



Gut microbiota dysbiosis, circulating microbial genetic traces, and their role in gestational diabetes

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Abstract

Diabetes mellitus is a leading metabolic and non-communicable disease, affecting nearly 537 million adults worldwide. Recent research highlights the gut microbiota as a crucial factor in the onset and progression of diabetes. Gut microbial dysbiosis, an imbalance in microbial composition, has been increasingly recognized as a contributor to diabetes pathogenesis during pregnancy. The gut microbiome is influenced by multiple internal and external factors, which can worsen diabetes-related complications. A higher abundance of pathogenic microbes may lead to the release of microbial metabolites or DNA into circulation, contributing to metabolic disorders such as obesity, cardiovascular disease, and liver dysfunction. Microbial nucleic acids have been identified in the bloodstream of individuals with diabetes and in pregnant women, suggesting the existence of a circulating or blood microbiome. Various physiological and pathological conditions may permit gut microbes or their components to enter the bloodstream. This review introduces the concept that the blood microbiome may play a critical role during pregnancy, potentially increasing susceptibility to diabetes. It emphasizes the mechanistic link between gut dysbiosis, microbial translocation, and pregnancy-associated metabolic disturbances. Exploring gut and blood microbiome interactions in pregnancy could reveal early biomarkers and therapeutic targets for gestational diabetes mellitus. Future studies should focus on longitudinal microbiome analyses and interventions to restore microbial balance, offering new preventive strategies against diabetes during pregnancy.

Key Words: Gut dysbiosis; Gestational diabetes mellitus; Microbial DNA; Systemic inflammation; Maternal-foetal health; Biomarkers

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Core Tip: Pregnancy represents a unique metabolic state, where immune tolerance and insulin sensitivity are tightly regulated. Recent evidence suggests that gut microbiota dysbiosis may compromise the intestinal barrier, leading to the release of microbial genetic traces into the bloodstream. These microbial signals can activate host immune pathways and may aggravate systemic inflammation, thereby exacerbating gestational diabetes mellitus. This review highlights emerging insights into the link between gut dysbiosis, microbial translocation into circulation, and the worsening of diabetic outcomes in pregnancy. Understanding this gut-blood axis could open new opportunities for predictive biomarkers and targeted interventions to improve maternal and foetal health.

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INTRODUCTION

Diabetes during pregnancy is a major global health concern, with gestational diabetes mellitus (GDM) affecting approximately 7%-15% of pregnancies worldwide[1]. Pregnancy represents a unique immunometabolic state characterized by extensive physiological adaptations that support foetal growth and maternal energy balance. These adaptations involve tightly regulated changes in insulin sensitivity, immune tolerance, and hormonal modulation[2]. Although insulin resistance is a physiological feature of late gestation, its exaggeration in genetically or metabolically predisposed women contributes to GDM[3]. This condition not only increases the risk of obstetric complications but also confers long-term cardiometabolic consequences for both mother and child, including type 2 diabetes mellitus (T2DM) and metabolic syndrome[4]. Understanding the molecular and microbial mechanisms that exacerbate hyperglycaemia in this unique physiological context is therefore an important research priority[5].

The human gastrointestinal tract harbours a dense and diverse microbial ecosystem collectively known as the gut microbiota, which plays a crucial role in maintaining metabolic, immune, and endocrine homeostasis[6]. These microbial communities influence nutrient metabolism, immune regulation, and gut barrier integrity, thereby contributing to systemic metabolic balance[7]. Perturbation of this delicate equilibrium, termed dysbiosis, has been implicated in the development of metabolic and inflammatory disorders, including T2DM, obesity, cardiovascular disease, and GDM[8,9]. Mechanistically, dysbiosis contributes to metabolic dysfunction through altered short-chain fatty acid (SCFA) production, endotoxin release, impaired intestinal permeability, and low-grade systemic inflammation[10].

Beyond the gut, emerging evidence suggests that microbial components and genetic material, including cell-free microbial DNA, RNA, lipopolysaccharides (LPS), and extracellular vesicles (EVs), can enter the bloodstream through a process known as microbial translocation[11,12]. These microbial-derived molecules interact with host pattern recognition receptors such as toll-like receptors (TLRs) and NOD-like receptors (NLRs), activating pro-inflammatory pathways that exacerbate insulin resistance and glucose dysregulation[13,14]. Circulating microbial genetic material has been detected in metabolic disorders such as obesity, T2DM, and non-alcoholic fatty liver disease[15,16]. In the context of pregnancy, limited studies have identified microbial DNA signatures in maternal circulation and associated them with GDM risk[17,18]. However, it remains unclear whether gut microbiota dysbiosis directly increases the abundance of circulating microbial DNA during pregnancy and whether this contributes to gestational hyperglycaemia. Given the unique immunometabolic state of pregnancy, this question represents a critical but understudied research gap.

This review synthesizes current knowledge on the interplay between gut microbiota dysbiosis, microbial genetic traces in circulation, and diabetes during pregnancy. We first describe physiological and immunometabolic adaptations during pregnancy and their dysregulation in GDM. We then summarize evidence on gut dysbiosis, intestinal barrier dysfunction, and microbial translocation, highlighting studies that have detected microbial DNA in maternal blood. Finally, we discuss potential mechanistic pathways linking circulating microbial DNA to insulin resistance and identify key knowledge gaps to guide future research. By addressing this emerging gut-blood-metabolism interface, this review aims to provide a novel perspective that may inform biomarker discovery and microbiota-targeted strategies for improving maternal and offspring metabolic health.

GUT MICROBIOTA DYSBIOSIS IN PREGNANCY

Pregnancy is a period of extensive physiological remodeling encompassing metabolic, endocrine, and immune systems, accompanied by notable alterations in the gut microbiota. While some of these microbial changes facilitate maternal adaptation and foetal growth, excessive perturbations, termed gut microbiota dysbiosis, have been associated with adverse metabolic outcomes, including GDM. Understanding these interactions requires an integrative view of microbial composition, intestinal barrier function, and systemic immune-metabolic signaling (Figure 1).

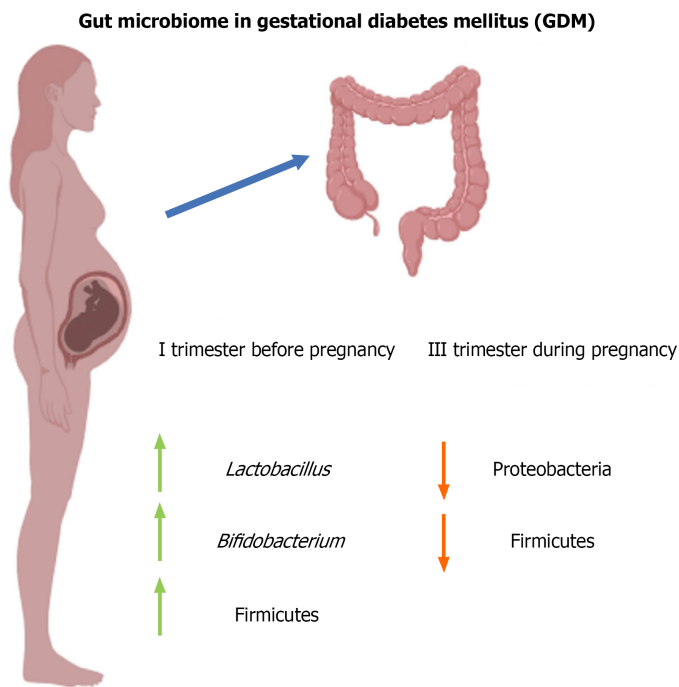


Figure 1 Microbiome changes during pregnancy. Typical changes in gut microbiota composition before and during pregnancy. It shows a normal, healthy microbiome with a balance of beneficial bacteria (e.g., *Lactobacillus*, *Bifidobacterium*) and a more diverse microbial community, contrasted with a dysbiotic microbiome in pregnant women with gestational diabetes. GDM: Gestational diabetes mellitus.

Microbiota remodeling during normal pregnancy

During early gestation, gut microbial diversity remains relatively stable, whereas late pregnancy is characterized by reduced alpha diversity, expansion of *Proteobacteria* and *Actinobacteria*, and enrichment of taxa such as *Enterobacteriaceae* and *Streptococcus*[8]. These patterns resemble those observed in obesity and low-grade inflammation, indicating that pregnancy itself induces a physiological, “controlled dysbiosis”. Experimental evidence supports this notion that faecal microbiota transplantation (FMT) from third-trimester women to germ-free mice induces insulin resistance, adiposity, and mild inflammation, underscoring the functional relevance of microbial remodeling during gestation[8].

Dysbiosis associated with GDM

In women with GDM, microbial changes extend beyond physiological adaptation. Several studies report a reduction in butyrate-producing bacteria, including *Faecalibacterium prausnitzii* and *Roseburia spp.*, which are essential for maintaining epithelial integrity and insulin sensitivity[19]. Concurrently, there is an enrichment of pro-inflammatory taxa such as *Collinsella*, *Ruminococcus*, and *Desulfovibrio*, linked to enhanced endotoxin production and metabolic inflammation[4]. Reduced microbial diversity and community instability further suggest a loss of ecological resilience to dietary or environmental challenges[20]. Collectively, these observations indicate that dysbiosis in GDM represents a maladaptive state with functional consequences for maternal glucose metabolism.

Gut barrier dysfunction and systemic microbial signaling

Dysbiosis contributes to intestinal barrier dysfunction by decreasing SCFA production, particularly butyrate, a primary energy source for colonocytes and regulator of tight junction proteins, and by enriching mucin-degrading and LPS-producing bacteria. This compromise in barrier integrity permits the translocation of microbial components such as LPS, peptidoglycans, and microbial nucleic acids into maternal circulation[15,16]. This process, termed microbial translocation, provides a mechanistic explanation for the detection of microbial genetic material in the plasma of pregnant women[11, 21].

Immune, placental, and metabolic consequences

Once in circulation, microbial molecules engage host pattern-recognition receptors such as TLRs and NLRs, activating nuclear factor kappa-B (NF-κB) signaling and pro-inflammatory cytokine release[22]. In pregnancy, where insulin resistance is physiologically heightened, this low-grade inflammation can exacerbate glucose intolerance and β-cell stress. Preliminary studies further suggest that microbial components in maternal blood may reach the placenta, influencing trophoblast signaling, inflammatory tone, and nutrient transport. However, current evidence remains limited and largely correlative. Further mechanistic and clinical investigations are needed to substantiate causal relationships between maternal microbial translocation and placental dysfunction.

Integrated conceptual framework

The interplay between gut microbiota, barrier integrity, and systemic immune-metabolic signaling can be summarized across multiple levels. Microbial level: Loss of beneficial butyrate producers and enrichment of inflammatory taxa. Barrier level: Reduced epithelial integrity and SCFA depletion. Systemic level: Circulating microbial components activate innate immune receptors. Metabolic level: Inflammatory signaling exacerbates insulin resistance, promoting GDM progression. Overall, gut microbiota dysbiosis represents a systemic perturbation rather than a mere compositional shift within the intestine. Circulating microbial signatures could therefore serve as potential biomarkers of gut health and GDM risk during pregnancy.

MICROBIAL TRANSLOCATION AND THE CIRCULATION OF MICROBIAL GENETIC MATERIAL

The concept of microbial translocation has transformed understanding of the gut as a dynamic regulator of systemic physiology. Traditionally considered a contained microbial niche, the intestinal lumen is now recognized as a potential source of circulating microbial molecules under conditions of dysbiosis and impaired barrier integrity. In pregnancy, physiological changes in metabolism, immunity, and gut permeability may render this process particularly relevant, linking maternal gut disturbances to systemic and placental effects (Figure 2).

Mechanisms of microbial translocation

The intestinal barrier comprising epithelial tight junctions, mucus layers, secretory immunoglobulin A (IgA), and resident immune cells maintains controlled separation between gut microbes and host tissues. Dysbiosis can disrupt this defence through multiple pathways: Tight junction disruption: A decline in butyrate-producing bacteria such as *Faecalibacterium prausnitzii* reduces epithelial energy supply and tight junction protein expression (occludin, claudin)[23]. Mucus degradation: Overgrowth of mucin-degrading taxa (*Akkermansia muciniphila*, *Bacteroides fragilis*) thins the protective mucosal layer[24]. Endotoxin accumulation: Enrichment of gram-negative pathobionts elevates luminal LPS levels, predisposing to systemic endotoxemia[16]. Local immune alteration: Dysbiosis impairs IgA coating and mucosal immune regulation[25]. Through these mechanisms, intact microbes rarely translocate; instead, microbial components such as cell wall fragments, metabolites, EVs, and particularly microbial nucleic acids can cross into maternal circulation.

Circulating microbial genetic material

The detection of microbial DNA and RNA in human plasma challenges the traditional notion of blood sterility. Using next-generation sequencing and quantitative polymerase chain reaction (PCR), several studies have identified cell-free microbial DNA in the circulation of healthy and pregnant individuals[10,11]. This material likely originates from the gut, though contributions from oral and skin microbiota cannot be excluded. Microbial genetic material circulates in distinct forms: (1) Cell-free microbial DNA, often fragmented and occasionally bound to host nucleoproteins; (2) RNA fragments, which may reflect active microbial metabolism or vesicle-mediated release; and (3) EVs, nanosized structures carrying DNA, RNA, and proteins that facilitate stable systemic transport[26]. Once in the bloodstream, these microbial signals engage pattern recognition receptors such as TLR9 and TLR7/8, promoting innate immune activation and low-grade inflammation[17].

Microbial translocation in metabolic disease and pregnancy

In non-pregnant populations, microbial translocation has been linked to obesity, T2DM and non-alcoholic fatty liver disease. Elevated circulating LPS and microbial DNA levels predict incident diabetes and metabolic inflammation[12,13]. During pregnancy, physiological insulin resistance and immune modulation heighten vulnerability to these microbial signals. Women with GDM exhibit distinct circulating microbial DNA profiles compared with normoglycemic controls [14], and taxa enriched during pregnancy, such as *Enterobacteriaceae*, are potent endotoxin producers[4]. Together, these findings suggest that microbial translocation in pregnancy may exacerbate inflammation, impair insulin signaling, and contribute to glucose intolerance. Preliminary studies also indicate that microbial DNA fragments can cross the maternal-foetal interface, potentially influencing placental immune signaling and nutrient transport[27]. While this raises intriguing possibilities for foetal metabolic programming, current evidence remains limited and primarily associative. Mechanistic and longitudinal studies are needed to clarify causal pathways.

Detection and clinical implications

Recent advances in 16S rRNA gene sequencing, shotgun metagenomics, and quantitative PCR have enabled increasingly sensitive detection of microbial DNA in plasma[18]. Complementary approaches such as cell-free DNA fragmentomics and EV profiling now allow deeper characterization of circulating microbial signatures. Despite challenges related to low biomass and potential contamination, refined analytical protocols are improving reliability. Clinically, early detection of elevated microbial DNA in maternal plasma could offer a non-invasive biomarker for GDM risk prediction and monitoring of responses to dietary or probiotic interventions during pregnancy.

Conceptual integration

Collectively, current evidence supports a framework in which gut dysbiosis weakens intestinal barrier function, permitting translocation of microbial genetic material into maternal blood. These circulating microbial signals activate innate immune pathways, drive systemic inflammation, and contribute to gestational insulin resistance. Microbial

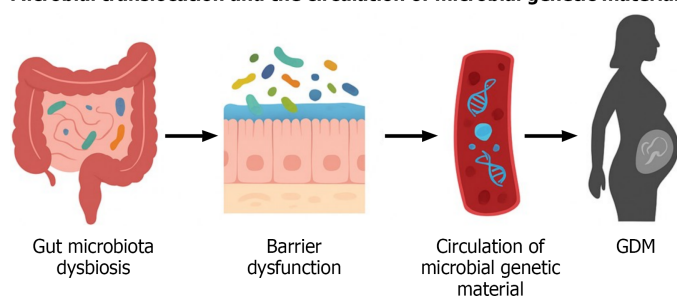
Microbial translocation and the circulation of microbial genetic material

Figure 2 Microbial translocation and gestational diabetes mellitus. Gut microbiota dysbiosis leads to intestinal barrier dysfunction, allowing microbial components and genetic material to translocate into the circulation. The presence of circulating microbial genetic material can trigger immune activation and metabolic disturbances, thereby contributing to the pathogenesis of gestational diabetes mellitus. GDM: Gestational diabetes mellitus.

translocation thus represents a mechanistic bridge between maternal gut dysbiosis, placental signaling, and diabetes risk in pregnancy.

GUT MICROBIOTA DYSBIOSIS, MICROBIAL DNA, AND DIABETES DURING PREGNANCY

Pregnancy represents a unique metabolic and immunological state in which the maternal body must balance competing demands of foetal nutrient supply and maternal health. Insulin resistance naturally increases in the second and third trimesters to ensure adequate glucose transport to the foetus, but when compensatory insulin secretion is insufficient, GDM develops. GDM not only affects short-term pregnancy outcomes but also predisposes mothers to T2DM and children to long-term metabolic disorders[6,7]. While genetic predisposition and environmental factors such as diet are well-established contributors, recent advances suggest that gut microbiota dysbiosis and the consequent presence of microbial DNA in the circulation may play a central role in exacerbating insulin resistance during pregnancy (Figure 3).

Gut dysbiosis and metabolic reprogramming in pregnancy

Longitudinal studies show that gut microbial diversity decreases progressively during late gestation, with enrichment of *Proteobacteria* and *Actinobacteria* taxa associated with pro-inflammatory responses[8]. These changes mirror alterations observed in metabolic syndrome, suggesting that maternal microbiota remodeling may mimic a diabetogenic profile. While some shifts are adaptive, excessive dysbiosis is increasingly linked to impaired glucose tolerance. Women with GDM consistently display enrichment of *Collinsella*, *Ruminococcus*, and *Desulfovibrio*, alongside depletion of butyrate-producing taxa such as *Roseburia* and *Faecalibacterium prausnitzii*[4,28]. This compositional imbalance weakens intestinal epithelial function and promotes systemic inflammation, two critical risk factors for insulin resistance.

Microbial DNA in the circulation: A novel diabetogenic mediator

The breakdown of epithelial barrier integrity during dysbiosis facilitates microbial translocation, allowing microbial components including LPS, EVs, and microbial DNA fragments to enter maternal circulation[16,29]. These microbial DNA fragments, detectable even in healthy individuals, increase significantly in metabolic disorders and during pregnancy complications[20,30].

It is important to note, however, that the detection of microbial DNA in circulation remains a technically challenging and evolving area. Because blood is a low-biomass environment, there is an inherent risk of sequencing contamination and background noise. While multiple studies have provided supportive evidence, current methodologies such as metagenomic sequencing and quantitative PCR are still being refined and validated for reliable detection of circulating microbial DNA in pregnancy-related contexts. Once in circulation, microbial DNA interacts with host immune sensors such as TLR9 and cytosolic DNA sensors like cyclic guanosine monophosphate-adenosine monophosphate synthase-stimulator of interferon genes. Activation of these pathways leads to the induction of type I interferons, NF- κ B signaling, and downstream pro-inflammatory cytokines including interleukin (IL)-6 and tumor necrosis factor (TNF)- α [22,31]. These cytokines interfere with insulin signaling by promoting serine phosphorylation of insulin receptor substrates and impairing glucose uptake in maternal tissues. Thus, while mechanistic links are biologically plausible, further validation of microbial DNA detection and functional relevance is needed to establish its role as an active mediator of insulin resistance during pregnancy.

Evidence linking microbial DNA to GDM

Emerging studies support a potential association between circulating microbial DNA and gestational diabetes. Neri *et al* [20] demonstrated that distinct bacterial DNA signatures could be detected in plasma samples from women with GDM, with enrichment of pro-inflammatory taxa correlating with higher glucose levels. Similarly, increases in circulating microbial DNA load have been reported in women with obesity, a major risk factor for GDM, linking gut permeability and microbial translocation with metabolic dysfunction[13]. Nevertheless, these findings should be interpreted cautiously

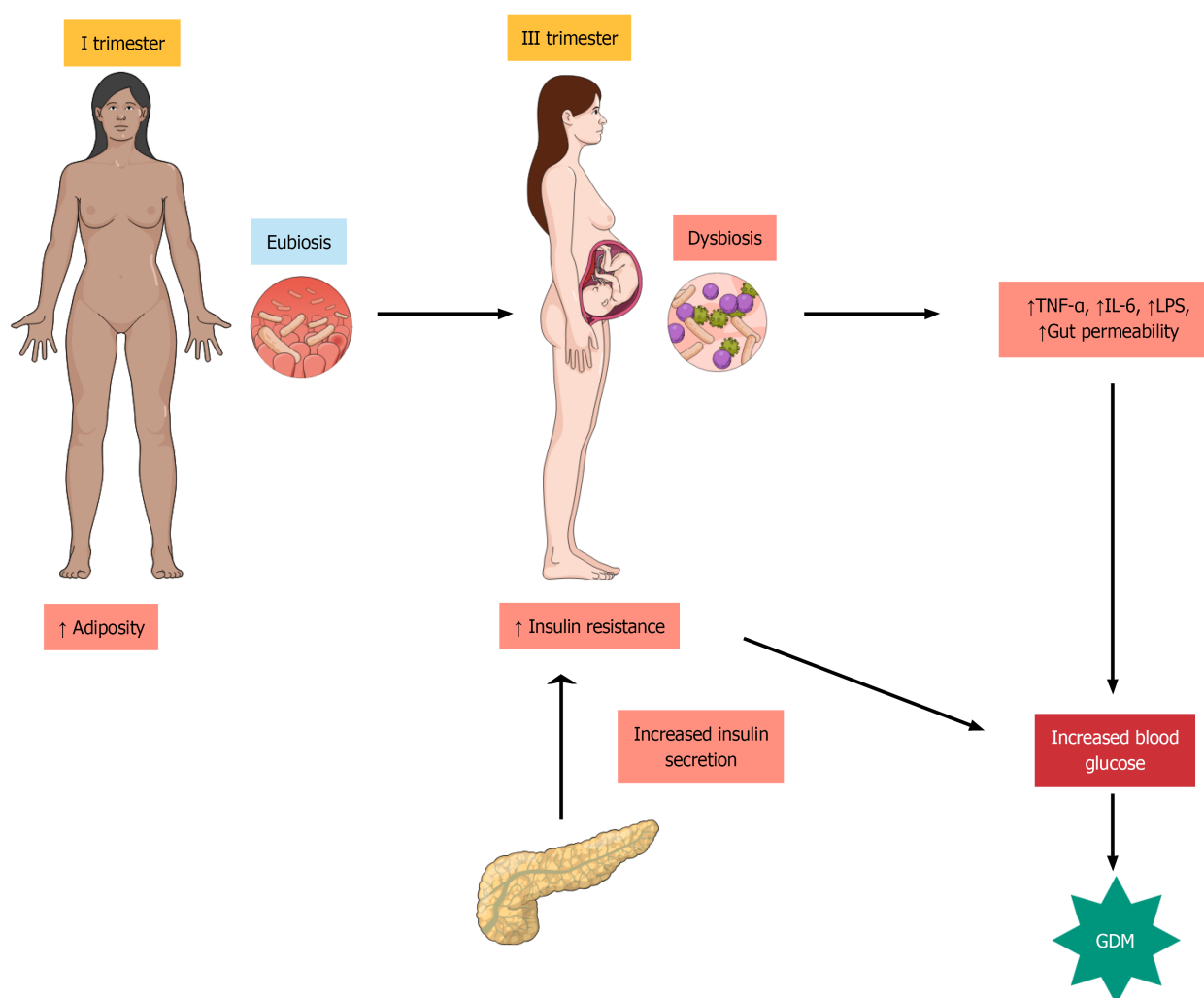


Figure 3 Gut microbiota dysbiosis, microbial DNA, and gestational diabetes mellitus. Gut microbiota dysbiosis during pregnancy reduces microbial diversity, weakens intestinal barrier integrity, and facilitates microbial DNA translocation into circulation. Circulating microbial DNA activates immune pathways such as toll-like receptor 9 and cyclic guanosine monophosphate-adenosine monophosphate synthase-stimulator of interferon genes, inducing pro-inflammatory cytokines (interleukin-6 and tumor necrosis factor- α) that impair insulin signaling. This immune-metabolic disruption promotes insulin resistance, contributing to the pathogenesis of gestational diabetes mellitus and adverse maternal-foetal outcomes. TNF: Tumor necrosis factor; IL: Interleukin; LPS: Lipopolysaccharides; GDM: Gestational diabetes mellitus.

given ongoing methodological debates. Low-biomass conditions, differences in sample processing, and contamination control remain major challenges, underscoring the need for standardized protocols and independent replication to confirm these associations.

Translational potential and future directions

The detection of microbial DNA in maternal plasma offers an innovative biomarker for predicting GDM risk. Compared to traditional risk factors such as body mass index and family history, microbial DNA profiles may provide earlier, non-invasive insights into maternal metabolic health. At the same time, it is crucial to acknowledge that circulating microbial DNA remains an emerging biomarker, and detection methods are still undergoing validation for clinical use. Rigorous quality control, contamination-aware sequencing pipelines, and quantitative standardization are essential before translation into diagnostics. Additionally, interventions aimed at restoring gut microbial balance through diet, probiotics, prebiotics, or synbiotics could reduce microbial DNA translocation and mitigate systemic inflammation. Future studies should employ longitudinal sampling, integrating microbiome, metagenomic, and immunological analyses to establish causal pathways and clarify whether reducing circulating microbial DNA improves glucose tolerance in pregnancy.

IMPLICATIONS FOR MATERNAL AND FOETAL HEALTH

GDM is not only a transient metabolic complication of pregnancy but also a condition with far-reaching implications for both maternal and foetal health. The emerging recognition that gut microbiota dysbiosis and microbial DNA translocation into maternal circulation contribute to the pathophysiology of GDM underscores the need to examine their short-

and long-term consequences. These effects extend beyond hyperglycaemia, influencing maternal systemic inflammation, placental function, and foetal metabolic programming. It is important to note, however, that evidence for microbial DNA-mediated effects remain evolving, and while several studies suggest plausible mechanisms, methodological and interpretive challenges persist. Nonetheless, current data provide a strong conceptual framework linking microbial signals with pregnancy outcomes.

Maternal health implications

Exacerbation of insulin resistance and inflammation: Pregnancy is characterized by a physiologic increase in insulin resistance, but dysbiosis-driven inflammation can magnify this effect. Circulating microbial DNA and bacterial products engage innate immune receptors such as TLRs, leading to overproduction of pro-inflammatory cytokines (IL-6, TNF- α) that interfere with insulin signaling[22,31]. This creates a self-reinforcing cycle of worsening glucose intolerance and chronic low-grade inflammation, heightening the risk of GDM and related complications such as preeclampsia[32,33].

Increased obstetric complications: Women with GDM face elevated risks of preeclampsia, preterm birth, and caesarean delivery[6,7]. Gut dysbiosis and circulating microbial DNA may exacerbate endothelial dysfunction and systemic inflammation which are both key drivers of preeclampsia[34]. Moreover, microbial DNA-induced immune activation could impair uterine vascular function, potentially contributing to abnormal placental perfusion and growth restriction in some pregnancies.

Long-term metabolic risk for mothers: Up to 50% of women with GDM develop type 2 diabetes within 10 years[35]. Persistent gut dysbiosis, coupled with continued microbial DNA translocation, may sustain systemic inflammation and metabolic dysregulation beyond pregnancy. This chronic inflammatory milieu may also contribute to elevated cardiovascular and metabolic syndrome risk later in life[36]. Thus, exposure to dysbiosis and microbial genetic traces during pregnancy may have enduring metabolic repercussions for the mother.

Foetal health implications

Altered intrauterine environment: Microbial DNA and associated inflammatory mediators in maternal blood may cross the placenta and influence foetal development. Increasing evidence indicates that the placenta, though low in microbial biomass, is exposed to microbial signals during gestation[27]. Excessive exposure to microbial DNA or inflammatory cytokines could alter placental immune regulation, nutrient transport, and hormone signaling. These perturbations may contribute to foetal overgrowth (macrosomia), a hallmark complication of GDM, which increases risks of birth trauma and neonatal hypoglycaemia[37].

Foetal immune system programming: In utero exposure to microbial DNA fragments and metabolites may shape the developing immune system. While limited microbial signaling is likely beneficial for immune tolerance, dysregulated exposure may predispose to immune imbalance. Infants born to mothers with GDM exhibit altered gut colonization, with reductions in beneficial taxa such as *Bifidobacterium* and enrichment of pro-inflammatory species[38]. This dysbiotic start may increase susceptibility to obesity, asthma, and allergic diseases later in life.

Increased risk of childhood and lifelong metabolic disease: The “developmental origins of health and disease” hypothesis posits that adverse intrauterine environments program long-term metabolic outcomes. Infants of mothers with GDM have a higher lifetime risk of obesity, impaired glucose tolerance, and type 2 diabetes[39]. These effects may arise not only from intrauterine hyperglycaemia but also from microbial DNA-driven placental inflammation and epigenetic reprogramming in foetal tissues. For instance, exposure to pro-inflammatory cytokines in utero may alter insulin signaling pathways, predisposing children to insulin resistance in adolescence and adulthood.

Intergenerational consequences

The maternal gut microbiota, microbial DNA, and GDM form an interconnected triad that may perpetuate metabolic dysfunction across generations. Mothers affected by GDM are more likely to experience persistent dysbiosis and transmit altered microbial communities to their infants during delivery and breastfeeding[8,38]. Combined with foetal exposure to microbial DNA and maternal hyperglycaemia, this may establish a developmental trajectory favoring obesity and diabetes in offspring. Thus, improving maternal gut health and minimizing microbial DNA translocation during pregnancy may offer a preventive strategy not only for maternal outcomes but also for reducing intergenerational transmission of metabolic risk (Figure 4).

CLINICAL EVIDENCE AND RESEARCH GAPS

The interplay between gut microbiota dysbiosis, microbial translocation, and the presence of microbial genetic material in circulation is increasingly recognized in pregnancy-associated metabolic disorders such as GDM. Although emerging data support these links, the clinical evidence remains preliminary, largely derived from small or pilot-scale studies, and requires replication in larger, well-characterized pregnancy cohorts (Figure 5 and Table 1).

Existing clinical evidence

Several studies report altered gut microbial diversity and composition in women with GDM compared with healthy pregnancies. Notably, reductions in butyrate-producing taxa such as *Faecalibacterium prausnitzii* and enrichment of pro-

Table 1 Summary of key human studies investigating gut microbiota dysbiosis and circulating microbial DNA in relation to gestational diabetes mellitus[4,55-66]

No.	Citation	Year	Country	Design	Gut microbiota assessed	Circulating cfDNA assessed	Sequencing Methodology	Contamination controls	Antibiotics reported/controlled	Longitudinal	Key findings	Limitations
1	Gomez-Arango <i>et al</i> [55]	2016	Australia	Cross-sectional; overweight/obese pregnant women; <i>n</i> = 70	Yes (fecal 16S)	No	16S rRNA (Illumina)	Not reported	Not reported	No	<i>Collinsella</i> associated with insulin; gut taxa correlate with metabolic hormones	Small sample, overweight/obese cohort, no cfDNA data
2	Crusell <i>et al</i> [4]	2018	Denmark	Case-control and longitudinal postpartum; GDM <i>n</i> = 50, controls <i>n</i> = 157	Yes (fecal 16S + metagenomics)	No	16S rRNA/shotgun (variable)	Not clearly stated	Not reported	Yes (postpartum)	GDM associated with altered fecal microbiota (<i>Collinsella</i> , <i>Rothia</i> , <i>Desulfovibrio</i>)	Heterogeneous methods, observational
3	Ferrocino <i>et al</i> [56]	2018	Italy	Prospective observational; GDM <i>n</i> = 41, controls	Yes (fecal 16S)	No	16S rRNA	Not reported	Not reported	Yes (pregnancy)	Microbiota changes during pregnancy in GDM; links to diet and metabolic markers	Small sample, observational
4	Pinto <i>et al</i> [57]	2023	United Kingdom/Israel (multi-centre)	Prospective cohort; early sampling before GDM diagnosis; sizeable cohort (development and validation)	Yes (multi-omics fecal)	No	16S/shotgun metagenomics, metabolomics	Reported (standard pipelines)	Partially reported	Yes (samples months before diagnosis)	Microbiota-induced inflammation precedes GDM; decreased fecal SCFAs in those who developed GDM	Requires mechanistic validation
5	Hu <i>et al</i> [58]	2021	China	Prospective cohort; early pregnancy sampling; moderate N	Yes	No	16S rRNA	Not reported	Not reported	Yes	Early pregnancy gut microbiota associated with later GDM risk	Needs replication in other populations
6	Witt <i>et al</i> [59]	2020	United States	Case-control; chorioamnionitis cases <i>vs</i> controls; small N	No	Yes (mcfDNA sequencing in maternal plasma)	Shotgun cfDNA sequencing (NGS)	Described (negative controls)	Not central to study	No	mcfDNA detected in maternal and cord plasma in chorioamnionitis; higher levels <i>vs</i> controls	Not GDM-focused; small sample
7	Tang <i>et al</i> [60]	2024	China/International	Longitudinal cfDNA study; GDM <i>n</i> = 299, controls <i>n</i> = 299	Partially (integrative analyses)	Yes (deep cfDNA sequencing)	High-depth cfDNA sequencing (Illumina)	Reported (bioinformatic filters)	Not fully reported	Yes	cfDNA fragment features associated with GDM across pregnancy; potential predictive signals	Needs external replication; novel methods
8	Wang <i>et al</i> [61]	2023	China	Large cohort (<i>n</i> > 5000), cfDNA sequencing data for GDM prediction	No	Yes (cfDNA features)	NIPT-style cfDNA sequencing	Not fully described in abstract	Not reported	No (screening dataset)	Machine learning on cfDNA can screen/predict GDM	Early; requires independent validation and contamination-aware analysis
9	Su <i>et al</i>	2021	China	Case-control; GDM <i>vs</i>	Yes (fecal 16S)	No	16S rRNA	Not reported	Not reported	No	Distinct gut	Cross-sectional;

	[62]			controls; small N							microbiota signatures in GDM	small sample
10	Liu <i>et al</i> [63]	2019	China	Case-control/prospective; moderate N	Yes (fecal metagenomics)	No	Shotgun metagenomics	Not reported	Not reported	Some follow-up	Fecal microbiota linked to plasma lipidome and GDM risk	Causality not established
11	Zheng <i>et al</i> [64]	2020	China	Prospective; first half of pregnancy; sample size moderate	Yes (16S)	No	16S rRNA	Not reported	Not reported	Yes	Reduced dynamics of gut microbiota during early pregnancy associated with GDM	Population-specific; replication needed
12	Ma <i>et al</i> [65]	2020	China	Cross-sectional; first trimester	Yes	No	16S rRNA	Not reported	Not reported	No	Altered early pregnancy microbiota in GDM patients	Small; cross-sectional
13	Ponzo <i>et al</i> [66]	2019	Italy	Associated with Ferrocino dataset; maternal and offspring microbiome studies	Yes	No	16S rRNA	Not reported	Not reported	Yes (infant follow-up)	Offspring microbiota influenced by maternal GDM	Cohort-specific

The table includes study characteristics, methodologies, and major findings. cfDNA: Circulating free DNA; GDM: Gestational diabetes mellitus; mcfDNA: Microbial cell-free DNA; NGS: Next-generation sequencing; NIPT: Non-invasive prenatal testing; SCFA: Short-chain fatty acid.

inflammatory genera such as *Collinsella* and *Prevotella* have been observed[4,28]. These microbial shifts reflect a pro-inflammatory intestinal environment that may compromise epithelial integrity and facilitate microbial translocation. Emerging studies have detected microbial circulating free DNA (cfDNA) in maternal blood, with higher concentrations noted in individuals with metabolic dysfunction[30]. In GDM, small exploratory studies suggest that circulating bacterial DNA fragments are elevated and correlate with inflammatory markers such as C-reactive protein and IL-6[40]. These findings raise the possibility that microbial cfDNA contributes to systemic inflammation and metabolic dysregulation during pregnancy. Metagenomic analyses further indicate that the microbial signatures in blood often resemble gut-associated taxa such as *Bacteroides*, *Escherichia*, and *Clostridium*[41], supporting a gut origin of these circulating fragments. Despite these intriguing associations, most studies are cross-sectional and underpowered, precluding causal inference. Furthermore, maternal factors such as genetic polymorphisms in innate immune or barrier-regulatory genes (*e.g.*, TLR variants) may modify susceptibility to microbial translocation, yet these influences remain largely unexplored. Maternal antibiotic exposure, which profoundly alters microbial communities and immune tone, also represents a potential confounder that warrants greater consideration in study design and analysis.

Limitations of current evidence

Current research is constrained by methodological and conceptual limitations: (1) Heterogeneity in study design: Differences in sequencing platforms, diagnostic definitions of GDM, and gestational timing of sampling complicate data integration; (2) Small cohort sizes: Most studies include fewer than 100 participants, limiting statistical power and adjustment for confounders such as diet, body mass index, ethnicity, and antibiotic use; (3) Lack of longitudinal follow-up: Few studies track microbiome or cfDNA dynamics across gestation, leaving unclear whether these alterations precede

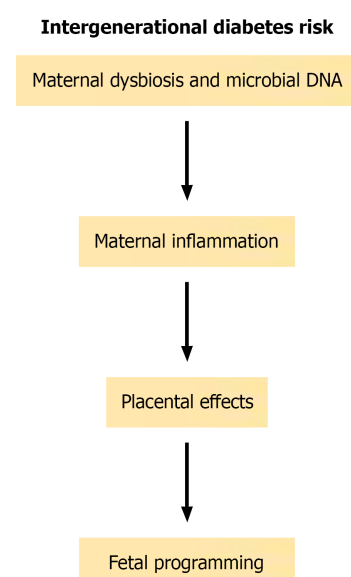


Figure 4 Intergenerational diabetes risk mediated by maternal dysbiosis and microbial DNA. Gut microbiota dysbiosis and microbial DNA in maternal circulation trigger inflammation, leading to placental alterations and impaired nutrient transfer. These processes contribute to foetal programming, thereby increasing susceptibility to obesity and diabetes in the offspring.

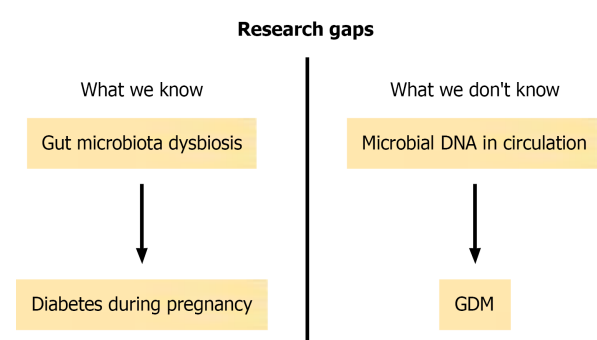


Figure 5 Research gaps in the gut microbiota-gestational diabetes mellitus axis. Current evidence links gut microbiota dysbiosis with diabetes during pregnancy. However, the role of circulating microbial DNA as a mechanistic driver of gestational diabetes mellitus remains poorly understood, highlighting a key area for future investigation. GDM: Gestational diabetes mellitus.

or follow GDM onset; (4) Nascent biomarker validation: While circulating microbial DNA is a promising candidate biomarker, its diagnostic and prognostic utility in GDM remains untested, and detection methods continue to face challenges related to contamination and low biomass; and (5) Mechanistic uncertainty: The causal pathways linking microbial cfDNA and metabolic dysfunction in pregnancy remain speculative. Whether cfDNA acts as an immunostimulant, interacts with other microbial components such as LPS, or merely reflects compromised gut barrier function is yet to be determined.

THERAPEUTIC IMPLICATIONS

Understanding the interplay between gut microbiota dysbiosis, microbial translocation, and the circulation of microbial genetic material during pregnancy carries important therapeutic relevance. If dysbiosis-induced microbial DNA contributes to the onset or progression of GDM, interventions aimed at modulating the gut microbiome and fortifying barrier function may represent novel preventive and therapeutic strategies. However, it is crucial to acknowledge that current clinical evidence remains preliminary, often derived from small, cross-sectional cohorts and must be replicated in larger, longitudinal pregnancy studies before translation to clinical practice (Figure 6).

Probiotics and prebiotics

Probiotics, which are live microorganisms that confer health benefits, have been investigated for their ability to modulate the maternal gut microbiome. Randomized controlled trials suggest that supplementation with specific strains such as *Lactobacillus rhamnosus* and *Bifidobacterium lactis* may improve glucose metabolism and reduce GDM risk in selected

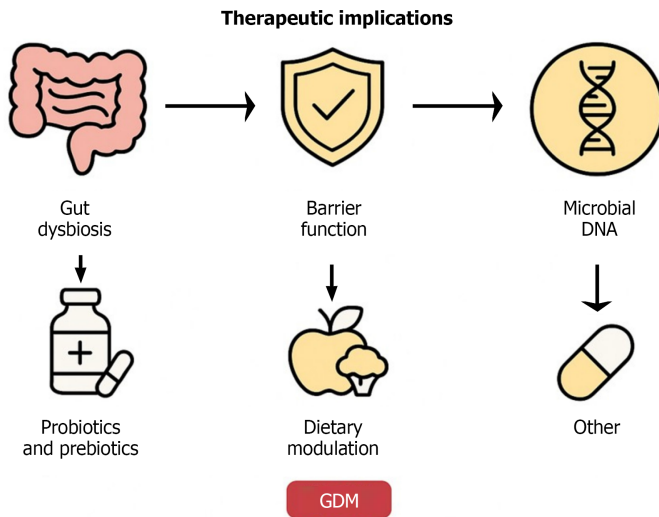


Figure 6 Therapeutic implications of the gut microbiota-microbial DNA axis in gestational diabetes mellitus. Gut dysbiosis contributes to impaired barrier function and increased microbial DNA translocation, which may exacerbate gestational diabetes mellitus. Potential therapeutic strategies include probiotics, prebiotics, dietary modulation, and other interventions aimed at restoring microbiota balance, strengthening barrier integrity, and reducing microbial DNA-mediated inflammation. GDM: Gestational diabetes mellitus.

populations[42,43]. Prebiotics, non-digestible fibres that selectively stimulate beneficial microbes, may complement these effects by enhancing microbial diversity and SCFA production, which promotes anti-inflammatory and insulin-sensitizing effects[44]. Synbiotic interventions combining both have shown promise, although results remain inconsistent. Heterogeneity in probiotic strains, dosage, timing, and study design complicates interpretation and limits the formulation of standardized recommendations. Moreover, maternal-foetal safety data are still limited, necessitating careful evaluation in future trials.

Dietary modulation

Diet remains the most practical and safe strategy to shape the gut microbiota during pregnancy. Fibre-rich, plant-based, and Mediterranean-style diets enhance microbial diversity, reinforce barrier integrity, and improve metabolic and inflammatory profiles[8,45]. Conversely, high-fat, high-sugar diets foster dysbiosis and gut permeability. Since maternal diet influences both microbiota composition and the amount of microbial DNA that may enter circulation, targeted nutritional interventions could help prevent or attenuate GDM. Culturally sensitive, individualized dietary plans integrating microbiome data may therefore represent a low-risk, high-impact approach.

Targeting intestinal barrier integrity

Because microbial DNA and other microbial products enter circulation primarily through compromised epithelial and placental barriers, therapies that strengthen these interfaces are of particular interest. Nutrients such as glutamine, zinc, and vitamin D contribute to maintaining tight junction integrity[46]. SCFAs and other probiotic-derived metabolites can further enhance mucosal defense and modulate inflammatory signaling. Early-stage studies suggest that selective inhibition of TLR pathways may dampen the inflammatory response triggered by circulating microbial DNA[47]. However, these strategies remain experimental, and robust safety evaluations in pregnancy are needed before clinical application.

Pharmacological approaches

Standard pharmacologic management of GDM includes insulin and, in some cases, metformin. Interestingly, metformin has been shown to beneficially alter gut microbiota composition, enriching *Akkermansia muciniphila* and SCFA-producing species[48]. These effects may partly mediate its metabolic benefits by improving barrier integrity and reducing microbial DNA translocation. Beyond metformin, targeted small-molecule inhibitors of microbial metabolic pathways, such as trimethylamine N-oxide synthesis inhibitors, are being investigated for cardiometabolic disease modulation[49]. Although not yet tested in pregnancy, these approaches open new avenues for microbiome-informed pharmacotherapy once safety and efficacy are established in reproductive contexts.

FMT

FMT has emerged as a highly effective therapy for restoring microbial diversity in non-pregnant populations, particularly in recurrent *Clostridioides difficile* infection. Experimental evidence suggests that FMT can reduce gut permeability and systemic inflammation, improving metabolic outcomes[50]. However, FMT remains unsuitable during pregnancy due to ethical and safety concerns. Postpartum application in women with prior GDM, however, may hold promise for mitigating long-term metabolic risks and reducing recurrence in subsequent pregnancies.

Controversies and current limitations

Despite growing enthusiasm, therapeutic strategies targeting the microbiome face several challenges. Many studies rely on small, cross-sectional cohorts, limiting generalizability[51-55]. Methodological variability, including inconsistent microbial DNA sequencing protocols, further complicates comparisons. The ongoing “sterile womb” debate and the risk of contamination in low-biomass microbial DNA studies highlight the need for rigorous validation and contamination controls before microbial DNA can be established as a reliable biomarker or therapeutic target in pregnancy.

CONCLUSION

Emerging evidence suggests that gut microbiota dysbiosis and the presence of microbial genetic material in circulation may contribute to the pathophysiology of diabetes during pregnancy by promoting inflammation and insulin resistance. However, most findings are preliminary, based on small cohorts, and require replication through longitudinal and mechanistic studies. Future research should focus on establishing causal links between dysbiosis, microbial DNA translocation, and metabolic dysfunction by integrating multi-omics analyses across maternal gut, plasma, and placental compartments. Particular attention should be given to host genetic factors (e.g., TLR and barrier-related gene variants) and maternal exposures such as antibiotics, which may modify microbiome-host interactions. Standardization of microbial cfDNA detection methods and the development of validated biomarkers will be essential for clinical translation. Furthermore, rigorously designed trials testing microbiota-targeted interventions including dietary modulation and next-generation probiotics could clarify whether restoring microbial balance can mitigate gestational diabetes risk and its long-term metabolic sequelae.

FOOTNOTES

Author contributions: Vasudevan D contributed, conceived and wrote the manuscript.

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REFERENCES

- Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. *BMJ* 2018; **361**: k2179 [RCA] [PMID: 29899036 DOI: 10.1136/bmj.k2179] [FullText]
- Thursby E, Juge N. Introduction to the human gut microbiota. *Biochem J* 2017; **474**: 1823-1836 [RCA] [PMID: 28512250 DOI: 10.1042/BCJ20160510] [FullText] [Full Text(PDF)]
- Larsen N, Vogensen FK, van den Berg FW, Nielsen DS, Andreasen AS, Pedersen BK, Al-Soud WA, Sørensen SJ, Hansen LH, Jakobsen M. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. *PLoS One* 2010; **5**: e9085 [RCA] [PMID: 20140211 DOI: 10.1371/journal.pone.0009085] [FullText] [Full Text(PDF)]
- Crusell MKW, Hansen TH, Nielsen T, Allin KH, Rühlemann MC, Damm P, Vestergaard H, Rørbye C, Jørgensen NR, Christiansen OB, Heinsen FA, Franke A, Hansen T, Lauenborg J, Pedersen O. Gestational diabetes is associated with change in the gut microbiota composition in third trimester of pregnancy and postpartum. *Microbiome* 2018; **6**: 89 [RCA] [PMID: 29764499 DOI: 10.1186/s40168-018-0472-x] [Full Text] [Full Text(PDF)]
- Butte NF. Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. *Am J Clin Nutr* 2000; **71**: 1256S-1261S [RCA] [PMID: 10799399 DOI: 10.1093/ajcn/71.5.1256s] [FullText]
- McIntyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational diabetes mellitus. *Nat Rev Dis Primers* 2019; **5**: 47 [RCA] [PMID: 31296866 DOI: 10.1038/s41572-019-0098-8] [FullText]
- Buchanan TA, Xiang AH. Gestational diabetes mellitus. *J Clin Invest* 2005; **115**: 485-491 [RCA] [PMID: 15765129 DOI: 10.1172/JCI24531] [FullText]
- Koren O, Goodrich JK, Cullender TC, Spor A, Laitinen K, Bäckhed HK, Gonzalez A, Werner JJ, Angenent LT, Knight R, Bäckhed F, Isolauri E, Salminen S, Ley RE. Host remodeling of the gut microbiome and metabolic changes during pregnancy. *Cell* 2012; **150**: 470-480 [RCA] [PMID: 22863002 DOI: 10.1016/j.cell.2012.07.008] [FullText]

- 9 Wu N, Zhou J, Mo H, Mu Q, Su H, Li M, Yu Y, Liu A, Zhang Q, Xu J, Yu W, Liu P, Liu G. The Gut Microbial Signature of Gestational Diabetes Mellitus and the Association With Diet Intervention. *Front Cell Infect Microbiol* 2021; **11**: 800865 [RCA] [PMID: 35096649 DOI: 10.3389/fcimb.2021.800865] [FullText] [Full Text(PDF)]
- 10 Ji C, Guo X. The clinical potential of circulating microRNAs in obesity. *Nat Rev Endocrinol* 2019; **15**: 731-743 [RCA] [PMID: 31611648 DOI: 10.1038/s41574-019-0260-0] [FullText]
- 11 Pietrzak B, Kawacka I, Olejnik-Schmidt A, Schmidt M. Circulating Microbial Cell-Free DNA in Health and Disease. *Int J Mol Sci* 2023; **24**: 3051 [RCA] [PMID: 36769374 DOI: 10.3390/ijms24033051] [FullText]
- 12 Amar J, Lange C, Payros G, Garret C, Chabo C, Lantieri O, Courtney M, Marre M, Charles MA, Balkau B, Burcelin R; D. E.S.I.R. Study Group. Blood microbiota dysbiosis is associated with the onset of cardiovascular events in a large general population: the D.E.S.I.R. study. *PLoS One* 2013; **8**: e54461 [RCA] [PMID: 23372728 DOI: 10.1371/journal.pone.0054461] [FullText] [Full Text(PDF)]
- 13 Lelouvier B, Servant F, Païssé S, Brunet AC, Benyahya S, Serino M, Valle C, Ortiz MR, Puig J, Courtney M, Federici M, Fernández-Real JM, Burcelin R, Amar J. Changes in blood microbiota profiles associated with liver fibrosis in obese patients: A pilot analysis. *Hepatology* 2016; **64**: 2015-2027 [RCA] [PMID: 27639192 DOI: 10.1002/hep.28829] [FullText]
- 14 Dias S, Pheiffer C, Adam S. The Maternal Microbiome and Gestational Diabetes Mellitus: Cause and Effect. *Microorganisms* 2023; **11**: 2217 [RCA] [PMID: 37764061 DOI: 10.3390/microorganisms11092217] [FullText] [Full Text(PDF)]
- 15 Brown K, DeCoffe D, Molcan E, Gibson DL. Diet-induced dysbiosis of the intestinal microbiota and the effects on immunity and disease. *Nutrients* 2012; **4**: 1095-1119 [RCA] [PMID: 23016134 DOI: 10.3390/nu4081095] [FullText] [Full Text(PDF)]
- 16 Cani PD, Amar J, Iglesias MA, Poggi M, Knauf C, Bastelica D, Neyrinck AM, Fava F, Tuohy KM, Chabo C, Waget A, Delmée E, Cousin B, Sulpice T, Chamontin B, Ferrières J, Tanti JF, Gibson GR, Casteilla L, Delzenne NM, Alessi MC, Burcelin R. Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes* 2007; **56**: 1761-1772 [RCA] [PMID: 17456850 DOI: 10.2337/db06-1491] [FullText]
- 17 Kawasaki T, Kawai T. Toll-like receptor signaling pathways. *Front Immunol* 2014; **5**: 461 [RCA] [PMID: 25309543 DOI: 10.3389/fimmu.2014.00461] [FullText] [Full Text(PDF)]
- 18 Lo YM, Chan KC, Sun H, Chen EZ, Jiang P, Lun FM, Zheng YW, Leung TY, Lau TK, Cantor CR, Chiu RW. Maternal plasma DNA sequencing reveals the genome-wide genetic and mutational profile of the fetus. *Sci Transl Med* 2010; **2**: 61ra91 [RCA] [PMID: 21148127 DOI: 10.1126/scitranslmed.3001720] [FullText]
- 19 Kuang YS, Lu JH, Li SH, Li JH, Yuan MY, He JR, Chen NN, Xiao WQ, Shen SY, Qiu L, Wu YF, Hu CY, Wu YY, Li WD, Chen QZ, Deng HW, Papasian CJ, Xia HM, Qiu X. Connections between the human gut microbiome and gestational diabetes mellitus. *Gigascience* 2017; **6**: 1-12 [RCA] [PMID: 28873967 DOI: 10.1093/gigascience/gix058] [FullText] [Full Text(PDF)]
- 20 Neri C, Serafino E, Morlando M, Familiari A. Microbiome and Gestational Diabetes: Interactions with Pregnancy Outcome and Long-Term Infant Health. *J Diabetes Res* 2021; **2021**: 9994734 [RCA] [PMID: 34869780 DOI: 10.1155/2021/9994734] [FullText] [Full Text(PDF)]
- 21 Whittle E, Leonard MO, Harrison R, Gant TW, Tonge DP. Multi-Method Characterization of the Human Circulating Microbiome. *Front Microbiol* 2018; **9**: 3266 [RCA] [PMID: 30705670 DOI: 10.3389/fmicb.2018.03266] [FullText] [Full Text(PDF)]
- 22 Acosta IC, Alonzo F 3rd. The Intersection between Bacterial Metabolism and Innate Immunity. *J Innate Immun* 2023; **15**: 782-803 [RCA] [PMID: 37899025 DOI: 10.1159/000534872] [FullText]
- 23 Peng L, Li ZR, Green RS, Holzman IR, Lin J. Butyrate enhances the intestinal barrier by facilitating tight junction assembly via activation of AMP-activated protein kinase in Caco-2 cell monolayers. *J Nutr* 2009; **139**: 1619-1625 [RCA] [PMID: 19625695 DOI: 10.3945/jn.109.104638] [FullText]
- 24 Pelaseyed T, Bergström JH, Gustafsson JK, Ermund A, Birchenough GM, Schütte A, van der Post S, Svensson F, Rodríguez-Piñero AM, Nyström EE, Wising C, Johansson ME, Hansson GC. The mucus and mucins of the goblet cells and enterocytes provide the first defense line of the gastrointestinal tract and interact with the immune system. *Immunol Rev* 2014; **260**: 8-20 [RCA] [PMID: 24942678 DOI: 10.1111/imr.12182] [FullText]
- 25 Palm NW, de Zoete MR, Cullen TW, Barry NA, Stefanowski J, Hao L, Degnan PH, Hu J, Peter I, Zhang W, Ruggiero E, Cho JH, Goodman AL, Flavell RA. Immunoglobulin A coating identifies colitogenic bacteria in inflammatory bowel disease. *Cell* 2014; **158**: 1000-1010 [RCA] [PMID: 25171403 DOI: 10.1016/j.cell.2014.08.006] [FullText]
- 26 Toyofuku M, Nomura N, Eberl L. Types and origins of bacterial membrane vesicles. *Nat Rev Microbiol* 2019; **17**: 13-24 [RCA] [PMID: 30397270 DOI: 10.1038/s41579-018-0112-2] [FullText]
- 27 Stinson LF, Boyce MC, Payne MS, Keelan JA. The Not-so-Sterile Womb: Evidence That the Human Fetus Is Exposed to Bacteria Prior to Birth. *Front Microbiol* 2019; **10**: 1124 [RCA] [PMID: 31231319 DOI: 10.3389/fmicb.2019.01124] [FullText] [Full Text(PDF)]
- 28 Camilleri M. Leaky gut: mechanisms, measurement and clinical implications in humans. *Gut* 2019; **68**: 1516-1526 [RCA] [PMID: 31076401 DOI: 10.1136/gutjnl-2019-318427] [FullText]
- 29 Duan D, Wang M, Han J, Li M, Wang Z, Zhou S, Xin W, Li X. Advances in multi-omics integrated analysis methods based on the gut microbiome and their applications. *Front Microbiol* 2024; **15**: 1509117 [RCA] [PMID: 39831120 DOI: 10.3389/fmicb.2024.1509117] [FullText] [Full Text(PDF)]
- 30 Sun L, Wu J, Du F, Chen X, Chen ZJ. Cyclic GMP-AMP synthase is a cytosolic DNA sensor that activates the type I interferon pathway. *Science* 2013; **339**: 786-791 [RCA] [PMID: 23258413 DOI: 10.1126/science.1232458] [FullText]
- 31 Edwards SM, Cunningham SA, Dunlop AL, Corwin EJ. The Maternal Gut Microbiome During Pregnancy. *MCN Am J Matern Child Nurs* 2017; **42**: 310-317 [RCA] [PMID: 28787280 DOI: 10.1097/NMC.0000000000000372] [FullText]
- 32 Yang Y, Wu N. Gestational Diabetes Mellitus and Preeclampsia: Correlation and Influencing Factors. *Front Cardiovasc Med* 2022; **9**: 831297 [RCA] [PMID: 35252402 DOI: 10.3389/fcvm.2022.831297] [FullText] [Full Text(PDF)]
- 33 Roberts JM, Escudero C. The placenta in preeclampsia. *Pregnancy Hypertens* 2012; **2**: 72-83 [RCA] [PMID: 22745921 DOI: 10.1016/j.preghy.2012.01.001] [FullText]
- 34 Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. *Diabetes Care* 2002; **25**: 1862-1868 [RCA] [PMID: 12351492 DOI: 10.2337/diacare.25.10.1862] [FullText]
- 35 Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet* 2009; **373**: 1773-1779 [RCA] [PMID: 19465232 DOI: 10.1016/S0140-6736(09)60731-5] [FullText]
- 36 Catalano PM, Kirwan JP, Haugel-de Mouzon S, King J. Gestational diabetes and insulin resistance: role in short- and long-term implications for mother and fetus. *J Nutr* 2003; **133**: 1674S-1683S [RCA] [PMID: 12730484 DOI: 10.1093/jn/133.5.1674S] [FullText]
- 37 Soderborg TK, Carpenter CM, Janssen RC, Weir TL, Robertson CE, Ir D, Young BE, Krebs NF, Hernandez TL, Barbour LA, Frank DN,

- Kroehl M, Friedman JE. Gestational Diabetes Is Uniquely Associated With Altered Early Seeding of the Infant Gut Microbiota. *Front Endocrinol (Lausanne)* 2020; **11**: 603021 [RCA] [PMID: 33329403 DOI: 10.3389/fendo.2020.603021] [FullText] [Full Text(PDF)]
- 38 Damm P, Houshmand-Oeregaard A, Kelstrup L, Lauenborg J, Mathiesen ER, Clausen TD. Gestational diabetes mellitus and long-term consequences for mother and offspring: a view from Denmark. *Diabetologia* 2016; **59**: 1396-1399 [RCA] [PMID: 27174368 DOI: 10.1007/s00125-016-3985-5] [FullText]
- 39 Gabriel CL, Ferguson JF. Gut Microbiota and Microbial Metabolism in Early Risk of Cardiometabolic Disease. *Circ Res* 2023; **132**: 1674-1691 [RCA] [PMID: 37289901 DOI: 10.1161/CIRCRESAHA.123.322055] [FullText]
- 40 Zozaya-Valdés E, Wong SQ, Raleigh J, Hatzimihailis A, Ftouni S, Papenfuss AT, Sandhu S, Dawson MA, Dawson SJ. Detection of cell-free microbial DNA using a contaminant-controlled analysis framework. *Genome Biol* 2021; **22**: 187 [RCA] [PMID: 34162397 DOI: 10.1186/s13059-021-02401-3] [FullText] [Full Text(PDF)]
- 41 Lindsay KL, Kennelly M, Culliton M, Smith T, Maguire OC, Shanahan F, Brennan L, McAuliffe FM. Probiotics in obese pregnancy do not reduce maternal fasting glucose: a double-blind, placebo-controlled, randomized trial (Probiotics in Pregnancy Study). *Am J Clin Nutr* 2014; **99**: 1432-1439 [RCA] [PMID: 24646819 DOI: 10.3945/ajcn.113.079723] [FullText]
- 42 Jarde A, Lewis-Mikhael AM, Moayyedi P, Stearns JC, Collins SM, Beyene J, McDonald SD. Pregnancy outcomes in women taking probiotics or prebiotics: a systematic review and meta-analysis. *BMC Pregnancy Childbirth* 2018; **18**: 14 [RCA] [PMID: 29310610 DOI: 10.1186/s12884-017-1629-5] [FullText] [Full Text(PDF)]
- 43 Canfora EE, Meex RCR, Venema K, Blaak EE. Gut microbial metabolites in obesity, NAFLD and T2DM. *Nat Rev Endocrinol* 2019; **15**: 261-273 [RCA] [PMID: 30670819 DOI: 10.1038/s41574-019-0156-z] [FullText]
- 44 Assaf-Balut C, García de la Torre N, Durán A, Fuentes M, Bordiú E, Del Valle L, Familiar C, Ortolá A, Jiménez I, Herraiz MA, Izquierdo N, Perez N, Torrejon MJ, Ortega MI, Illana FJ, Runkle I, de Miguel MP, Montañez C, Barabash A, Cuesta M, Rubio MA, Calle-Pascual AL. A Mediterranean diet with additional extra virgin olive oil and pistachios reduces the incidence of gestational diabetes mellitus (GDM): A randomized controlled trial: The St. Carlos GDM prevention study. *PLoS One* 2017; **12**: e0185873 [RCA] [PMID: 29049303 DOI: 10.1371/journal.pone.0185873] [FullText] [Full Text(PDF)]
- 45 Gao Y, Li W, Huang X, Lyu Y, Yue C. Advances in Gut Microbiota-Targeted Therapeutics for Metabolic Syndrome. *Microorganisms* 2024; **12**: 851 [RCA] [PMID: 38792681 DOI: 10.3390/microorganisms12050851] [FullText]
- 46 Wang C, Li Q, Ren J. Microbiota-Immune Interaction in the Pathogenesis of Gut-Derived Infection. *Front Immunol* 2019; **10**: 1873 [RCA] [PMID: 31456801 DOI: 10.3389/fimmu.2019.01873] [FullText] [Full Text(PDF)]
- 47 Wu H, Esteve E, Tremaroli V, Khan MT, Caesar R, Mannerås-Holm L, Ståhlman M, Olsson LM, Serino M, Planas-Félix M, Xifra G, Mercader JM, Torrents D, Burcelin R, Ricart W, Perkins R, Fernández-Real JM, Bäckhed F. Metformin alters the gut microbiome of individuals with treatment-naïve type 2 diabetes, contributing to the therapeutic effects of the drug. *Nat Med* 2017; **23**: 850-858 [RCA] [PMID: 28530702 DOI: 10.1038/nm.4345] [FullText]
- 48 Tang WH, Hazen SL. Microbiome, trimethylamine N-oxide, and cardiometabolic disease. *Transl Res* 2017; **179**: 108-115 [RCA] [PMID: 27490453 DOI: 10.1016/j.trsl.2016.07.007] [FullText]
- 49 Kootte RS, Levin E, Salojärvi J, Smits LP, Hartstra AV, Udayappan SD, Hermes G, Bouter KE, Koopen AM, Holst JJ, Knop FK, Blaak EE, Zhao J, Smidt H, Harms AC, Hankemeijer T, Bergman JJGHM, Romijn HA, Schaap FG, Olde Damink SWM, Ackermans MT, Dallinga-Thie GM, Zoetendal E, de Vos WM, Serlie MJ, Stoes ESG, Groen AK, Nieuwdorp M. Improvement of Insulin Sensitivity after Lean Donor Feces in Metabolic Syndrome Is Driven by Baseline Intestinal Microbiota Composition. *Cell Metab* 2017; **26**: 611-619.e6 [RCA] [PMID: 28978426 DOI: 10.1016/j.cmet.2017.09.008] [FullText]
- 50 Dimova T, Dimitrova V, Grozdanov P, Markova N. Placenta of BCG-Vaccinated Women in early Pregnancy is Colonized with Non-Immunogenic Mycobacterial L-forms. *Am J Reprod Immunol* 2023; **89**: e13650 [RCA] [PMID: 36331422 DOI: 10.1111/aji.13650] [FullText]
- 51 Vander Haar EL, Wu G, Gyamfi-Bannerman C, Thomas C, Wapner RJ, Reddy UM, Zhao L, Silver RM, Goldenberg RL, Han YW. Microbial Analysis of Umbilical Cord Blood Reveals Novel Pathogens Associated with Stillbirth and Early Preterm Birth. *mBio* 2022; **13**: e0203622 [RCA] [PMID: 35993728 DOI: 10.1128/mbio.02036-22] [FullText] [Full Text(PDF)]
- 52 Vanstokstraeten R, Mackens S, Callewaert E, Blotwijk S, Emmerechts K, Crombé F, Soetens O, Wybo I, Vandoorslaer K, Mostert L, De Geyter D, Muyldermans A, Blockeel C, Piérard D, Demuyser T. Culturomics to Investigate the Endometrial Microbiome: Proof-of-Concept. *Int J Mol Sci* 2022; **23**: 12212 [RCA] [PMID: 36293066 DOI: 10.3390/ijms232012212] [FullText]
- 53 Williams N, Vella R, Zhou Y, Gao H, Mass K, Townsel C, Campbell W, Luo G. Investigating the origin of the fetal gut and placenta microbiome in twins. *J Matern Fetal Neonatal Med* 2022; **35**: 7025-7035 [RCA] [PMID: 34130585 DOI: 10.1080/14767058.2021.1936487] [FullText]
- 54 Yu J, Peng T, Lu J, Li X, Hu R. Analysis of the Microbiome Based on 16S rRNA Gene Signature in Women with Preterm versus Term Birth. *Reprod Dev Med* 2021; **5**: 81-89 [RCA] [DOI: 10.4103/2096-2924.320887] [FullText]
- 55 Gomez-Arango LF, Barrett HL, McIntyre HD, Callaway LK, Morrison M, Dekker Nitert M; SPRING Trial Group. Connections Between the Gut Microbiome and Metabolic Hormones in Early Pregnancy in Overweight and Obese Women. *Diabetes* 2016; **65**: 2214-2223 [RCA] [PMID: 27217482 DOI: 10.2337/db16-0278] [FullText]
- 56 Ferrocino I, Ponzo V, Gambino R, Zarovska A, Leone F, Monzeglio C, Goitre I, Rosato R, Romano A, Grassi G, Broglio F, Cassader M, Coccolin L, Bo S. Changes in the gut microbiota composition during pregnancy in patients with gestational diabetes mellitus (GDM). *Sci Rep* 2018; **8**: 12216 [RCA] [PMID: 30111822 DOI: 10.1038/s41598-018-30735-9] [FullText] [Full Text(PDF)]
- 57 Pinto Y, Frishman S, Turjeman S, Eshel A, Nuriel-Ohayon M, Shrossel O, Ziv O, Walters W, Parsonnet J, Ley C, Johnson EL, Kumar K, Schweitzer R, Khatib S, Magzal F, Muller E, Tamir S, Tenenbaum-Gavish K, Rautava S, Salminen S, Isolauri E, Yariv O, Peled Y, Poran E, Pardo J, Chen R, Hod M, Borenstein E, Ley RE, Schwartz B, Louzoun Y, Hadar E, Koren O. Gestational diabetes is driven by microbiota-induced inflammation months before diagnosis. *Gut* 2023; **72**: 918-928 [RCA] [PMID: 36627187 DOI: 10.1136/gutjnl-2022-328406] [FullText] [Full Text(PDF)]
- 58 Hu P, Chen X, Chu X, Fan M, Ye Y, Wang Y, Han M, Yang X, Yuan J, Zha L, Zhao B, Yang CX, Qi XR, Ning K, Debelius J, Ye W, Xiong B, Pan XF, Pan A. Association of Gut Microbiota during Early Pregnancy with Risk of Incident Gestational Diabetes Mellitus. *J Clin Endocrinol Metab* 2021; **106**: e4128-e4141 [RCA] [PMID: 34015117 DOI: 10.1210/clinem/dgab346] [FullText]
- 59 Witt RG, Blair L, Frascio M, Rosen MJ, Nguyen QH, Bercovici S, Zompi S, Romero R, Mackenzie TC. Detection of microbial cell-free DNA in maternal and umbilical cord plasma in patients with chorioamnionitis using next generation sequencing. *PLoS One* 2020; **15**: e0231239 [RCA] [PMID: 32294121 DOI: 10.1371/journal.pone.0231239] [FullText] [Full Text(PDF)]

- 60 **Tang Z**, Wang S, Li X, Hu C, Zhai Q, Wang J, Ye Q, Liu J, Zhang G, Guo Y, Su F, Liu H, Guan L, Jiang C, Chen J, Li M, Ren F, Zhang Y, Huang M, Li L, Zhang H, Hou G, Jin X, Chen F, Zhu H, Li L, Zeng J, Xiao H, Zhou A, Feng L, Gao Y, Liu G. Longitudinal integrative cell-free DNA analysis in gestational diabetes mellitus. *Cell Rep Med* 2024; **5**: 101660 [RCA] [PMID: 39059385 DOI: 10.1016/j.xcrm.2024.101660] [FullText] [Full Text(PDF)]
- 61 **Wang Y**, Sun P, Zhao Z, Yan Y, Yue W, Yang K, Liu R, Huang H, Wang Y, Chen Y, Li N, Feng H, Li J, Liu Y, Chen Y, Shen B, Zhao L, Yin C. Identify gestational diabetes mellitus by deep learning model from cell-free DNA at the early gestation stage. *Brief Bioinform* 2023; **25**: bbad492 [RCA] [PMID: 38168840 DOI: 10.1093/bib/bbad492] [FullText]
- 62 **Su Y**, Wang HK, Gan XP, Chen L, Cao YN, Cheng DC, Zhang DY, Liu WY, Li FF, Xu XM. Alterations of gut microbiota in gestational diabetes patients during the second trimester of pregnancy in the Shanghai Han population. *J Transl Med* 2021; **19**: 366 [RCA] [PMID: 34446048 DOI: 10.1186/s12967-021-03040-9] [FullText] [Full Text(PDF)]
- 63 **Liu H**, Pan LL, Lv S, Yang Q, Zhang H, Chen W, Lv Z, Sun J. Alterations of Gut Microbiota and Blood Lipidome in Gestational Diabetes Mellitus With Hyperlipidemia. *Front Physiol* 2019; **10**: 1015 [RCA] [PMID: 31447702 DOI: 10.3389/fphys.2019.01015] [FullText] [Full Text (PDF)]
- 64 **Zheng W**, Xu Q, Huang W, Yan Q, Chen Y, Zhang L, Tian Z, Liu T, Yuan X, Liu C, Luo J, Guo C, Song W, Zhang L, Liang X, Qin H, Li G. Gestational Diabetes Mellitus Is Associated with Reduced Dynamics of Gut Microbiota during the First Half of Pregnancy. *mSystems* 2020; **5**: e00109-e00120 [RCA] [PMID: 32209715 DOI: 10.1128/mSystems.00109-20] [FullText] [Full Text(PDF)]
- 65 **Ma S**, You Y, Huang L, Long S, Zhang J, Guo C, Zhang N, Wu X, Xiao Y, Tan H. Alterations in Gut Microbiota of Gestational Diabetes Patients During the First Trimester of Pregnancy. *Front Cell Infect Microbiol* 2020; **10**: 58 [RCA] [PMID: 32175285 DOI: 10.3389/fcimb.2020.00058] [FullText] [Full Text(PDF)]
- 66 **Ponzo V**, Ferrocino I, Zarovska A, Amenta MB, Leone F, Monzeglio C, Rosato R, Pellegrini M, Gambino R, Cassader M, Ghigo E, Coccolin L, Bo S. The microbiota composition of the offspring of patients with gestational diabetes mellitus (GDM). *PLoS One* 2019; **14**: e0226545 [RCA] [PMID: 31841548 DOI: 10.1371/journal.pone.0226545] [FullText] [Full Text(PDF)]



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