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Review Article

Role of Gut Microbiome in Metabolic Syndrome: A Comprehensive Review

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Abstract:
This current review explains the complex relationship between gut microbiota and metabolic syndrome, focusing on the significant role of gut microbiota along with genetics, and environmental factors in the pathogenesis of the metabolic syndrome. This microbiota with beneficial bacteria plays a pivotal role in the balance of metabolic health by supporting gut barrier integrity, immune function, and the production of short-chain fatty acids (SCFAs), which regulate glucose and lipid metabolism. Any imbalance in the delicate relationship between gut bacteria and the host's immune system increases the gut permeability and drives chronic inflammation. This leads to Insulin resistance characteristic of metabolic syndrome, which promotes pro-inflammatory adipokines thereby significantly raising the risk of cardiovascular diseases and type 2 diabetes. Host genetics, specifically genetic variations in NOD2 and FUT2 can influence both microbial populations and metabolic consequences. Lifestyle also increases the likelihood of developing metabolic syndrome particularly with diets rich in refined sugars and fats, exacerbating dysbiosis. This study demonstrates the addition of gut microbiota based therapeutic strategies in animal and human studies, including probiotics, prebiotics, and fecal microbiota transplantation (FMT), all of which have demonstrated promising results in lowering inflammation and re-establishing microbial balance . It also focuses on diet modifications like Mediterranean diet can enhance metabolic health and encourage microbial diversity. Considering all of the above, this review article focuses on the requirement of personalized microbiome-focused strategies in preventing and treating metabolic syndrome .Further research works are required on microbiome targeted therapies and their usage clinically.

Keywords: Metabolic Syndrome, Gut Microbiota, Insulin Resistance, Fecal Microbiota Transplantation, Short-Chain Fatty Acids.

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Introduction

Metabolic syndrome is a collective term for interrelated metabolic risk factors that increase the likelihood of developing cardiovascular disease and type 2 diabetes. The main components of metabolic syndrome are central adiposity, high blood pressure, increased fasting glucose concentration, increased serum triglyceride concentration, and decreased high-density lipoprotein (HDL) cholesterol concentration [1].

In turn metabolic disorder showcases the complex network between underlying pathophysiological mechanisms, genetic predisposition and lifestyle factors. Rapidly increasing prevalence of metabolic syndrome signifies the need to understand underlying biological mechanisms that contribute to the disease development and progression. Recent developments in microbiome research have revealed the major role of gut bacteria in maintaining healthy metabolism. A human gut should contain a healthy and balanced gut microbiota in order to maintain metabolic equilibrium. Disruption of microbial composition known as dysbiosis would increase gut permeability, promote systemic inflammation and disrupt metabolic signaling pathways. This in turn leads to lipid dysregulation, progression of insulin resistance and contributes to pathogenesis of metabolic syndrome.

Genetic variations in genes like NOD2 and FUT2 can alter microbiome composition promoting dysbiosis and are exacerbated by environmental and dietary factors which increase inflammation and disrupt metabolisms leading to metabolic syndrome. Preserving microbial equilibrium, improving integrity of gut health are some of the benefits of using Probiotics, prebiotics, and fecal microbiota transplantation (FMT). Some dietary modifications like having fiber- rich or polyphenol-enriched diets improve metabolic outcomes and reduce the risk of metabolic syndrome significantly. All these interventions using comprehensive strategies focusing on gut microbiota would bring impactful outcomes in metabolic syndrome.

This literature review gives a wholesome picture of understanding metabolic syndrome with main focus on the role played by gut microbiota in its etiology, pathophysiology, and management. We emphasize how environmental influences, genetic factors and microbial composition work together in influencing metabolic outcomes. Considering findings from latest studies on gut microbiota and metabolic syndrome this review emphasizes personalized microbiome centered strategies in treating this rising global health issue.

Pathogenesis:

Insulin resistance, a central component of metabolic syndrome, is a condition wherein body cells, including muscle and adipose tissues, become less responsive to insulin. As a result, glucose uptake by these cells is impaired, leading to elevated blood glucose concentrations. To counteract this impaired glucose utilization, the pancreas increases insulin secretion, resulting in hyperinsulinemia. This compensatory mechanism may temporarily maintain glucose levels but contributes to long-term metabolic disturbances and plays a pivotal role in the development of type 2 diabetes [2]. Excessive visceral fat accumulation leads to insulin resistance. Adipose tissue, especially in the abdomen, acts as an active endocrine organ secreting free fatty acids, adipokines and inhibits insulin action [3]. Additionally, the adipose tissue secretes a variety of hormones and cytokines, collectively known as adipokines, including leptin and adiponectin. An imbalance in these adipokines promotes systemic inflammation and further impairs insulin sensitivity, creating a cycle that perpetuates metabolic complications [4].

Chronic low-grade inflammation is another defining feature of metabolic syndrome. Elevated levels of inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), are not only associated with insulin resistance but also play a critical role in endothelial dysfunction. This dysfunction impairs the ability of blood vessels to dilate properly and increases vascular permeability, laying the groundwork for atherosclerosis. The resulting build-up of arterial plaque heightens the risk of cardiovascular events and contributes to the development of hypertension [5]. Genetic predisposition also influences the development of metabolic syndrome. Variations in genes related to immunity and metabolism, such as NOD2 and FUT2, are linked to alterations in the gut microbiota composition. These genetic variations may influence the abundance and balance of specific microbial populations, impacting metabolic health and inflammation [6] [7]. Beyond genetics, environmental and lifestyle factors further exacerbate metabolic syndrome. Sedentary behavior and a diet rich in saturated fats, processed carbohydrates, and sugars promote weight gain and worsen insulin resistance. Additionally, chronic stress adversely affects glucose metabolism, further complicating the body's metabolic landscape [8]. Insulin resistance also significantly disrupts lipid metabolism. It leads to elevated triglyceride levels and reduced high-density lipoprotein (HDL) cholesterol, a condition known as dyslipidemia. This imbalance fosters the formation of atherogenic particles that accumulate within the arterial walls, accelerating the development of atherosclerosis and heightening the risk of cardiovascular disease [9] Collectively, the interplay of genetic, inflammatory, and environmental factors amplifies the severity of metabolic syndrome, increasing susceptibility to severe outcomes such as type 2 diabetes, cardiovascular disease, and organ damage.

Methodology:

A comprehensive and systematic methodology was used in the preparation of the above review, integrating both primary and secondary sources of peer-reviewed scientific literature; a detailed literature search was conducted using well-known biomedical databases such as PubMed, Science Direct, and Google Scholar, and a comprehensive literature review was conducted by the authors of the review, providing broad and focused coverage of the pathophysiology, etiology and gut microbiota role in metabolic syndrome. Selection criteria included systematic reviews, meta-analyses, and recent publications with robust data, prioritizing key studies that provide insights into molecular and genetic mechanisms. Data extraction focused on key findings on insulin resistance, lipid metabolism, inflammation, and microbial-host interactions, and selected studies were critically appraised. Narrative synthesis uses thematic analysis to organize the content into clear and interrelated chapters, enriched with the latest theories on the impact of genetic predisposition and dietary interventions on gut health. Relevant clinical trials and intervention approaches are reviewed to clarify therapeutic implications and provide a coherent and substantial discussion based on contemporary biomedical research.

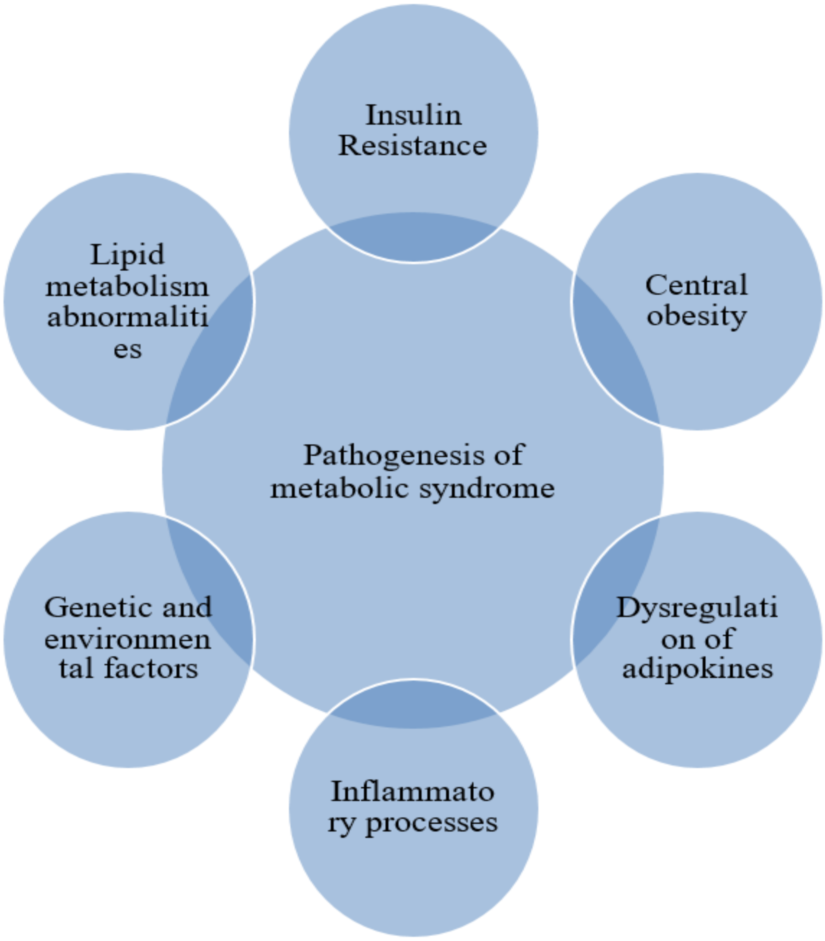

Figure 1: Figure outlining the key mechanisms driving the pathogenesis of metabolic syndrome.

Pathophysiology:

Insulin resistance impairs glucose uptake by muscle and adipose tissues, resulting in elevated blood glucose levels, or hyperglycemia. Over time, persistent hyperglycemia can cause dysfunction of pancreatic beta cells, leading to a further reduction in insulin secretion and worsening metabolic control [10]. Additionally, hyperglycemia and dyslipidemia—characterized by abnormal lipid levels—exert damaging effects on the vascular endothelium. Endothelial dysfunction, which arises from this damage, is an early indicator of atherosclerosis and plays a significant role in increasing vascular resistance and the risk of developing hypertension [11]. Moreover, insulin resistance, along with the accompanying state of hyperinsulinemia, promotes sodium retention in the kidneys and activates the sympathetic nervous system. These effects collectively contribute to elevated blood pressure and increased cardiovascular strain [12]. In metabolic syndrome, the presence of elevated levels of plasminogen activator inhibitor-1 (PAI-1) and fibrinogen further complicates the situation by enhancing blood clotting potential, thereby raising the risk of thrombotic events such as deep vein thrombosis [13].

The interplay between hyperglycemia, hypertension, and dyslipidemia causes widespread damage to various organs. This damage manifests in significant clinical consequences, including cardiovascular events, kidney disease (nephropathy), and damage to the eyes (retinopathy) [14]. The cumulative impact of these metabolic disturbances underscores the importance of early intervention and comprehensive management to mitigate the risks associated with metabolic syndrome and its complications.

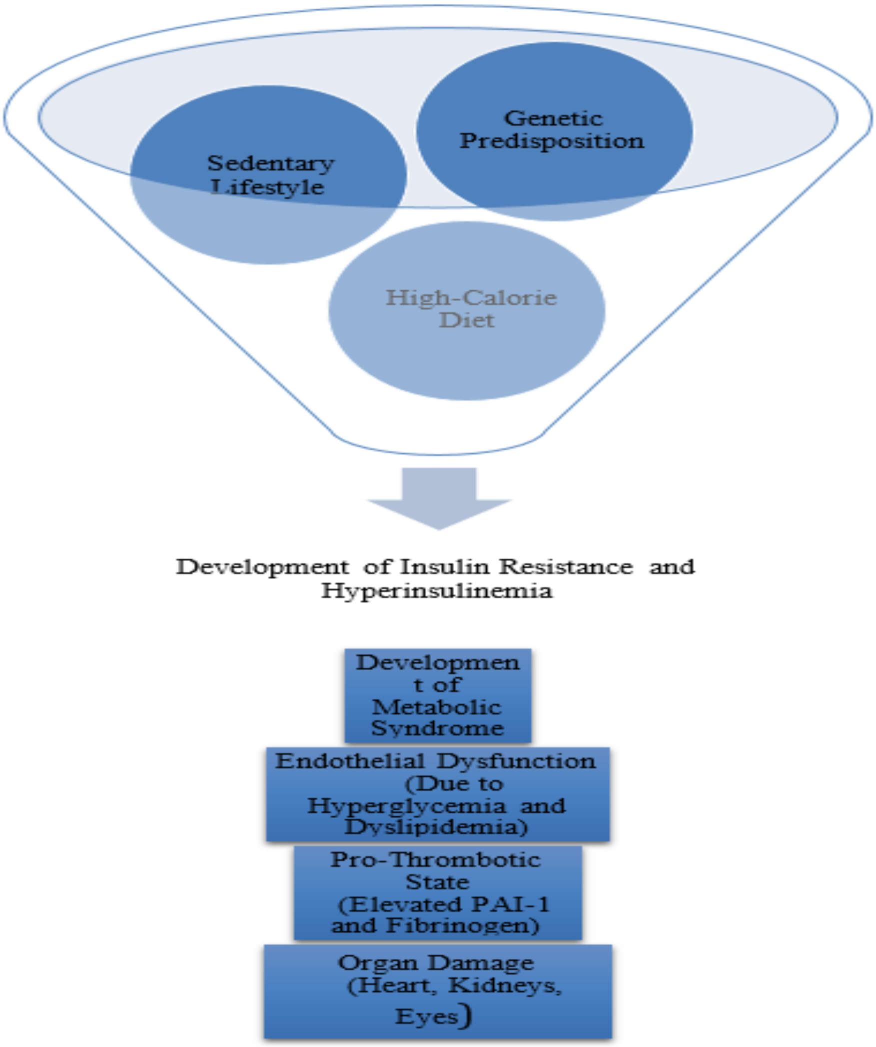

Figure 2: Depicts factors involved in metabolic syndrome resulting in various pathological manifestations.

Role of normal microflora in gut health: Beneficial bacteria in the gut promote the expression of proteins that help maintain gut integrity, thereby strengthening the intestinal barrier and protecting against harmful substances that could otherwise enter the bloodstream [15]. By modulating immune responses, probiotics play a crucial role in balancing Th17 and regulatory T (Treg) cells. This shift favors regulatory T cells, which help to reduce inflammation and support immune homeostasis [16]. These bacteria also contribute to metabolic health by enhancing key signaling pathways.

They activate AMP-activated protein kinase (AMPK) and produce short-chain fatty acids (SCFAs) and other beneficial metabolites, which together improve glucose uptake and promote lipid oxidation, aiding in energy metabolism and overall metabolic efficiency [17]. Additionally, beneficial gut microbes have a positive impact on the secretion of glucagon-like peptide-1 (GLP-1), a hormone that enhances insulin secretion and supports glucose homeostasis, contributing to better regulation of blood sugar levels [18].

Preventive role and aspects in case of metabolic syndrome: Restoring microbial balance through the use of probiotics, such as strains of Lactobacillus and Bifidobacterium, is a promising approach in regulating the composition of the gut microbiota. These probiotics increase the population of beneficial bacteria while inhibiting the growth of pathogenic microbes, promoting a healthy and diverse microbiome [19].

A well-balanced gut microbiota is essential for overall health, as it influences immune function, nutrient absorption, and metabolic processes. One of the critical benefits of probiotics is their ability to improve the intestinal barrier function. By enhancing the strength and integrity of tight junctions between epithelial cells, probiotics reduce the translocation of endotoxins from the gut into the bloodstream, lowering endotoxemia and mitigating systemic inflammation. This improved barrier function is crucial in preventing the onset of inflammatory diseases and maintaining a robust immune system [20].

Additionally, probiotics contribute to the production of beneficial metabolites, such as short-chain fatty acids (SCFAs), through the enhanced fermentation of dietary fiber. Elevated SCFA levels, particularly butyrate, acetate, and propionate, are associated with improved insulin sensitivity and reduced inflammation. SCFAs play a pivotal role in energy metabolism, gut health, and the modulation of the immune response, making them key players in metabolic regulation [21]. SCFAs also influence appetite and energy expenditure. They stimulate the secretion of satiety hormones like peptide YY (PYY) and glucagon-like peptide-1 (GLP-1), promoting a feeling of fullness and reducing food intake. Furthermore, SCFAs activate the AMP-activated protein kinase (AMPK) pathway, enhancing energy expenditure and facilitating fat oxidation. This dual effect on appetite regulation and metabolic rate underscores the potential of SCFAs in managing body weight and preventing metabolic syndrome [22]. Beneficial gut bacteria also modulate bile acid metabolism by activating receptors such as the farnesoid X receptor (FXR) and the G protein-coupled bile acid receptor (TGR5). These changes in bile acid profiles improve receptor signaling, which is crucial for optimizing glucose and lipid metabolism. Enhanced bile acid receptor activity has been shown to lower blood glucose levels, improve lipid profiles, and promote metabolic homeostasis [23].

Another significant aspect of a balanced microbiome is the reduction of toxic metabolites. Dietary interventions that support a beneficial microbial community can lower the production of harmful compounds like trimethylamine N-oxide (TMAO), which has been associated with an increased risk of cardiovascular diseases. By reducing TMAO levels, these interventions help to lower cardiovascular risk and improve overall heart [24]. Moreover, beneficial bacteria can suppress pro-inflammatory signaling pathways, such as the nuclear factor kappa B (NF-κB) pathway. This suppression reduces the production of pro-inflammatory cytokines, alleviating chronic inflammation, which is a risk factor for numerous metabolic and autoimmune diseases [25]. At the same time, beneficial microorganisms promote the production of anti-inflammatory cytokines, including interleukin-10 (IL-10), which plays a crucial role in dampening inflammatory responses and maintaining immunity [26]. Prebiotics, such as inulin and fructooligosaccharides (FOS), are dietary fibers that support the growth and activity of beneficial bacteria in the gut. These prebiotics serve as fuel for gut microbes, fostering a favorable environment that enhances the microbiome's health-promoting effects [27].

In addition, polyphenol-rich diets—featuring foods like berries, tea, and dark chocolate—exert positive effects on gut microbiota composition. Polyphenols act as prebiotic compounds, regulating microbial diversity and supporting metabolic health by reducing inflammation and oxidative stress [28]. In summary, the integration of probiotics, prebiotics, and polyphenol-rich diets presents a comprehensive approach to promoting gut health, enhancing metabolic function, and reducing the risk of chronic diseases. These dietary strategies support a healthy microbiota that is essential for maintaining a balanced immune system and optimal metabolic health.

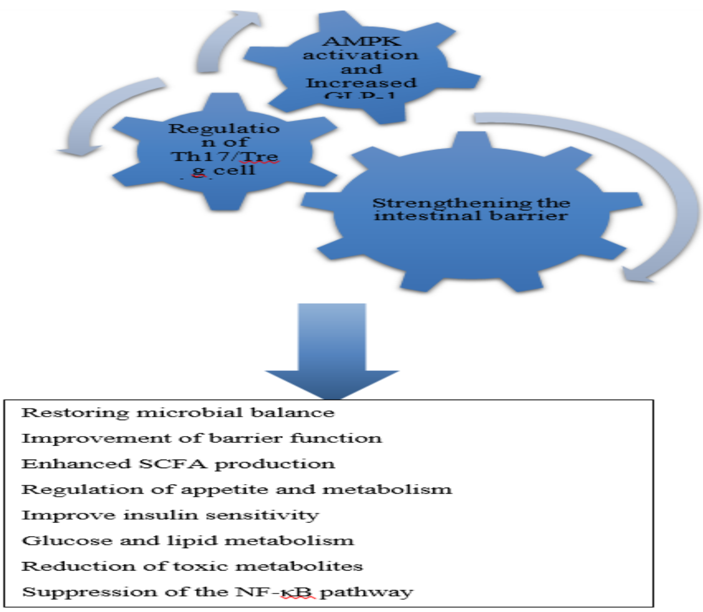

Figure 3: Depicts the functions of gut microbiota and underlying mechanism.

Experimental evidences:

Table 1: Human studies:

Authors	**Larsen N., Vogensen F.K., van den Berg F.W.J., et al. [29]**	**Vrieze A., Holleman F., Zoetendal E.G., et al [30]**
Year	**2010**	**2012**
Title	Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults.	Transfer of intestinal microbiota from lean donors increases insulin sensitivity in individuals with metabolic syndrome.
Place of Study	Denmark	The Netherlands
Objective	To compare gut microbiota composition between adults with type 2 diabetes and non-diabetic controls	To assess whether fecal microbiota transplantation (FMT) from lean donors improves insulin sensitivity in individuals with metabolic syndrome
Methods	In a cross-sectional study involving 36 male adults (18 with type 2 diabetes and 18 controls); 16S rRNA gene sequencing used to analyze fecal samples	Randomized controlled trial with 18 male subjects with metabolic syndrome; participants received either allogenic FMT from lean donors or autologous FMT; insulin sensitivity measured using hyperinsulinemic-euglycemic clamp technique
Findings	Diabetic individuals had a decreased ratio of Firmicutes to Bacteroidetes and increased levels of Proteobacteria; specific changes in gut microbiota correlated with glucose levels and HbA1c.	Allogenic FMT resulted in a significant 44% increase in peripheral insulin sensitivity after six weeks compared to autologous FMT; an increased abundance of butyrate-producing intestinal microbiota was observed in recipients of lean donor microbiota.
Conclusions	Altered gut microbiota composition is associated with type 2 diabetes, suggesting a potential role in metabolic syndrome development and progression.	Modulating gut microbiota via FMT from lean donors can substantially improve insulin sensitivity, highlighting a therapeutic potential for metabolic syndrome through microbiota manipulation.

Table 2: Animal studies:

Authors	**Bäckhed F., Ding H., Wang T., et al. [31]**	**Turnbaugh P.J., Bäckhed F., Fulton L., Gordon J.I. [32]**	**Cani P.D., Amar J., Iglesias M.A., et al. [33]**	**Everard A., Lazarevic V., Derrien M., et al. [34]**
Year	**2004**	**2008**	**2007**	**2011**
Title	The gut microbiota is an environmental factor that regulates fat storage.	Diet-induced obesity is linked to marked but reversible alterations in the mouse distal gut microbiome.	Metabolic endotoxemia initiates obesity and insulin resistance.	Responses of gut microbiota and glucose and lipid metabolism to prebiotics in genetically obese and diet-induced leptin-resistant mice.
Place of Study	United States	United States	Belgium and France	Belgium and Switzerland
Objective	To investigate the role of gut microbiota in regulating fat storage and energy balance in mice.	To examine how a high-fat diet affects gut microbiome composition and contributes to obesity in mice.	To explore the impact of gut microbiota-induced endotoxemia on obesity and insulin resistance.	To evaluate the effects of prebiotic treatment on gut microbiota and metabolic parameters in obese mice.
Methods	Germ-free (GF) mice were colonized with microbiota from conventional mice; body fat content, food intake, and	Mice were fed either a standard diet or a high-fat, high-sugar "Western" diet; gut microbiota were analyzed using 16S rRNA gene	Mice were fed a normal or high-fat diet; plasma lipopolysaccharide (LPS) levels were measured to assess metabolic	Obese and leptin-resistant mice were administered prebiotics (oligofructose) for five weeks; gut microbiota was analyzed using 16S rRNA gene sequencing;

	metabolic rates were measured; gene expression analysis was conducted to assess host metabolic responses.	sequencing; body weight and fat mass were measured; microbiota transplantation experiments were conducted.	endotoxemia; antibiotic treatment was used to modulate gut microbiota; metabolic parameters including weight gain, glucose tolerance, and insulin sensitivity were evaluated.	metabolic assessments included glucose tolerance tests, lipid profiling, and gene expression analysis of metabolic markers.
Findings	Colonization of GF mice led to a 60% increase in body fat within 14 days without increased food intake or decreased energy expenditure; increased hepatic lipogenesis and decreased fatty acid oxidation were observed; upregulation of host genes involved in lipid storage was identified.	High-fat diet-induced significant shifts in gut microbiota, notably an increase in Firmicutes and a decrease in Bacteroidetes; these changes enhanced energy harvest from the diet, leading to increased fat deposition and obesity; microbiota changes were reversible upon diet normalization.	High-fat diet increased gut permeability and plasma LPS levels, leading to metabolic endotoxemia; metabolic endotoxemia induced low-grade inflammation, weight gain, adipose tissue accumulation, insulin resistance, and diabetes; antibiotic treatment reduced LPS levels and improved metabolic parameters.	Prebiotic treatment increased beneficial bacteria such as Akkermansia muciniphila and Bifidobacterium spp.; improved glucose tolerance, reduced fat mass, decreased plasma endotoxin levels, and modulated expression of genes involved in lipid metabolism and inflammation were observed.
Conclusions	Gut microbiota plays a critical role in energy harvest and fat storage, influencing host metabolism and contributing to the development of metabolic syndrome	Diet alters gut microbiota composition, which in turn influences energy harvest and fat storage, contributing to obesity and metabolic syndrome; microbiota modulation may be a target for therapeutic intervention.	Gut microbiota-induced metabolic endotoxemia plays a causative role in initiating obesity and insulin resistance; targeting gut microbiota to reduce endotoxemia may offer a therapeutic strategy for metabolic syndrome.	Prebiotics beneficially modulate gut microbiota composition and improve metabolic health, indicating that dietary interventions targeting gut microbiota may be effective in combating metabolic syndrome and associated disorders.

Gut microbiota composition and host genetics: Heritability of the gut microbiota has been a topic of significant interest, with twin studies on monozygotic and dizygotic twins demonstrating that certain components of the gut microbiota are influenced by genetic factors. These studies have shown that the abundance and composition of specific bacterial taxa are partially inherited, underscoring the genetic contribution to gut microbiome [35] For instance, certain bacterial taxa, such as Faecalibacterium prausnitzii, a beneficial bacterium known for its anti-inflammatory properties, have been linked to genetic variations in the host.

The abundance of this bacterium is associated with specific genetic factors, suggesting that host genetics can influence the presence of bacteria that play crucial roles in immune modulation and gut for instance, certain bacterial taxa, such as Faecalibacterium prausnitzii, a beneficial bacterium known for its anti-inflammatory properties, have been linked to genetic variations in the host. The abundance of this bacterium is associated with specific genetic factors, suggesting that host genetics can influence the presence of bacteria that play crucial roles in immune modulation and gut health [36] Genome-wide association studies (GWAS) have further elucidated the genetic influences on the gut microbiota. Bonder et al. (2016) identified multiple host loci that are associated with variations in microbiota diversity, providing evidence that genetic factors contribute to shaping the gut microbial community. These loci underscore the complex interplay between human genetics and the gut. Additionally, genes related to immunity and metabolism, such as NOD2 and FUT2, have been associated with differences in microbiota composition. Variations in these genes can influence the abundance of certain microbial populations, thereby affecting the host's metabolic and immune responses [37]. Gut microbiota composition and functioning can be influenced by genetic variations that can finally have an impact on metabolic outcomes. For example, genetic polymorphisms in APOE are associated with differences in gut microbiota composition and lipid metabolism, highlighting the link between genetic predisposition and metabolic health. This interplay illustrates the significant role that genetic predisposition plays in determining how gut microbes influence metabolic health [38]. The interplay between host genetics, the gut microbiota, and metabolic syndrome is an area of growing research interest.

Similarly, the FUT2 gene, which determines an individual's secretor status, plays a significant role in shaping the gut microbiota. Individuals with the non-secretor status exhibit altered microbiota profiles that are associated with metabolic traits, including an increased risk of obesity and metabolic syndrome. These variations emphasize how genetic factors can influence the risk of metabolic disorders by affecting the microbiota's composition and function [40]. Understanding the interaction between genetic disposition and the gut microbiota is crucial in explaining individual susceptibility to metabolic syndrome. Genetic factors may determine how the gut microbiota influences metabolic processes, including glucose and lipid metabolism, thereby contributing to disease risk. This knowledge paves the way for the development of personalized medicine, where targeted interventions can be designed based on an individual's genetic and microbiome profiles. By understanding these complex interactions, it becomes possible to develop personalized strategies that mitigate the risk of metabolic syndrome, combining genetic insights with microbiota-based therapies to improve health outcomes [41].

Therapeutic implications of alterations in gut microbiota in metabolic syndrome and other medical conditions: The gut microbiota is a highly complex community of microorganisms residing in the human gastrointestinal tract, playing a crucial role in maintaining metabolic health and overall well-being. Alterations in the composition of the gut microbiota have significant implications for the treatment of metabolic syndrome, a cluster of conditions—including obesity, insulin resistance, hypertension, and dyslipidemia—that elevate the risk of cardiovascular disease and type 2 diabetes [42]. Modulating the gut microbiota offers promising potential not only for managing metabolic syndrome but also for treating a variety of other diseases. This discussion delves into the therapeutic applications of microbiota modulation, presenting specific examples and mechanisms of action.

One therapeutic approach to metabolic syndrome is the use of probiotics. Probiotics are live microorganisms that provide various health benefits when taken in appropriate doses [43]. Probiotics can regulate the composition of the gut microbiota by increasing beneficial bacteria and suppressing harmful bacteria [44]. Additionally, they improve intestinal barrier function by tightening junctions between intestinal cells, reducing permeability, and lowering endotoxemia and systemic inflammation [45]. Furthermore, probiotics exert anti-inflammatory effects by reducing inflammatory cytokines and modulating the immune response [46]. These mechanisms lead to enhanced metabolic outcomes, such as improved insulin sensitivity and a healthier lipid profile [47] Specific bacterial strains, such as Lactobacillus and Bifidobacterium, have been shown to reduce body weight and visceral fat while enhancing insulin sensitivity in individuals with metabolic syndrome [48] [49].

Another strategy is prebiotics. Prebiotics are non-digestible food components that selectively promote the growth of healthy and useful gut microorganisms [50]. Prebiotics stimulate the growth of beneficial bacteria such as bifidobacteria and lactic acid bacteria [51]. Through fermentation, prebiotics increase the production of short-chain fatty acids (SCFAs), which have been shown to improve glucose and lipid metabolism [52]. They also influence the secretion of hormones such as glucagon-like peptide-1 (GLP-1) and peptide Y (PYY), which promote satiety and aid in weight management [53]. For example, inulin-type fructans have been associated with weight loss, improved lipid profiles, and increased insulin sensitivity in obese individuals [54]. Symbiotics, which combine probiotics and prebiotics, offer a synergistic effect by simultaneously enhancing gut microbiota composition and metabolic activity. Prebiotics serve as a substrate for probiotics, boosting their survival and efficacy [55] [56]. Symbiotics simultaneously increase beneficial bacteria and their metabolic activity and thus comprehensively regulate the gut microbiota [57]; studies have shown that synbiotic supplementation improved various metabolic parameters such as fasting blood glucose levels and inflammatory markers in type 2 diabetes patients [58].

Fecal microbiota transplantation (FMT) is the transplantation of gut microbiota from a healthy donor to a recipient to restore the composition of a healthy microbiota [59]. FMT replaces the dysbiotic microbiota with a diverse and balanced community [60]. . In cases of metabolic syndrome, FMT from lean donors has been shown to improve insulin sensitivity and positively modify gut microbiota composition, suggesting that restoring microbial diversity can favorably influence metabolic pathways [61]. This suggests that restoration of the microbiota has a positive impact on metabolic pathways and the metabolism of the host. Improved nutrition also plays an important role. Diets rich in fiber, whole grains, fruits, and vegetables promote healthy gut microbiota by increasing microbial diversity and beneficial species [62]. High-fiber diets promote SCFA production and improve metabolic health [63]. The Mediterranean diet, for instance, has been linked to a reduction in components of metabolic syndrome and an increase in gut microbiota diversity, further underscoring the connection between diet and gut [64].

The therapeutic effects of altering the gut microbiota are mediated by several mechanisms. Modulation of the immune response by the gut microbiota alters the balance of the immune system and suppresses inflammation and autoimmunity [65]. Improving gut barrier function increases mucosal integrity, prevents the transfer of toxic substances, and reduces systemic inflammation [66]. The gut microbiota also influences host metabolism by regulating energy production, lipid metabolism, and glucose homeostasis It influences host metabolism by regulating energy production, lipid metabolism, and glucose homeostasis [67]. The production of bioactive compounds, such as SCFAs, neurotransmitters, and vitamins, also plays a critical role, impacting distant organs and systems [68]. The gut-brain axis is another crucial pathway through which the gut microbiota influences the central nervous system, affecting mood, cognition, and the body's response to stress [69].

In conclusion, altering the gut microbiota composition holds great therapeutic potential for managing metabolic syndrome and a variety of other health conditions. Interventions such as probiotics, prebiotics, symbiotics, FMT, and dietary modifications have shown promise in improving metabolic health, modulating immune function, and influencing the gut-brain axis. Continued research into these mechanisms will pave the way for personalized medicine, enabling targeted therapies that harness the power of a healthy gut microbiota to improve health outcomes. The below illustration depicts the use of gut microbiota in various other conditions.

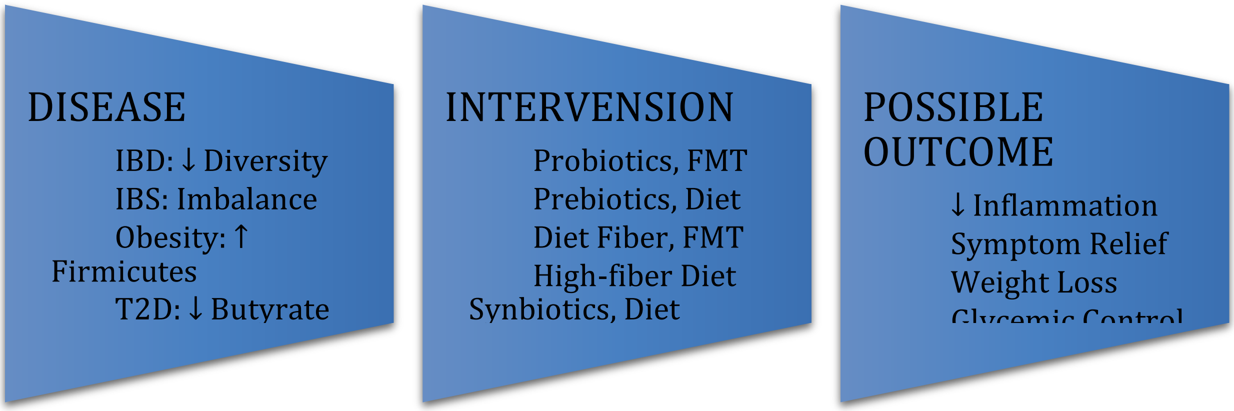

Figure 4: Depicts the various applications of gut microbiota.

Discussion

Metabolic syndrome is a complex interplay of risk factors, including central adiposity, hypertension, insulin resistance, elevated triglycerides, and low HDL cholesterol, all of which heighten the risk of type 2 diabetes and cardiovascular disease. At its core, insulin resistance disrupts glucose uptake, while excess visceral fat acts as an endocrine organ, releasing inflammatory adipokines that further impair metabolic balance. This chronic low-grade inflammation, marked by elevated CRP and IL-6, contributes to endothelial dysfunction and atherosclerosis, exacerbating cardiovascular risk. Genetic factors, such as variations in NOD2 and FUT2, influence gut microbiota composition, but environmental factors like poor diet and inactivity significantly worsen metabolic outcomes, highlighting a blend of inherited and lifestyle-driven influences.

The gut microbiota plays a vital role in metabolic health by strengthening gut barrier function, modulating immune responses, and producing beneficial metabolites like short-chain fatty acids (SCFAs) that enhance glucose and lipid metabolism. Therapeutic strategies, including probiotics, prebiotics, and dietary interventions like the Mediterranean diet, have shown promise in improving metabolic parameters by restoring microbial balance. Fecal Microbiota Transplantation (FMT) is a novel approach that has demonstrated potential in re-establishing healthy gut flora and improving insulin sensitivity. As research advances, personalized medicine that leverages genetic and microbiome insights could pave the way for tailored interventions to manage and mitigate metabolic syndrome effectively.

Research gap and future direction: While significant progress has been made in understanding metabolic syndrome and the gut microbiota's role, crucial research gaps persist, particularly in identifying the exact mechanisms linking microbiota composition to metabolic outcomes. The causative pathways remain unclear, and individual variability in responses to probiotics, prebiotics, and dietary interventions complicates treatment efficacy. Future research should prioritize personalized approaches, incorporating genetic, microbial, and environmental factors to tailor therapies more effectively. Additionally, longitudinal studies are needed to evaluate the long-term impacts of microbiota-based interventions, while exploration of the gut-brain axis and early-life influences, like maternal diet and antibiotic exposure, may unlock new therapeutic opportunities.

Conclusion

In conclusion, the gut microbiota is an important factor leading to the pathogenesis of metabolic syndrome by modulating primary processes like lipid metabolism, inflammation and insulin resistance. If composition of gut microbiota gets disturbed it can cause damage to metabolic equilibrium and lead to various disorders like cardiovascular diseases, type2 diabetes and obesity. Lifestyle, genetic factors and diet containing high fat, high sugar further worsens these balances. Microbiota-based therapies, including probiotics, prebiotics, and fecal microbiota transplantation (FMT) have shown promising roles in modulating microbial balance and decreasing inflammation offering potential interventions for managing metabolic syndrome. The complex nature of host and microbiome interaction signifies the requirement for a personalized strategy that will treat and prevent metabolic syndrome. Further studies are needed in order to gain a clear understanding of these interactions so that it can enhance clinical application of interventions which are microbiome centered, thereby advancing more effective and personalized treatment strategies for metabolic syndrome.

References

1. Alberti KGMM, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. Lancet. 2005; 366(9491):1059–1062. Doi: 10.1016/S0140-6736(05)67402-8 https://doi. org/10.1016/S0140-6736(05)67402-8
2. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes. 1988; 37(12):1595–1607. doi: 10.2337/diab.37.12.1595https://doi.org/10.2337/diab.37.12.1595
3. Després JP, Lemieux I. Abdominal obesity and metabolic syndrome. Nature. 2006; 444(7121): 881–887. Doi: 10.1038/nature05488 https://doi.org/10.1038/nature05488
4. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation, and immunity. Nature Reviews Immunology. 2006; 6(10):772–783. Doi: 10.1038/nri1937 https://doi.org/10.1038/nri1937
5. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006; 444(7121):860–867. Doi: 10.1038/nature05485 https://doi.org/10.1038/nature05485
6. Rausch P, Rehman A, Künzel S, Häsler R, Ott SJ, Schreiber S, et al. Colonic mucosa-associated microbiota is influenced by an interaction of Crohn's disease and FUT2 (Secretor) genotype. Proceedings of the National Academy of Sciences U.S.A. 2011; 108(47): 19030–19035. doi:10.1073/pnas.1106408108 https://doi.org/10.1073/pnas.1106408108
7. Franke A, McGovern DP, Barrett JC, Wang K, Radford-Smith GL, Ahmad T, et al. Genome-wide meta-analysis increases to 71 the number of confirmed Crohn's disease susceptibility loci. Nature Genetics. 2010; 42(12):1118–1125. doi:10.1038/ng.717https://doi.org/10.1038/ng.717
8. Grundy SM. Metabolic syndrome pandemic. Arteriosclerosis, Thrombosis, and Vascular Biology. 2008; 28(4):629–636. Doi: 10.1161/atvbaha.107.151092 https://doi.org/10.1161/atvbaha.107.151092
9. Ginsberg HN. Insulin resistance and cardiovascular disease. The Journal of Clinical Investigation. 2000; 106(4):453–458. doi:10.1172/JCI10762 https://doi.org/10.1172/JCI10762
10. DeFronzo RA. Dysfunctional fat cells, lipotoxicity and type 2 diabetes. International Journal of Clinical Practice Supplement. 2004; (143):9–21. doi:10.1111/j.1368-504X.2004.00393.xhttps://doi.org/10.1111/j.1368-504X.2004.00389.x
11. Bonetti PO, Lerman LO, Lerman A. Endothelial dysfunction: a marker of atherosclerotic risk. Arteriosclerosis, Thrombosis, and Vascular Biology. 2003; 23(2):168–175. doi:10.1161/01.ATV.0000051384.43104.FChttps://doi.org/10.1161/01.atv.0000051384.43104.FC
12. Hall JE. The kidney, hypertension, and obesity. Hypertension. 2003; 41(3):625–633. Doi: 10. 1161/01.HYP.0000052314.95497.78 https://doi.org/10.1161/01.HYP.0000052314.95497.78
13. Alessi MC, Juhan-Vague I. PAI-1 and the metabolic syndrome: links, causes, and consequences. Arteriosclerosis, Thrombosis, and Vascular Biology. 2008; 28(1):12–18. doi:10.1002/cphy.c160004

14. Anderson RC, Cookson AL, McNabb WC, Kelly WJ, Roy NC. Lactobacillus plantarum DSM 2648 is a potential probiotic that enhances intestinal barrier function. FEMS Microbiology Letters. 2010; 309(2):184–192. Doi: 10.1111/j.1574-6968.2010.02038.x https://doi.org/10.1111/j.1574-6968.2010.02038.x
15. Anderson RC, Cookson AL, McNabb WC, Kelly WJ, Roy NC. Lactobacillus plantarum DSM 2648 is a potential probiotic that enhances intestinal barrier function. FEMS Microbiology Letters. 2010; 309(2):184–192. doi:10.1111/j.1574-6968.2010.02038.x https://doi.org/10.1111/j.1574-6968.2010.02038.x
16. Round JL, Mazmanian SK. Inducible Foxp3+ regulatory T-cell development by a commensal bacterium of the intestinal microbiota. Proceedings of the National Academy of Sciences U.S.A. 2010; 107(27):12204–12209. doi:10.1073/pnas.0909122107https://doi.org/10.1073/pnas.0909122107
17. Yadav H, Lee JH, Lloyd J, Walter P, Rane SG. Beneficial metabolic effects of a probiotic via butyrate-induced GLP-1 hormone secretion. Journal of Biological Chemistry. 2013; 288(35):25088–25097. doi:10.1074/jbc.M113.452516https://doi.org/10.1074/jbc.M113.452516
18. Tolhurst G, Heffron H, Lam YS, Parker HE, Habib AM, Diakogiannaki E, et al. Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. Diabetes. 2012; 61(2):364–371. Doi: 10.2337/db11-1019 https://doi.org/10.2337/db11-1019
19. Roberfroid M, Gibson GR, Hoyles L, McCartney AL, Rastall RA, Rowland I, et al. Prebiotic effects: metabolic and health benefits. British Journal of Nutrition. 2010; 104(Suppl 2)–S63. Doi: 10.1017/S0007114510003363 https://doi.org/10.1017/S0007114510003363
20. Karczewski J, Troost FJ, Konings I, Dekker J, Kleerebezem M, Brummer RJ, et al. Regulation of human epithelial tight junction proteins by Lactobacillus plantarum in vivo and protective effects on the epithelial barrier. American Journal of Physiology-Gastrointestinal and Liver Physiology. 2010; 298(6)–G859. Doi: 10. 1152/ajpgi.00327.2009 https://doi.org/10.1152/ajpgi.00327.2009
21. Canfora EE, Jocken JW, Blaak EE. Short-chain fatty acids in control of body weight and insulin sensitivity. Nature Reviews Endocrinology. 2015; 11(10):577–591. doi:10.1038/nrendo.2015.128 https://doi.org/10.1038/ nrendo.2015.128
22. Gao Z, Yin J, Zhang J, Ward RE, Martin RJ, Lefevre M, et al. Butyrate improves insulin sensitivity and increases energy expenditure in mice. Diabetes. 2009; 58(7):1509–1517. Doi: 10.2337/db08-1637 https://doi.org/10.2337/db08-1637
23. Li T, Chiang JY. Bile acid signaling in metabolic disease and drug therapy. Pharmacological Reviews. 2014; 66(4):948–983. doi:10.1124/pr.113.008201https://doi.org/10.1124/pr.113.008201
24. [24] Koeth RA, Wang Z, Levison BS, Buffa JA, Org E, Sheehy BT, et al. Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. Nature Medicine. 2013; 19(5):576–585. doi:10.1038/nm.3145 https://doi.org/10.1038/nm.3145
25. Qin J, Li Y, Cai Z, Li S, Zhu J, Zhang F, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. Nature. 2012; 490(7418):55–60. Doi: 10.1038/nature11450 https://doi.org/10.1038/nature11450
26. Kwon HK, Lee CG, So JS, Chae CS, Hwang JS, Sahoo A, et al. Generation of regulatory dendritic cells and CD4+Foxp3+ T cells by probiotics administration suppresses immune disorders. Proceedings of the National Academy of Sciences U.S.A. 2010; 107(5):2159–2164. doi:10.1073/pnas.0904055107 https://doi.org/10.1073/pnas.0904055107
27. Slavin J. Fiber and prebiotics: mechanisms and health benefits. Nutrients. 2013; 5(4):1417–1435. Doi: 10.3390/nu5041417 https://doi.org/10.3390/nu5041417
28. Cardona F, Andrés-Lacueva C, Tulipani S, Tinahones FJ, Queipo-Ortuño MI. Benefits of polyphenols on gut microbiota and implications in human health. Journal of Nutritional Biochemistry. 2013; 24(8):1415–1422. Doi: 10. 1016/j.jnutbio.2013.05.001 https://doi.org/10.1016/j.jnutbio.2013.05.001
29. Larsen N, Vogensen FK, van den Berg FWJ, Nielsen DS, Andreasen AS, Pedersen BK, et al. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. PLoS One. 2010; 5(2). doi:10.1371/journal.pone.0009085https://doi.org/10.1371/journal.pone.0009085
30. Vrieze A, Van Nood E, Holleman F, Salojärvi J, Kootte RS, Bartelsman JFWM, et al. Transfer of intestinal microbiota from lean donors increases insulin sensitivity in individuals with metabolic syndrome. Gastroenterology. 2012; 143(4):913–916.e7. doi:10.1053/j.gastro.2012.06.031https://doi.org/10.1053/j.gastro.2012.06.031
31. Bäckhed F, Ding H, Wang T, Hooper LV, Koh GY, Nagy A, et al. The gut microbiota as an environmental factor that regulates fat storage. Proceedings of the National Academy of Sciences U.S.A. 2004; 101(44):15718–15723. doi:10.1073/pnas.0407076101https://doi.org/10.1073/pnas.0407076101

32. Turnbaugh PJ, Bäckhed F, Fulton L, Gordon JI. Diet-induced obesity is linked to marked but reversible alterations in the mouse distal gut microbiome. Cell Host & Microbe. 2008; 3(4):213–223. doi:10.1016/j.chom.2008.02.0 15https://doi.org/10.1016/j.chom.2008.02.015
33. Cani PD, Amar J, Iglesias MA, Poggi M, Knauf C, Bastelica D, et al. Metabolic endotoxemia initiates obesity and insulin resistance. Diabetes. 2007; 56(7):1761–1772. Doi: 10.2337/db06-1491 https://doi.org/10.2337/db 06-1491
34. Everard A, Lazarevic V, Derrien M, Girard M, Muccioli GG, Neyrinck AM, et al. Responses of gut microbiota and glucose and lipid metabolism to prebiotics in genetically obese and diet-induced leptin-resistant mice. Diabetes. 2011; 60(11):2775–2786. Doi: 10.2337/db11-0227 https://doi.org/10.2337/db11-0227
35. Goodrich JK, Waters JL, Poole AC, Sutter JL, Koren O, Blekhman R, et al. Human genetics shape the gut microbiome. Cell. 2014; 159(4):789–799. doi:10.1016/j.cell.2014.09.0 53 https://doi.org/10.1016/j.cell.2014.09.053
36. Turpin W, Espin-Garcia O, Xu W, Sargent M, Medina S, Haritunians T, et al. Association of host genome with intestinal microbial composition in a large healthy cohort. Nat Genet. 2016 Nov; 48(11):1413-1417. DOI: 10.1038/ ng.3693. https://doi.org/10.1038/ng.3693
37. Rausch P, Rehman A, Künzel S, Häsler R, Ott SJ, Schreiber S, et al. Colonic mucosa-associated microbiota is influenced by an interaction of Crohn disease and FUT2 (Secretor) genotype. Proc Natl Acad Sci U S A. 2011 Nov 22; 108(47):19030-19035. DOI: 10.1073/ pnas.1106408108https://doi.org/10.1073/pnas. 1106408108
38. Blekhman R, Goodrich JK, Huang K, Sun Q, Bukowski R, Bell JT, et al. Host genetic variation impacts microbiome composition across human body sites. Genome Biol. 2015 Apr 28; 16:191. DOI: 10.1186/s13059-015-0759-1. Htt ps://doi. org/10.1186/s13059-015-0759-1
39. Zajac, D.J., Green, S.J., Johnson, L.A. et al. APOE genetics influence murine gut microbiome. Sci Rep 12, 1906 (2022). https://doi. org/10.1038/s41598-022-05763-1
40. Qin J, Li Y, Cai Z, Li S, Zhu J, Zhang F, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. Nature. 2012 Oct 4; 490(7418):55-60. DOI: 10.1038/ nature11450 https://doi.org/10.1038/nature11450
41. Zeevi D, Korem T, Zmora N, Israeli D, Rothschild D, Weinberger A, et al. Personalized nutrition by prediction of glycemic responses. Cell. 2015 Nov 19; 163(5):1079-1094. DOI: 10.1016/j.cell.2015.11.001. https://doi.org/10.1 016/j.cell.2015.11.001
42. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. Lancet. 2005 Sep 24-30; 366(9491):1059-1062. DOI: 10.1016/S0140-6736(05)67402-8 https:// doi.org/10.1016/S0140-6736 (05)67402-8
43. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol. 2014 Aug; 11(8):506-514. DOI: 10.1038/ nrgastro.2014.66 https://doi.org/10.1038/nrgast ro.2014.66
44. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. Nutrients. 2017 Sep 15; 9(9):1021. DOI: 10.33 90/nu9091021.https://doi.org/10.3390/nu90910 21
45. Liotti, F., Marotta, M., Sorriento, D., Pagliuca, C., Caturano, V., Mantova, G., Scaglione, E., Salvatore, P., Melillo, R.M. and Prevete, N. (2022), Probiotic Lactobacillus rhamnosus GG (LGG) restrains the angiogenic potential of colorectal carcinoma cells by activating a pro-resolving program via formyl peptide receptor 1. Mol Oncol, 16: 2959-2980. https://doi.org/ 10.1002/1878-0261.13280
46. Plaza-Díaz J, Ruiz-Ojeda FJ, Vilchez-Padial LM, Gil A. Evidence of the anti-inflammatory effects of probiotics and synbiotics in intestinal chronic diseases. Nutrients. 2017 Jun 2; 9(6): 555. DOI: 10.3390/nu9060555. https://doi. org/10.3390/nu9060555
47. Khalili L, Alipour B, Asghari Jafarabadi M, Faraji I, Hassanalilou T. The effects of synbiotic supplementation on metabolic status in diabetic patients with coronary heart disease: A randomized, double-blind, placebo-controlled trial. Probiotics Antimicrob Proteins. 2019 Dec; 11(4):1249-1256. DOI: 10.1007/s12602-018-9500-3. https://doi.org/10.1007/s12602-01 8-9500-3
48. Agerholm-Larsen, L., Bell, M., Grunwald, G. et al. The effect of a probiotic milk product on plasma cholesterol: a meta-analysis of short-term intervention studies. Eur J Clin Nutr 54, 856–860 (2000). https://doi.org/10.1038/sj.ej cn.1601104
49. Maldonado Galdeano C, Cazorla SI, Lemme Dumit JM, Vélez E, Perdigón G. Beneficial effects of probiotic consumption on the immune system. Ann Nutr Metab. 2019; 74(2):115-124. DOI: 10.1159/000496426. https://doi.org/10. 1159/000496426
50. Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition

and scope of prebiotics. Nat Rev Gastroenterol Hepatol. 2017 Aug; 14(8):491-502. DOI: 10.1038/nrgastro.2017.75. https://doi.org/10.1038/nrgastro.2017.75
51. Roberfroid MB. Inulin-type fructans: Functional food ingredients. J Nutr. 2007 Nov; 137(11 Suppl):2493S-2502S. DOI: 10.1093/jn/137.11.2493S.https://doi.org/10.1093/jn/137.11.2493S
52. Canfora EE, Jocken JW, Blaak EE. Short-chain fatty acids in control of body weight and insulin sensitivity. Nat Rev Endocrinol. 2015 Oct; 11(10):577-591. DOI: 10.1038/nrendo.2015.128.https://doi.org/10.1038/nrendo.2015.128
53. Delzenne NM, Neyrinck AM, Cani PD. Gut microbiota and metabolic disorders: How prebiotic can work? Br J Nutr. 2013 Jun; 109 Suppl 2. DOI: 10.1017/S0007114512004047. https://doi.org/10.1017/S000711451200404
54. Liber A, Szajewska H. Effect of oligofructose supplementation on body weight in overweight and obese children: a randomised, double-blind, placebo-controlled trial. British Journal of Nutrition. 2014; 112(12):2068-2074. Doi: 10.1017/S000711451400311
55. Kolida S, Gibson GR. Synbiotics in health and disease. Annu Rev Food Sci Technol. 2011 Apr 10; 2:373-393. DOI: 10.1146/annurev-food-022510-133739. https://doi.org/10.1146/annurev-food-022510-133739
56. Swanson KS, Gibson GR, Hutkins R, Reimer RA, Reid G, Verbeke K, et al. The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of synbiotics. Nat Rev Gastroenterol Hepatol. 2020 Nov; 17(11):687-701. DOI: 10.1038/s41575-020-0344-2. https://doi.org/10.1038/s41575-020-0344-2
57. Pandey KR, Naik SR, Vakil BV. Probiotics, prebiotics and synbiotics—a review. J Food Sci Technol. 2015 Dec; 52(12):7577-7587. DOI: 10.1007/s13197-015-1921-1. https://doi.org/10.1007/s13197-015-1921-1
58. Soleimani, A., Motamedzadeh, A., Zarrati Mojarrad, M. et al. The Effects of Synbiotic Supplementation on Metabolic Status in Diabetic Patients Undergoing Hemodialysis: a Randomized, Double-Blinded, Placebo-Controlled Trial. Probiotics & Antimicro. Prot. 11, 1248–1256 (2019). https://doi.org/10.1007/s12602-018-9499-3
59. Smits LP, Bouter KE, de Vos WM, Borody TJ, Nieuwdorp M. Therapeutic potential of fecal microbiota transplantation. Gastroenterology. 2013 Nov; 145(5):946-953. DOI: 10.1053/j.gastro.2013.08.058.https://doi.org/10.1053/j.gastro.2013.08.058
60. Weingarden AR, Vaughn BP. Intestinal microbiota, fecal microbiota transplantation, and inflammatory bowel disease. Gut Microbes. 2017 May 4; 8(3):238-252. DOI: 10.1080/19490976.2017.1290757.https://doi.org/10.1080/19490976.2017.1290757
61. Vrieze A, Van Nood E, Holleman F, Salojärvi J, Kootte RS, Bartelsman JF, et al. Transfer of intestinal microbiota from lean donors increases insulin sensitivity in individuals with metabolic syndrome. Gastroenterology. 2012 Oct; 143(4):913-916.e7. DOI: 10.1053/j.gastro.2012.06.031.https://doi.org/10.1053/j.gastro.2012.06.031
62. Tilg H, Moschen AR. Food, immunity, and the microbiome. Gastroenterology. 2015 May; 148(6):1107-1119. DOI: 10.1053/j.gastro.2015.01.032.https://doi.org/10.1053/j.gastro.2015.01.032
63. Holscher HD. Dietary fiber and prebiotics and the gastrointestinal microbiota. Gut Microbes. 2017 Mar 4; 8(2):172-184. DOI: 10.1080/19490976.2017.1290756.https://doi.org/10.1080/19490976.2017.1290756
64. De Filippis F, Pellegrini N, Vannini L, Jeffery IB, La Storia A, Laghi L, et al. High-level adherence to a Mediterranean diet beneficially impacts the gut microbiota and associated metabolome. Gut. 2016 Nov; 65(11):1812-1821. DOI: 10.1136/gutjnl-2015-309957. https://doi.org/10.1136/gutjnl-2015-309957
65. Round JL, Mazmanian SK. The gut microbiota shapes intestinal immune responses during health and disease. Nat Rev Immunol. 2009 May; 9(5):313-323. DOI: 10.1038/nri2515. https://doi.org/10.1038/nri2515
66. Hooper LV, Littman DR, Macpherson AJ. Interactions between the microbiota and the immune system. Science. 2012 Jun 8; 336(6086):1268-1273. DOI: 10.1126/science.1223490.https://doi.org/10.1126/science.1223490
67. Bäckhed F, Ding H, Wang T, Hooper LV, Koh GY, Nagy A, et al. The gut microbiota as an environmental factor that regulates fat storage. Proc Natl Acad Sci U S A. 2004 Nov 2; 101(44):15718-15723. DOI: 10.1073/pnas.0407076101.https://doi.org/10.1073/pnas.0407076101
68. LeBlanc JG, Milani C, de Giori GS, Sesma F, van Sinderen D, Ventura M. Bacteria as vitamin suppliers to their host: A gut microbiota perspective. Curr Opin Biotechnol. 2013 Apr; 24(2):160-168. DOI: 10.1016/j.copbio.2012.08.005.https://doi.org/10.1016/j.copbio.2012.08.005
69. Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: Interactions between enteric microbiota, central and enteric nervous systems. Ann Gastroenterol. 2015 Apr-Jun; 28(2):203-209. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4367209/