of child-bearing potential who have IgG alloantibody-mediated diseases.[16]

Given the complexity and variability of immune-mediated diseases and their ability to be triggered during pregnancy, women and birthing people of childbearing age with underlying disease require proper diagnosis, medical care, and guidance during pregnancy planning throughout their pregnancy and in post-partum follow-up.[6,17] To minimize risk to both the mother and infant, their pregnancy should be carefully managed by a multidisciplinary team including obstetricians, obstetric medical physicians, and, where applicable, specialists in the care of mothers' underlying diseases (such as rheumatologists).[17] However, women of racially and ethnically diverse backgrounds often do not have access to this type of care.

Commitment to Advancing Maternal-Fetal Immunology Health and DE&I

In 2020, The Johnson & Johnson Family of Companies (Johnson & Johnson) launched the Our Race to Health Equity initiative to further guide our Diversity, Equity, and Inclusion

(DE&I) efforts. As part of Johnson & Johnson, Janssen has committed to a $100 million investment in health equity solutions over the next five years and is working to close the racial health equity gap by increasing diversity in clinical trials.

In 2022, Johnson & Johnson Innovation together with Janssen Research & Development and in collaboration with the Office of the Chief Medical Officer (OCMO) Health of Women team launched the Maternal-fetal Immune Disorders QuickFire Challenge: Innovating for Health Equity. This challenge was focused on finding innovative potential solutions aiming to enhance our understanding and improve treatment approaches in immune-mediated disease manifestations that disproportionately impact women in diverse communities.

Two companies were selected as the QuickFire Challenge awardees with the goal of helping to address inequities in maternal-fetal immunology. The first, Acclinate, is a company that helps pharmaceutical companies and healthcare organizations engage with communities of color with the aim to ensure that research is more inclusive and will be working to improve clinical trial recruitment among diverse people of child-bearing potential. The second, NX Prenatal Inc., is a molecular diagnostics company that aims to use novel biomarker technology to identify patients at risk for immune-mediated disorders of pregnancy.

Both companies received grants and access to the global Johnson & Johnson Innovation – JLABS network, a global life science network for innovation, providing startups with access to capital-efficient lab space and resources, as well as mentorship from experts across Johnson & Johnson.

When more racially and ethnically diverse people are enrolled in clinical trials, we could more accurately represent and improve diagnostics for early detection of high-risk immune-mediated pregnancies. New innovations, such as Acclinate's and NX Prenatal's cutting-edge solutions, may help overcome barriers to the diagnosis and treatment of immune-mediated pregnancy-related conditions.

Continuing to Prioritize Antibody Pathways

Current interventions for antibody-driven disorders such as HDFN are suboptimal. Our pathway-centric development strategy of identifying diseases driven by a common immune pathway – such as FcRn – and then pursuing novel therapeutics that can differentially modulate that pathway, positions us to deliver best-in-class treatments for patients managing a wide range of immune-mediated diseases.

At Janssen, we have more than two decades of immunology expertise and tools to inform our approach when addressing unmet needs for rare, antibody-driven diseases, many of which have few or no treatment options. We are working to advance the next generation of rare antibody-driven disease approaches and developing novel medicines, including treatments that aim to reduce the harmful effects of (auto- or allo-) antibodies while safely maintaining immune function.

We continue to take actionable steps toward our goals of delivering transformative therapies that provide lasting remission and restore immune balance. Together, we share enthusiasm for a future where maternal-fetal immunology is transformed and all communities can experience the high quality, healthy pregnancies and births they deserve.

Katie Abouzahr, M.D. is the Vice President and Portfolio Development Leader for autoantibody research at The Janssen Pharmaceutical Companies of Johnson & Johnson. She is passionate about transforming healthcare for women and addressing unmet needs in the maternal-fetal immunology space.

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