Weill Cornell Medicine

Methods to Improve Maternal-Fetal Tolerance and Pregnancy Success through AhR Receptor Modulation

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Background & Unmet Need

- Immune tolerance at the maternal-fetal interface (MFI) is required for fetal development, with dysregulation leading common pregnancy complications such as miscarriage or pre-term birth
- Maternal interferon gamma (IFNɣ) and interleukin-17 (IL-17) are normally protective during pregnancy, but high amounts are linked to adverse outcomes
- Myeloid-derived suppressor cells (MDSCs) and T regulatory cells (Treg) have been suggested to reduce inflammation during pregnancy
- Analysis of autoimmune conditions and associated pregnancy complications supports the conclusion that rampant inflammation lowers maternal-fetal tolerance
- **Unmet Need:** Therapies to regulate unchecked inflammation are needed to prevent pregnancy complications and improve maternal-fetal tolerance

Technology Overview

- **The Technology:** A therapeutic approach to improve maternal-fetal immune tolerance through aryl hydrocarbon receptor (AhR) activation by tryptophan metabolite supplementation
- **The Discovery:** Rates of fetal resorption in mice were higher in germ-free (GF) versus specific pathogen free (SPF) mice
- Gram-positive bacteria that release tryptophan (e.g. *Lactobacillus murinus*) increase MDSC and Treg activity, reducing IFN and IL-17 responses at the MFI to decrease incidence of complications via immunosuppression and downregulation of IFNɣ
- **PoC Data:** Administration of indole-3-carbinol as a proxy for tryptophan led to ~ less fetal resorption in germ-free (GF) mice
- Monocolonization with tryptophan-metabolizing *Lactobacillus murinus* reduced fetal resorption and restored immune tolerance markers compared to non-metabolizing bacteria or germ-free controls

Inventors:
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Patents:
Provisional Filed

Publications:
Brown et al. *Cell.* 2026.

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Cornell Reference:
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Technology Applications

- Therapeutic intervention for high-risk patients with dysregulated maternal-fetal immune tolerance
- Preventative supplementation to maintain healthy maternal-fetal interface tolerance throughout pregnancy

Technology Advantages

- May be formulated either as a small molecule or probiotic
- Utilizes naturally occurring compounds and safe bacterial strains, enabling faster regulatory approval pathways

Supporting Data / Figures

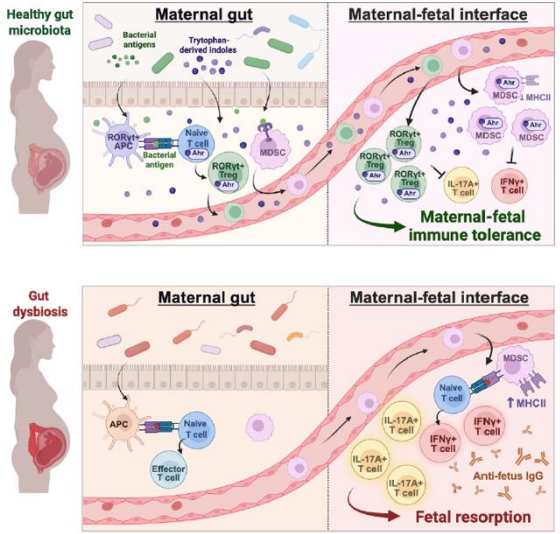

Figure 1: Healthy gut microbiota produces tryptophan-derived indoles that activate AhR on MDSCs and RORγt+ Tregs, promoting maternal-fetal tolerance. Dysbiosis disrupts this pathway, causing fetal resorption.

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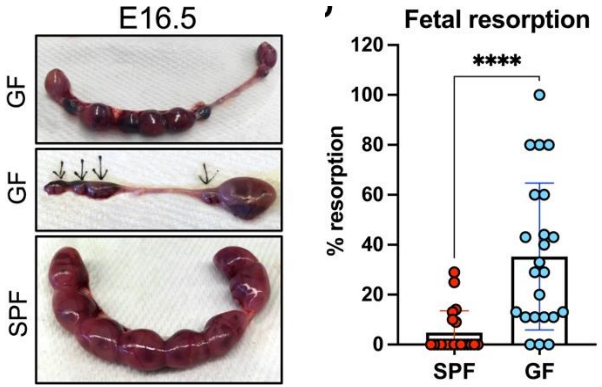

Figure 2: Germ-free mice (GF) have a higher incidence of resorption compared to specific pathogen-free mice (SPF).

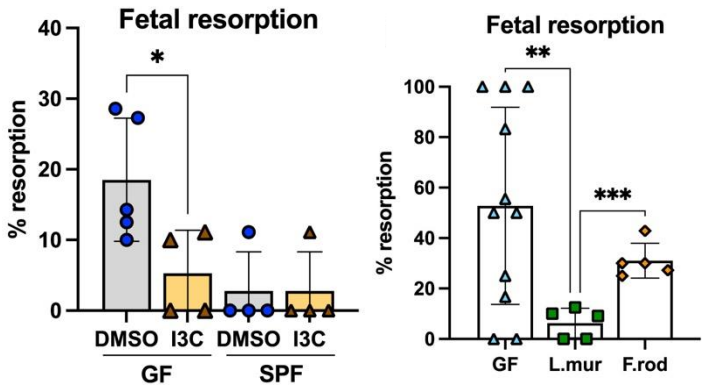

Figure 3: Oral administration of indole-3-carbinol (I3C) or a tryptophan producing bacteria, *Lactobacillus murinus,* to GF mice rescues fetal resorption rates to the level of SPF dams.

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