Intestinal flora and pregnancy complications: Current insights and future prospects

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Highlights

Pregnancy complications critically affect maternal and child health, necessitating urgent research and therapeutic strategies to reduce health and socio-economic impacts.

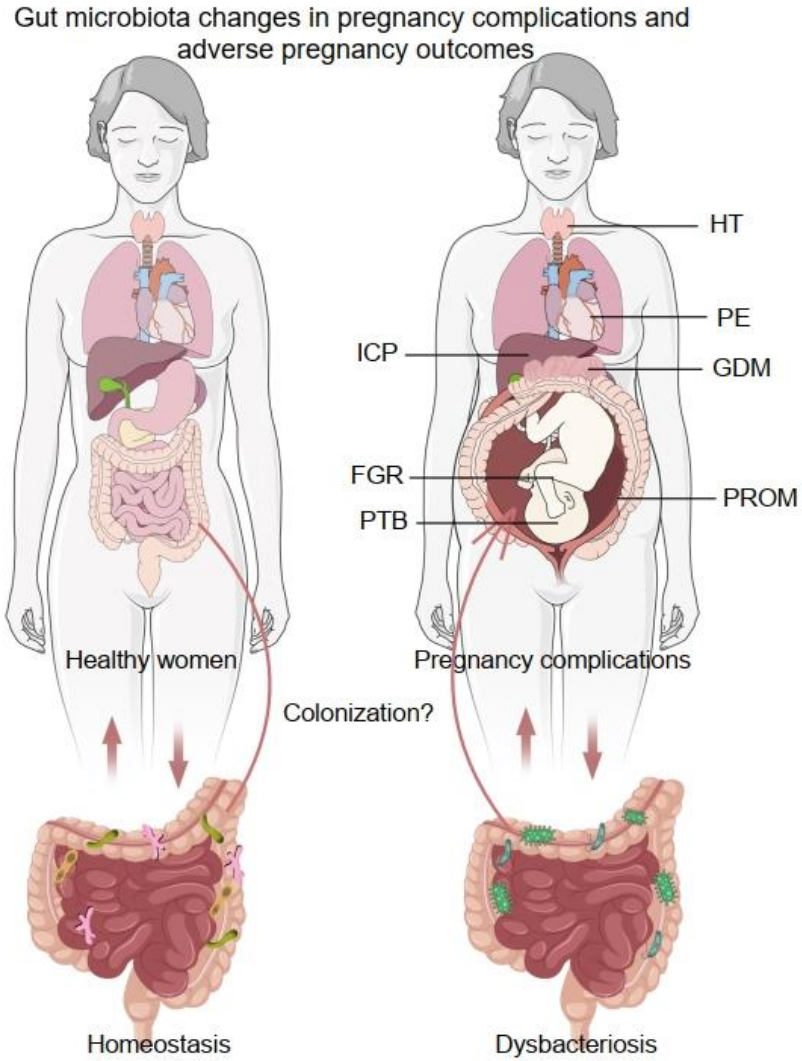
Gut microbiota dysbiosis in patients with various pregnancy complications acts as both a causal factor and a contributor to these conditions.

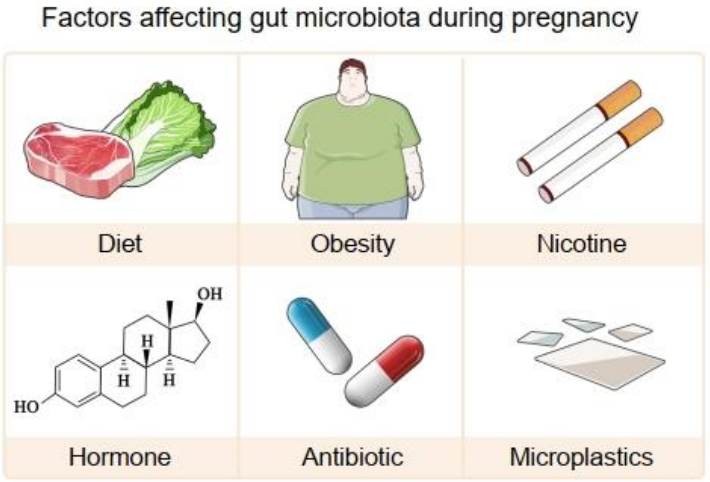
Gut microbiota-derived metabolites are involved in various pathophysiological pathways closely related to the pathogenesis of pregnancy complications, including intestinal barrier permeability, inflammatory responses, and glucose and lipid metabolism.

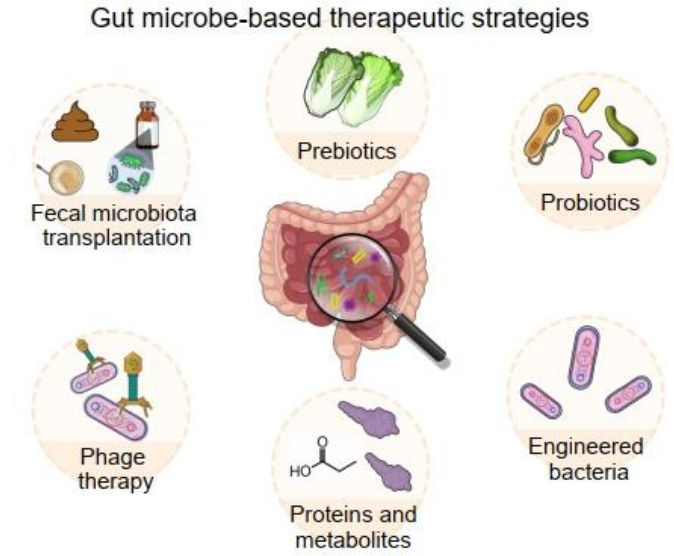
Emerging therapeutic strategies based on gut microbes show potential in treating pregnancy complications, yet there is a lack of evidence from randomized controlled trials (RCTs) to substantiate this approach.

Introduction

- In 2023, the World Health Organization (WHO) reported that approximately 287,000 women globally died from pregnancy-related complications in 2020, averaging one death every two minutes. This highlights that maternal and infant health has become an important social and scientific issue.
- Characteristic changes and etiological role of the gut microbiota in pregnancy complications.
- The possibility of existence of microbes in the uterus/placenta.
- The importance of gut microbe-based interventions







Changes during physiological pregnancy

☆ Immune system:

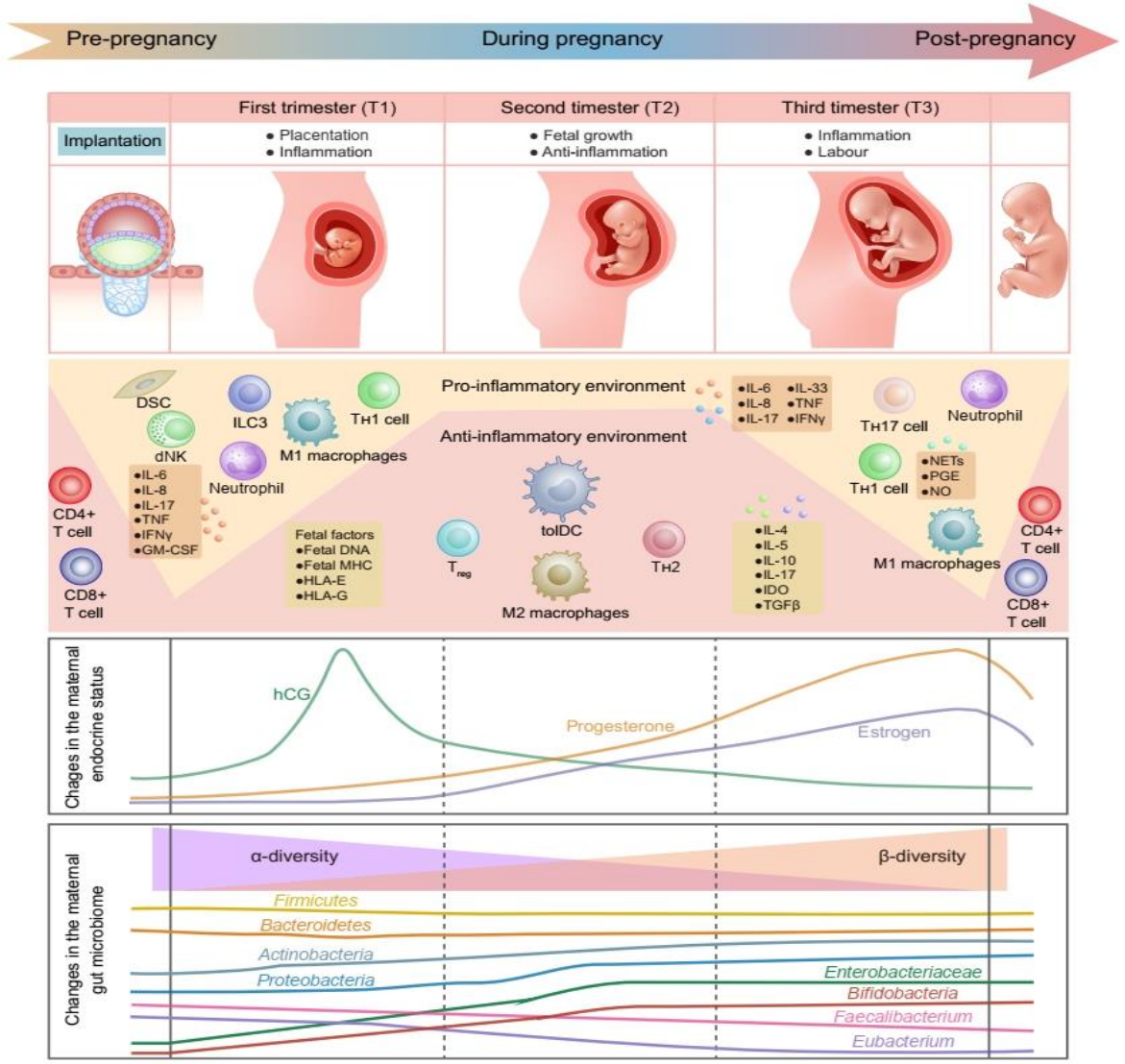
From the first to the third trimester, the changes in the immune system include shifts from a pro-inflammatory environment to an anti-inflammatory one, and then back to a pro-inflammatory state.

☆ Hormone:

A surge in human chorionic gonadotropin (hCG) levels early in gestation, followed by an escalating tide of progesterone and estrogen during the second trimester

☆ Gut microbiota:

A reduction in α-diversity and gut butyrate-producing bacteria such as Faecalibacterium. As the third trimester nears, there is a notable rise in Bifidobacteria, preparing the gut for the upcoming childbirth.

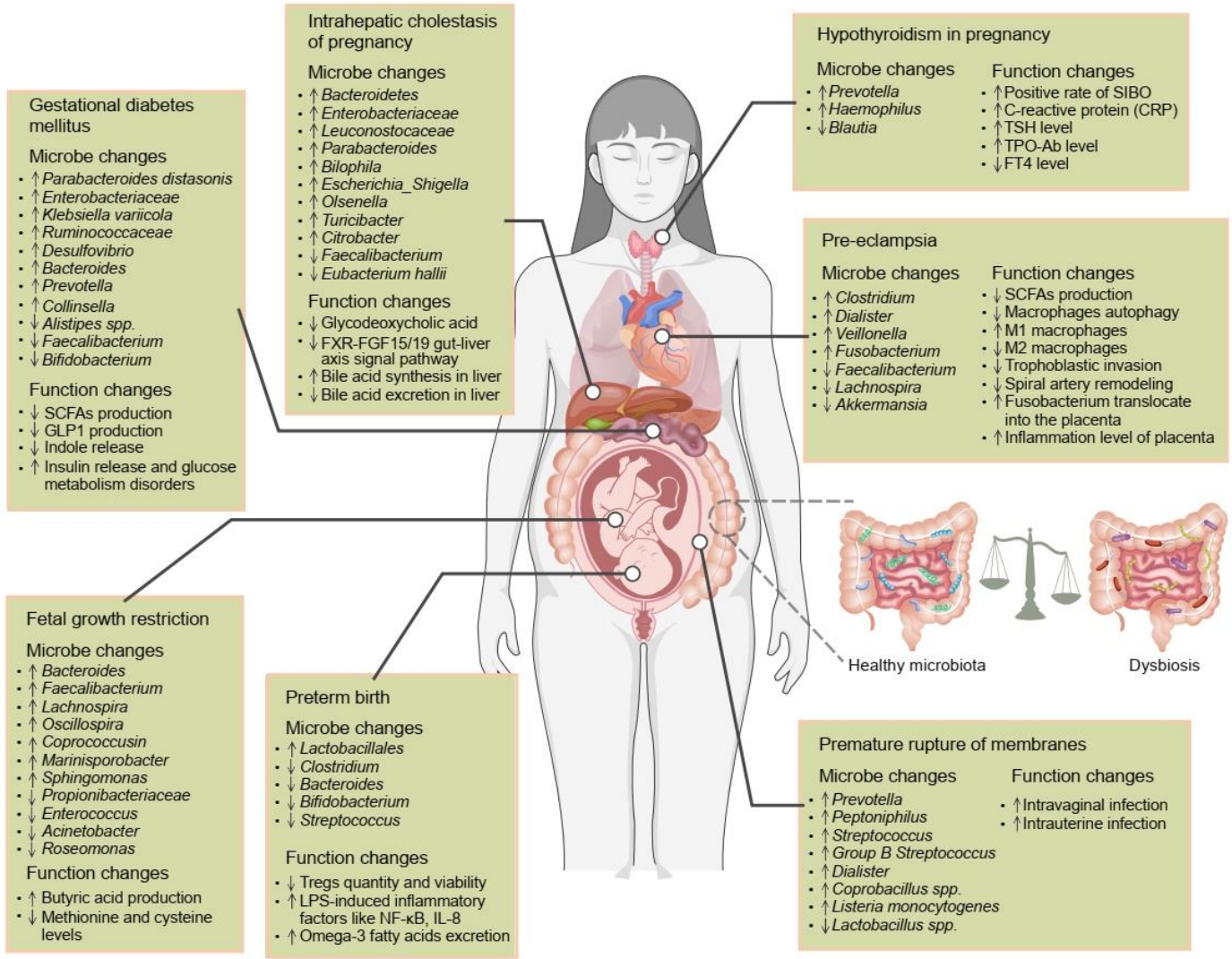


Evolution of immunological, hormonal, and gut microbiota profiles during physiological pregnancy.

Changes during pregnancy complications

☆ The gut microbiota and its derived metabolites experience significant changes, impacting various pregnancy complications and adverse outcomes. They participate in pathophysiological pathways related to pregnancy complications, affecting intestinal barrier, inflammation, and glucose and lipid metabolism.

☆ The figure presents findings from sequencing studies, detailing key microbes, functional features, and their roles in pregnancy complications and adverse outcomes.

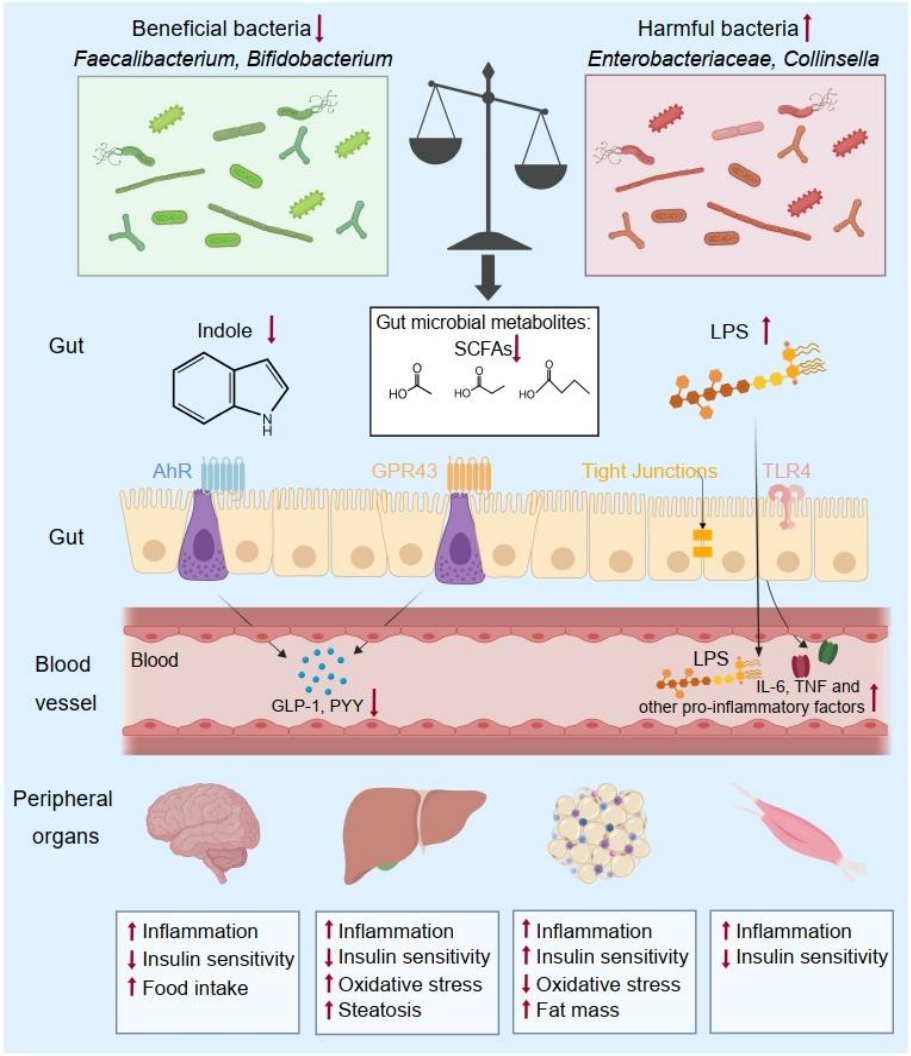


Enumeration of intestinal microbes and associated functional changes in pregnancy complications.

Two major pregnancy complications

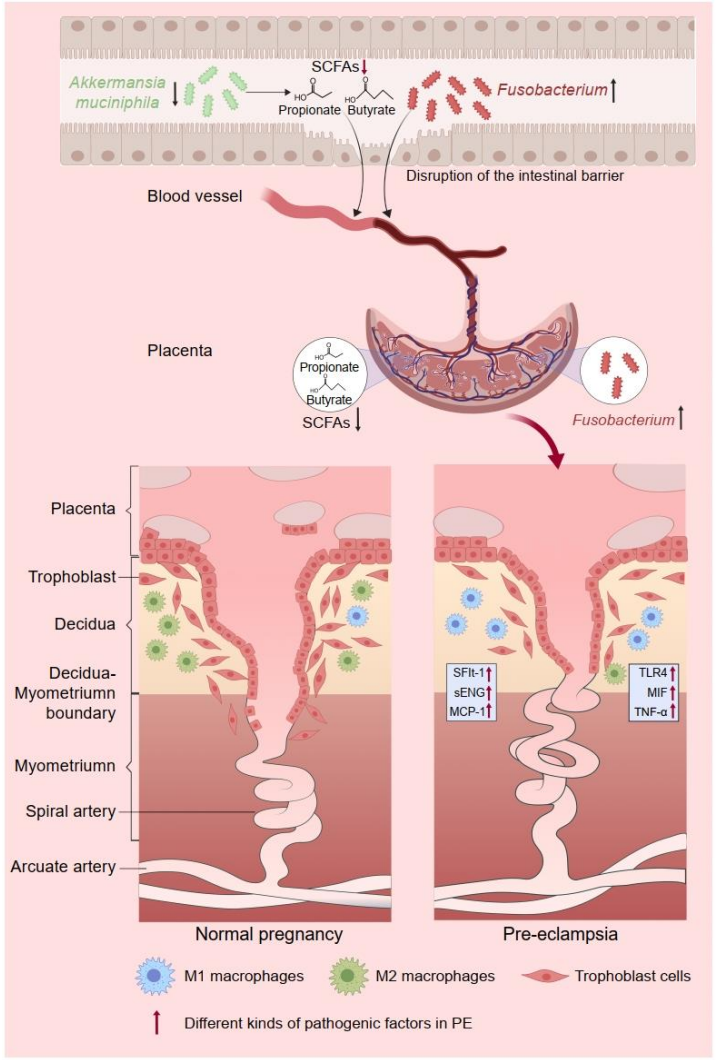
GDM

- **Gut**
  - Beneficial bacteria ↓
  - SCFAs and indole ↓
- **Blood**
  - GLP-1 ↓
  - LPS ↑
  - SCFA ↓
- **Peripheral organs**
  - Inflammation ↑
  - Insulin sensitivity ↓



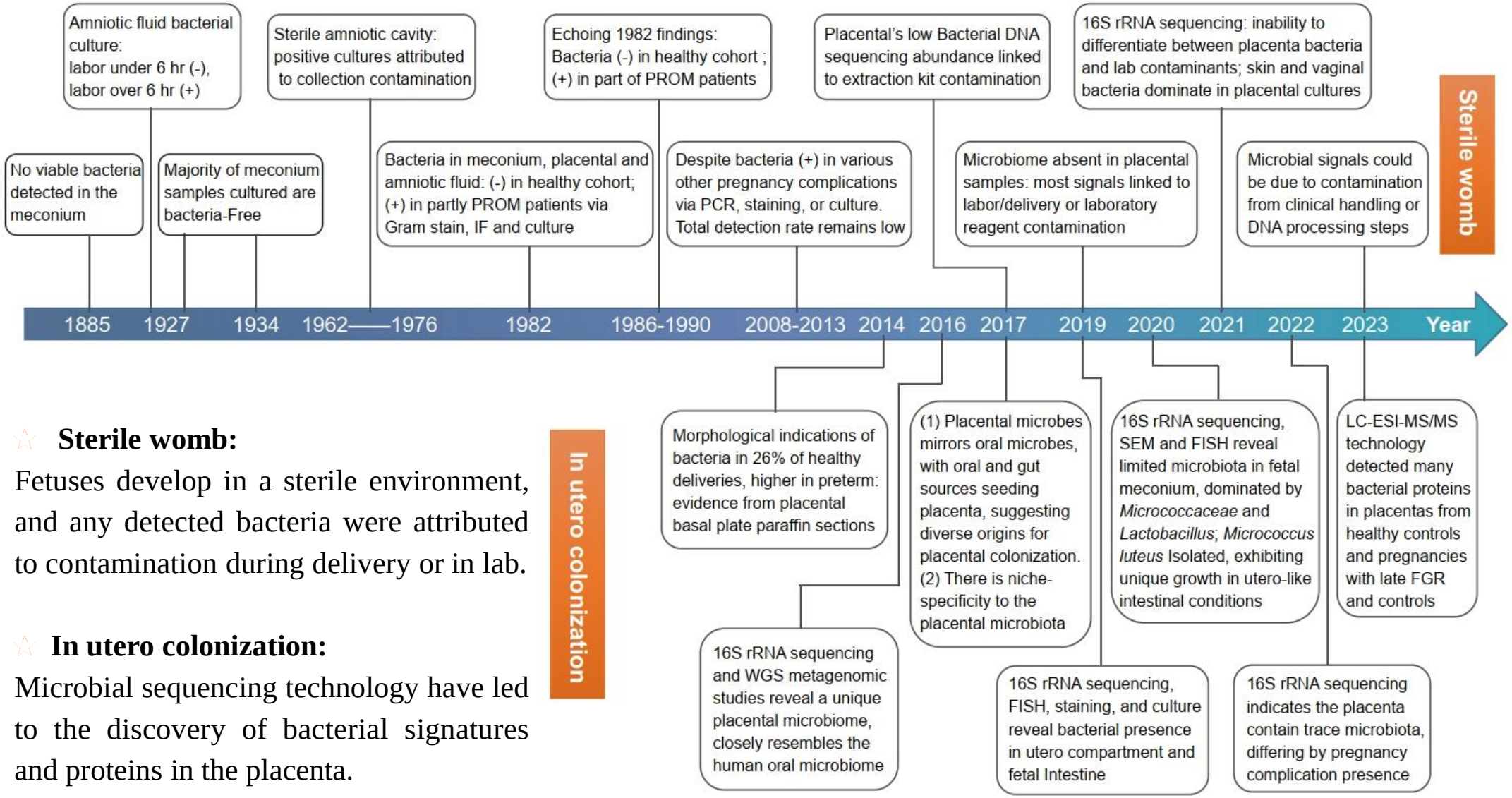
PE

- **Gut**
  - *Akkemansia* ↓
  - *Fusobacterium* ↑
  - SCFAs ↓
- **Blood**
  - SCFAs ↓
  - *Fusobacterium* ↑
- **Placenta**
  - Inflammation ↑
  - Trophoblast cells ↓



Conceptual depiction of mechanisms for gestational diabetes mellitus (GDM) and pre-eclampsia (PE).

Debate on 'sterile womb' versus 'in utero colonization'



☆ **Sterile womb:**

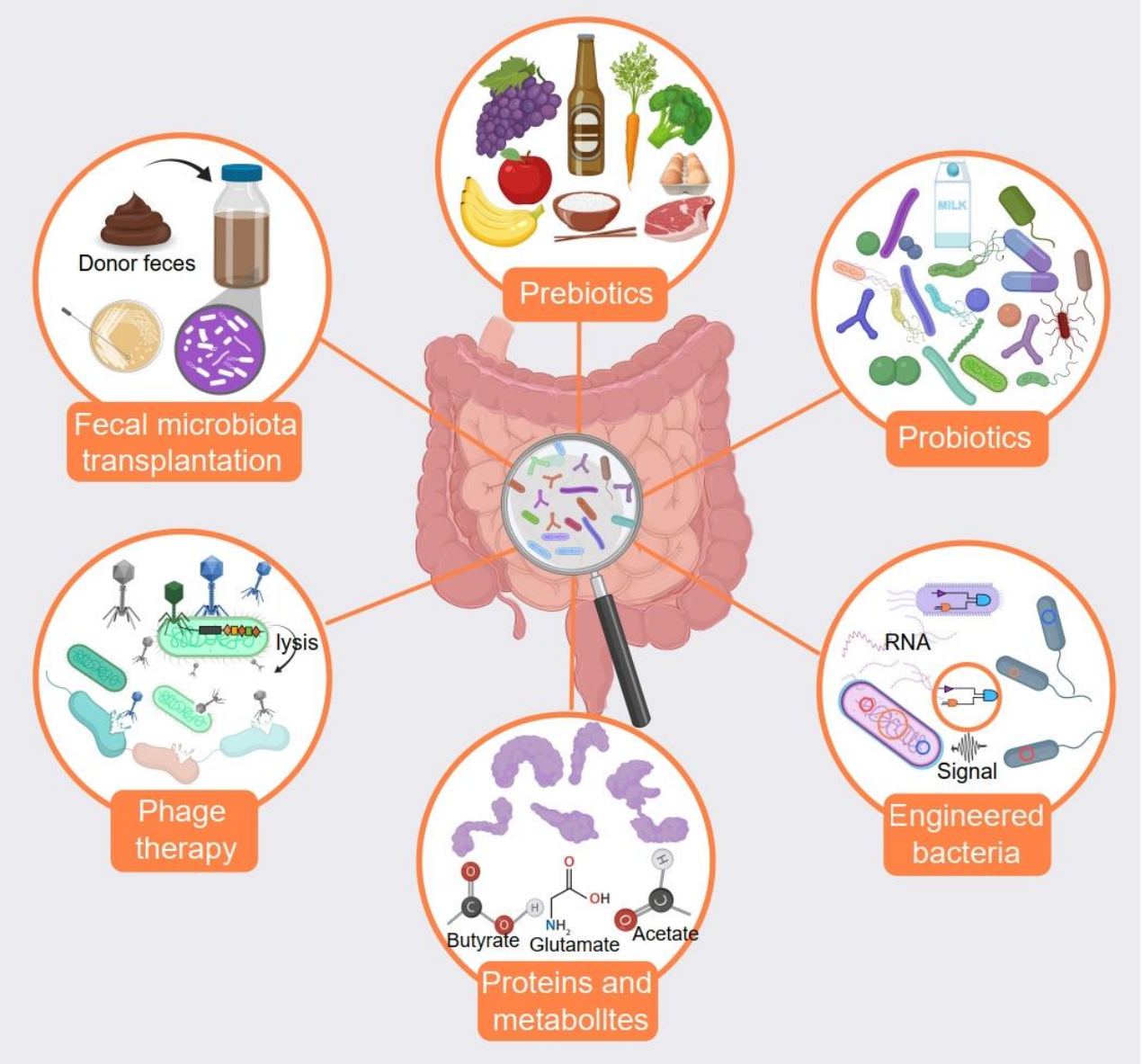
Fetuses develop in a sterile environment, and any detected bacteria were attributed to contamination during delivery or in lab.

☆ **In utero colonization:**

Microbial sequencing technology have led to the discovery of bacterial signatures and proteins in the placenta.

Timeline of the debate on 'sterile womb' versus 'in utero colonization'

Gut microbe-based treatment



Potential gut microbe-based treatment for pregnancy complications.

Summary

- Pregnancy complications are fatal and severely affect maternal and infant health.
- During pregnancy, the interplay among women's immune system, hormones, and gut microbiota significantly changes.
- Gut microbiota dysbiosisis an important cause of various pregnancy complications and adverse pregnancy outcomes, rather than a bystander.
- Metabolites produced by the gut microbiota, such as short-chain fatty acids and indoles, demonstrate significant value in the prevention and treatment of pregnancy complications.
- Gut microbiome therapy holds broad prospects for application in the treatment of pregnancy complications.

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