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Review Article

Review of the Gut Microbiota Dynamics in Type-2 Diabetes Mellitus (T2DM): A Focus on Human-Based Studies

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ABSTRACT

The gut microbiome contains a complex microbial community within the gastrointestinal tract (GIT), which benefits our health. Yet, studies have shown that persons with Type-2 diabetes mellitus (T2DM), compared to healthy controls, possess gut microbiota profile differences. Therefore, this study reviewed gut microbiome dynamics in the onset and progression of T2DM, starting from insulin resistance to how its modulation by drugs, food, and pre/postbiotics influences insulin resistance. First, an in-depth inquiry was executed on Google Scholar and PUBMED using the following keywords: Biomarker AND "Therapeutic targets" AND "Gut Microbiota" OR "Gut Microbiome" AND "Type 2 diabetes" NOT Cancer, and 755 papers were retrieved. Next, two independent authors screened the papers by title and abstract, leaving 64 articles for this study. Investigations revealed that some bacterial diversities occurred before the pathogenesis associated with T2DM. According to frequently published data, T2DM was adversely related with the genera *Bifidobacterium*, *Bacteroides*, *Faecalibacterium*, *Akkermansia*, and *Roseburia*, while it was positively associated with the genera *Ruminococcus*, *Fusobacterium*, and *Blautia*. Insulin sensitivity in T2DM was also improved with butyrate-producing short-chain fatty acid bacteria. Notably, patients with T2DM were mostly identified by increased specific infectious microbes, such as *Clostridium spp*, whereas the majority of control samples were enriched in butyrate-producing bacteria and *Lactobacillus spp*. In summary, we observed several inconsistencies in T2DM disease-linked organism(s) and knowledge gaps due to inadequate data. Hence, future studies must prove the relationships between dysbiosis and the onset/progression of T2DM to provide useful information that may guide better management of T2DM.

Keywords: Type 2 Diabetes Mellitus, Gut Microbiota, Short Chain Fatty Acids, Biomarkers, Butyrate-producing bacteria

Introduction

Diabetes is a group of diseases resulting in high sugar concentrations in the blood (hyperglycemia). Although the pathogenesis of diabetes is complex and unclear, accumulated evidence has implicated obesity, infection, genetics, immune disorders, and diet in diabetes pathogenesis.[1,2] Type 1 (T1) and Type 2 (T2) are the two major types of diabetes,[3] with T2 (diabetes mellitus) representing approximately 90% of all diabetes occurrences and is caused by a host's insufficient insulin secretion or rejection of the insulin produced. Consequently, it can result in severe and persistent abnormalities, ranging from blindness, cardiovascular disease, renal failure, loss of vital organs and early mortality. The international Diabetes Federation, reported that there are 463 million adult diabetics worldwide, and by 2045, that number is expected to rise to 700 million.[4] Dietary regulations, moderate exercise, antidiabetic medications, and insulin injections are the current standard measures for diabetes prevention and treatment.[5]

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Regrettably, however, neither of these routines has completely prevented the development of diabetes and its associated issues, causing the emergence of research on gut microbiome impacts to receive much attention over the last decade. Its function as a therapeutic measure for treating diabetes would be better understood if the gut microbiota relationship and influence were to be discovered.

The phrase "gut microbiota" refers to the microbial ecosystem of the GIT colonized by bacteria, archaea, and eukaryotes. They function to maintain a healthy state through energy recovery from dietary fiber metabolism, host protection from pathogenic invasion, as well as immunity regulation. The gut flora are specific in pathogen colonization, such that they contend for beneficial compounds/adhesion sites and generation of bioactive metabolites.[6,7] In turn, the gut microbiota induces the host's Paneth cells to generate antimicrobial properties such as adenosine monophosphates (AMPs), C-type lectins, cathelicidins, and pro-defensins *via* a PRR-mediated mechanism,[8] unfolding through all life stages with a significant role in propagating disease states or maintaining wellness.

The number of microbes in the intestinal tract is estimated to exceed 1014, and for many decades, the gut microbiota and its hosts have evolved together to create a complex and advantageous interaction,[9,10] containing roughly 100 times as much genetic information (microbiome) as the human genome and ten times as many bacterial cells as human cells.[6,9] As an outcome, the microbiota supports the host in differing ways, including enhancing gut health,[11] obtaining energy,[12] guarding against infections,[7] and modulating host defenses.[13] Unfortunately, imbalances of the gut microbiota (dysbiosis) have been identified: external factors that interfere with a host's metabolism, resulting in inflammatory bowel disorders (IBD), irritable bowel syndrome, and obesity, which are all manifestations of metabolic

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illness.[14-16] In addition, even though the diverse etiology of metabolic and gastrointestinal disorders has been linked to microbial species dysbiosis, the theory underlying its mode of action is poorly understood. Consequently, significant attempts have been made to characterize the components of a functional human microflora and its potential.[17-19] These investigations are then followed by comparable characterizations of the gut microbiota in certain illnesses like diabetes, which potentially leads to microbiome originated drugs addressing health and wellness.

Based on some microbiome-based studies that controlled inflammation, immune function, and metabolism, it has been established that bacterial metabolites of the gut microbiota influence the onset and advancement of T2DM. Similar to this, short-chain fatty acids (SCFA), imidazole propionate, lipopolysaccharide (LPS), secondary bile acid, and branched-chain amino acids (BCAA) have been identified in studies as significant molecules accounting for the onset and progression of T2DM. Numerous research findings have also looked into the contributions of gut microbiota in T2DM, specifically butyrate-producing bacteria.[20,21] Notably, however, a wide range of disparities in current data exist that have created difficulties in identifying microbiota targets or centers of focus. We have tagged these disparities as 'the gut microbiome dynamics.' Thus, this review attempts to present these dynamics to help researchers build a focus on the microbiome community as a target in further gut-microbiome T2DM therapeutics research.

Materials and Methods

We carried out a thorough, systematic literature search using different arrangements of the following phrases: Biomarker AND "Therapeutic targets" AND "Gut microbiome" OR "Gut microbiota" AND "Type 2 diabetes" NOT cancer, in the two biggest databases for health-related information, PUBMED and Google Scholar, up until January 2022. A total number of 755 publications were obtained, and the results were. The papers were then scrutinized by two separate authors by title and abstract, followed by full-text screening. Discussion with an impartial reviewer was used to settle disagreements based on opinions. We chose peer-reviewed/original publications that describe the isolation of particular gut microorganisms and how those microbes contribute to the development and progression of type 2 diabetes, starting with insulin resistance and how that is influenced by medications, food, and pre/postbiotics.

Also, only those papers that reported human-based studies from a wide range of populations, and considered T2DM as the subject with healthy adults as control, analyzing fecal gut microbiota, were included. We excluded review articles, articles that used animals, articles reporting any other microbiota asides from those in the gut, those that reported other diseases not involving T2DM, case studies, short communications, and articles without abstracts or incomplete text. Studies that did not previously isolate or reference isolated microbes in their study/microbe data sources, continuing clinical *in vivo* or *in vitro* studies, review articles, non-English literature or protocol papers, other types of diabetes mellitus or metabolic diseases other than T2DM, and research papers that did not relate gut microbiota in T2DM to that of healthy controls were also excluded. Subsequently, the following information was obtained from included research and used to compile a predesigned data collection table: author/publication year, microbes isolated, and significant findings/proposed mechanism.

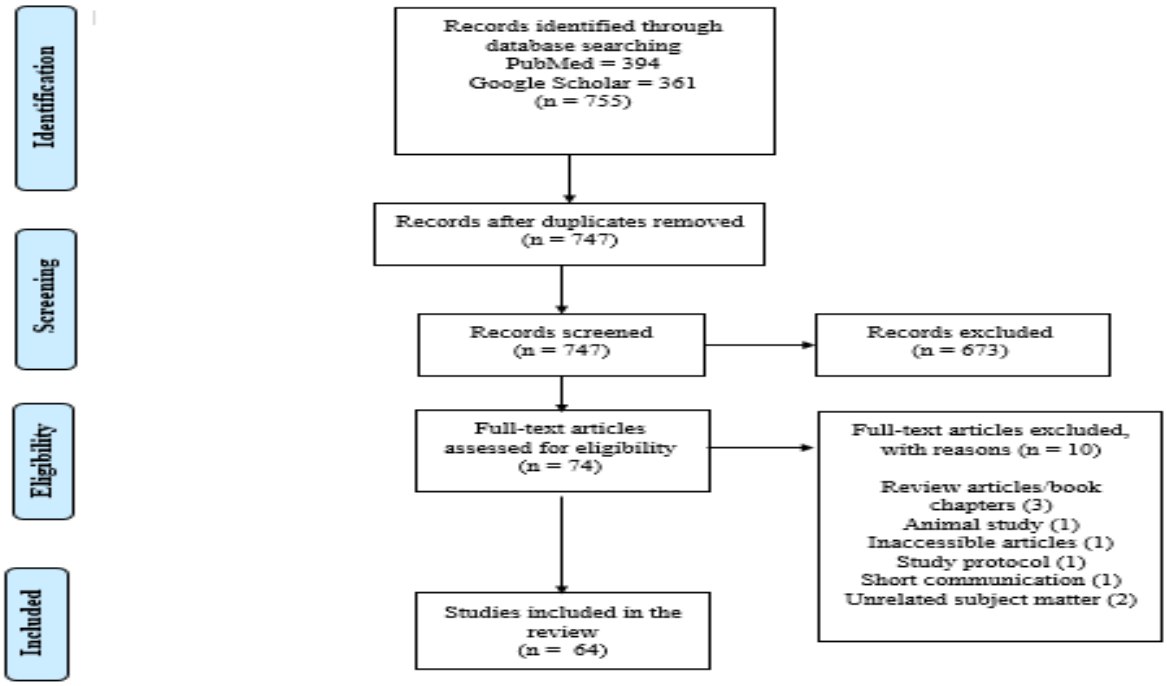

Figure 1: Flow chart showing the review progression of this study

Results and Discussion

Eight of the articles were withdrawn from the 755 articles obtained due to matching copies as shown in Figure. 1. A sum of 673 papers was further eliminated based on the following reasons: 30 had evaluated other pathologies asides from T2DM, 502 were review papers, 50 were animal studies, 5 were non-English papers, 7 were inaccessible articles, 1 was a study protocol, and 10 were short communications, 30 addressed other microbiota communities asides that of the gut. Other papers either did not compare controls with T2DM patients or measured the T2DM-causing gut microbiome communities with other parameters like environmental factors (n = 48). Altogether, this study reviewed 64 papers from 22 countries (China, Cameron, Egypt, Japan, Canada, South Indian, Pakistani, Netherlands, Germany, Caucasian, Dutch, Korea, Denmark, United Arab Emirates, Sweden, Italy, United Kingdom, Australia, Finland, Indonesia, United States of America,

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Philippines). Furthermore, while all the selected articles described in Fig. 1 were *in silico* studies, others were conducted in combination with *in vitro* approaches, specifically through 16S rRNA sequencing by analyzing V_3–V_4 hyper variable regions. Alternatively, Table 1 presents the patient cohorts reviewed and the significant gut microbiota identified or understudied. All studies ranged from comparative to case-control, and pilot studies involving T2DM patients were included. At the same time, the control groups comprised hale and hearty people or individuals with standard glucose-tolerance levels. Participants were of both genders, ranging in age from 19 to 70, with females outnumbering males in both groups, and we majorly probed variances in gut microbiota conformations between healthy controls and T2DM patients in these research findings.

Highlighting that gut microbiota configurations were determined using differing methodologies was also crucial (Table 1). Noteworthily, some studies used untargeted approaches, like metagenomic next-generation sequencing (shotgun metagenomic sequencing), and targeted approaches, comprising 16S rRNA sequencing (Illumina MiSeq), polymerase chain reaction (PCR), pyrosequencing, quantitative real-time PCR (qPCR), and reverse transcription-qPCR. The ultimate result was the distinct conformation of the gut microbiome in the understudied communities. Also, our investigations revealed *Lactobacillus* as one of the most prominent genera that constantly represented a clear significance ($p < 0.05$) in T2DM patient's gut, followed by *Roseburia* and *Faecalibacterium*, which were augmented in the controls of two or more investigations; however, *Bifidobacterium* was inconsistent in some cases.

Gut microbiota dynamics in T2DM and controls

The advancement of microbial analysis tools has encouraged opportunities to examine gut microbiota's involvement in Type 2 diabetes mellitus pathogenesis. Based on this review, although total microbial populations and gene quantities were comparable in patients with type 2 diabetes control subjects, T2DM patients' bacterial diversity decreased dramatically. Gut microbiotas belonged to 4 prominent phyla: Proteobacteria, Firmicutes, Actinobacteria, and Bacteroidetes, with Firmicutes constituting the largest significant part of the gut microbiota under healthy physiological circumstances, followed by Actinobacteria, Bacteroidetes, and Proteobacteria. Additionally, we observed that Fusobacteria and Verrucomicrobia were two minor but important phyla.[3,21-40] On the basis of phylum distribution, however, patients with/without T2DM exhibited conflicting microbiota findings, including increased opportunistic pathogens and decreased butyrate-producing microbes (Table 1). While we observed a rise in Lactobacillus, Akkermansia was reduced in T2DM patients but significantly high in pre-diabetic patients. Also, although depletion in Clostridium species was observed, increased levels in Ruminococcus and Streptococcus were reported.

Our investigations also showed that participants with T2DM had a much corresponding reduction in Firmicute abundances, compared to a considerably elevated percentage of Proteobacteria and Bacteroidetes. For instance, after an oral glucose load, the Bacteroidetes:Firmicutes (B/F) ratio was linked to higher plasma glycemic index levels.[27,37,41,42] Conversely, while other investigations reported high levels of Proteobacteria and Firmicutes, Bacteroidetes were much lower, enhancing the F/B ratio in T2D patients compared than the non-diabetic controls. Investigations further compared problematic and uncomplicated T2DM cohorts with high F/B proportions to elucidate the heightened F/B ratio in individuals with T2DM. Accordingly, while opportunistic pathogens such as *Clostridium symbiosum*, *Escherichia coli*, *Clostridium ramosum*, *Bacteroides caccae*, *Eggerthella lenta*, and *Bacteroides stercoris* were usually encountered in Type 2 diabetes mellitus microbiome communities,[43-50] pre-diabetes patients had comparable findings in their microbiome populations, such as a reduction in microbe population, a decline in the genera *Clostridium* and *Akkermansia*, as well as an upsurge in *Streptococcus* and *Ruminococcus* levels.[26,28,31,41,51,52] Other research teams found no significant variations in the microbiome.

The review also showed that T2D patients had a deficiency in butyrate-producing microorganisms, specifically *Clostridiales*, comprising the genera *Subdoligranulum* and *Ruminococcus*, including *Faecali prausnitzii*, *Eubacterium rectale*, *Roseburia inulinivorans*, and *Roseburia intestinalis*.[51,53-55] However, *Bacteroides*, *Prevotella*, and *Bifidobacterium* were considerably reduced in T2DM patients, with the genus Bifidobacterium providing significant health benefits: improved intestinal permeability and diminished circulating endotoxin levels/systemic inflammation. This discovery is linked to enhanced glucose-induced insulin secretion and glycemic control in the host and, thus, a decline in inflammation. In addition, significantly decreased fasting glycemic control levels and enhanced glycated hemoglobin (HbA1c) levels were related to an increase in the Lactobacillus population. Thus, we hypothesize that if a 'universal' microbial T2DM profile can be established, these microbiota indicators, combined with clinical data in a machine learning prediction method, could reliably differentiate people susceptible to T2DM. Second, if this approach works, the chosen microbiological indicators could track patients' glucose tolerance and the launch of innovative medications.

Influence of SCFA on gut microbiome dynamics between T2DM patients and controls

BCAAs, SCFAs, succinate, imidazole, and indole are all microbial metabolites synthesized from gut anaerobic fermentation. They all contribute to microbe-to-host signaling.[59] Microbial taxa, including *Prevotella*, *Coprococcus*, *Ruminococus*, *Akkermansia*, *Faecalibacterium*, *Roseburia*, *Eubacterium*, *Clostridium*, *Bacteroides*, *Streptococcus*, *Propionibacterium*, *Lactobacillus*, and *Fusobacterium* are primarily responsible for these metabolites.[3,22-40,56] Unfortunately, our investigations revealed that most of these microbial communities were reduced in patients with T2DM. In healthy patients, while SCFAs directly serve as energy sources to intestinal mucosal cells, they can be circulated systematically, providing a vital host energy source and acting in signal transduction.[57] SCFAs also significantly impact glycolysis/gluconeogenesis since they adhere to specific G-protein-coupled receptors (GPRs). The gut, fat tissue, and immune cells are the primary expression sites. As a result, the incretin glucagon-like peptide-1 (GLP-1) is released by enteroendocrine L-cells when GPR43 and GPR119 are stimulated.[58,59] Then, GLP-1 increases insulin concentration in response to blood glycemic indices, inhibits glucagon release, stimulates cell multiplication, shields β-cells from cytotoxicity, and extends gastric emptying.[60]

Additionally, SCFAs can directly affect glucose metabolic processes in the liver, diminishing gluconeogenesis and glycolysis rates, stimulating glycogenolysis, and decreasing circulating fat levels. They stimulate hunger and enhance glucose-stimulated insulin production by reducing sympathetic activity.[61] Similarly, while they stimulate the glucose type 4 transporter (GLUT4) expressions *via* AMP-activated protein kinase (AMPK), enhancing peripheral glucose uptake, SCFAs inhibit glucose breakdown in the skeleton, leading to a secondary buildup of glucose-6-phosphate (G-6-P) and enhanced glycogenolysis.[39,47,62,63] Studies have also reported that the most predominant SCFA, acetate, is absorbed by the intestinal lining, hepatically transferred past the portal vein, and then disseminated to outlying tissues for metabolization.[31,64,65] Finally, circulating acetate can pass in the activated acetyl-CoA carboxylase form, increasing neuropeptide production/blood-brain membrane and resulting in hypothalamic neuronal activity/appetite repression.[66] Since incorporating a high-fiber diet can help enhance SCFAs and, in turn, T2DM control, patients should increase its consumption, thereby enhancing the quantity of SCFA-fabricating microbiota and diminishing HbA1c levels, aided by amplified GLP-1 production.[24,46,65,67]

Glucose and insulin metabolism dynamics based on gut microbiome composition

Fermentation-based metabolite synthesis and their subsequent effects: activating inflammatory reactions, releasing cytokines, intestinal mucosa disruption, enabling toxin influx, and directing signal transductions *via* incretin release, are all pathways by which the gut microbiome can significantly change host glucose/glucose-based homeostasis. Consequently, T2D patients experience increased BCAA transport, enriched sugar transport, xenobiotic degradation/metabolism, sulfate membrane decrease, and increased methane oxidation, including

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a deterioration in flagellar assembly, bacterial chemotaxis, vitamin/cofactor metabolism, and butyrate production. The combination of these events acts to worsen the conditions of T2DM patients[24-26,43,54,63,68]

Gut microbiome medication-dependent dynamics

Individual gut microbial diversity varies greatly and is constantly influenced by endogenous and external influences.[69] Diet, disease, lifestyle, cleanliness, and drugs, as well as regional and environmental factors, can all contribute to alterations.[70,71] Antibiotics can affect the gut microbiome ecology for years after being given.[60] However, more research should assess whether a link between the two exists. A study previously reported that since antibiotics increase the risk of Type 2 diabetes mellitus in patients, those at risk became susceptible to ailments during the yearly lead-ups to diagnoses.[72] In our review, metformin was a commonly administered oral drug for individuals with Type 2 diabetes mellitus and maintained the gut microbiome's unaltered state. Nonetheless, overwhelming evidence exists that the microbiota may amplify specific effects due to these medications.[40,41,52,62,73-76] For example, the predominance of the taxa Bifidobacterium, Lactobacillus, and Akkermansia increased after using metformin. Bacteroides, Prevotella, Butyricoccus, Butyrivibrio, and Megasphaera were also among the other enriched genre relationships.[60,77] Since these microbiota communities all synthesized SCFAs, the activity of endocrine cells could become promoted by boosting SCFA synthesis, influencing bile acid (BA) turnover, diminishing endotoxemia through metformin administration, increasing bacterial communities and frequent changes in gut microbiome composition, and enhancing intestinal performance.[77]

Prebiotics, probiotics, and synbiotics in gut microbiota dynamics

Synbiotics, probiotics, and prebiotics are appealing dietary supplements capable of altering gut microbiota composition and optimizing glucose metabolism. Evidence supports the clinical use of synbiotics, probiotics, and prebiotics to improve glycemic index management in T2DM patients.[78,79] However, problems have been identified in differing study techniques (study duration, patient demographics, and supplement quantity), including hampered study comparisons, availability, small population sizes, and a conspicuous absence of microbiome data. While probiotics are living microbes that can sufficiently boost a person's health,[80] prebiotics are food nutrients like indigestible fiber or polysaccharides with the ability to enhance a host's health by facilitating the growth or activity of numerous intestinal microbiota.[81,82] Conversely, a synbiotic is a combination of living bacteria and substrates selectively used by a host's intestinal flora to boost the host's health advantage.[83] Studies have shown that probiotics increase the intestinal flora population, resulting in improved Type 2 diabetes mellitus control, intestinal architecture, lowered circulating LPS, enhanced peripheral insulin sensitivity and lowered endoplasmic reticulum (ER) stress, whereas prebiotic supplement intake leads to better blood sugar control. Regardless, variations in techniques lead to many inconsistent literature reports.[46,62,84] Although the direct contribution of their favorable effects has thus been traced directly to the modulation of the gut microbiota and complicated metabolic systems, painstaking efforts are required to create a 'standard' technique. It is also unclear if their consequences are due to gut flora alterations or the increased prevalence of fermentation substrates. Nonetheless, mounting evidence shows that supplementing with synbiotics, prebiotics, and probiotics, can contribute to glycemic regulation, indicating the prospects for using these dietary changes to manage Type 2 diabetes once this association-based technique standard has been implemented.

Table 1: Detailed information on the identified gut microbiota community investigated and their results on the onset and influence of diabetes onset

Microbe(S) Isolated	Patient Population/Country	Major Findings/Mechanism Of Action	References
Lachnospiraceae, Escherichia, Shigella, Rhodospirillales, Prevotellaceae, Alistipes, Enterorhabdus	Finland	With the gut flora as a prognostic tool, machine learning was utilized to forecast numerous metabolic consequences (continuous insulin measurements, HbA1c, and glucose) over varying periods. The METSIM cohort is particularly beneficial for researching host-microbiome connections because of its thorough clinical description and long-term study design. Also, several unique microbial biomarkers have been found as potential predictors of metabolic features linked to the prediabetic condition. Moreover, a considerable resource for additional research into the causal link between the detected biomarkers and Type 2 diabetes progression has been generated.	67
Clostridia, Negativicutes, and *Firmicutes bacteria* were the most common, followed by *Verrucomicrobia, Proteobacteria , Elusimicrobia,* and *Bacteroidetes bacteria*.	60 Pakistani adults	Firmicutes bacteria, including *Clostridia* and *Negativicutes* bacteria, were common. *Bacteroidetes, Proteobacteria, Elusimicrobia,* and *Verrucomicrobia* bacteria, on the other hand, were less common among obese diabetics. Compared to obese T2DM Indians, *Eubacterium coprostanoligenes* and *Prevotella-9* were lower in overweight Pakistani people with T2DM. The obese T2DM samples had a high percentage of Firmicutes and declined Bacteroidete abundances. Furthermore, while the abundances of *Firmicutes/Actinobacteria* had a positive link with fasting glucose levels, Bacteroidetes and Proteobacteria had negatively correlated relationships. Another noteworthy finding was the lack of *Verrucomicrobia* in these seriously overweight populations with type-2 diabetes. This phylum is thought to effectively maintain the gut's anti-inflammatory state and improve insulin sensitivity. In T2DM-obese samples from the Pakistani population, the number of gram-negative bacteria (*Allisonella* and *Dialister*) increased dramatically. These bacteria are instrumental in T2DM development	88

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		because their increasing abundance raised lipopolysaccharide (LPS) levels in these patients.	
Victivallaceae, Phascolarctobacterium, Acidaminococcus, Mogibacterium, Basidiomycota, Bacteroides, Escherichia, Akkermansia muciniphila, and other unclassified *Enterobacteriales, R uminococcus*	T2DM was investigated in 50 adults from Emirati	The four significant enterotypes first reported in westernized cohorts were found in this Emirati group. While controls/T2DM subjects had distinct microbiota community members, with non-T2DM controls having a more significant dysbiotic fraction of Bacteroides, T2DM patients had a higher proportion of the dysbiotic Bacteroides 2. In contrast to data from westernized cohorts, there was no noteworthy difference in microbial varieties of T2DM people following the correction of confounding factors. Several enterotyping approaches revealed significant changes in microbiome composition between T2D and non-T2D groups. The control group had an enrichment in *Prevotella*, whereas the T2DM cluster was enriched in the *Ruminococcus* enterotype. Distinguishable taxonomic features between non-T2DM controls and T2DM categories were also investigated while developing linear genus abundance models based on age, BMI, and disease. Six bacterial genera were substantially linked to disorders (*P*-value 0.05), with four genera increasing in the diseased T2D cluster (*Mogibacterium, Unclassified Victivallaceae, Acidaminococcus,* and *Phascolarctobacterium*). In addition, we identified a substantial link (*P*-value 0.05) between three fungal species and disease states, with two (*Malessezia firfur* and Unclassified *Davidiella*) increasing and 1 (Basidiomycota) decreasing T2DM. While a spike in Ascomycota distinguished the T2DM groups, a reduction was detected in Basidiomycota at higher taxonomic levels. In T2DM participants, metformin improved the relative predominance of *Akkermansia muciniphila, E. coli*, and other unclassified *Enterobacteriale* lineages. In the T2D category, while noticed changes from *Candida albicans* to *glabrata* were recorded as well, the T2DM group had no substantial variations in functional or taxonomic diversity, according to the findings.	[41]
	Diabetes and prediabetes were among the reasons that were considered. After taking a placebo for two weeks, MID (30–50 years) and ELD (> 70 years), Canadian individuals ingested 30 g of *MSPrebiotic*® or placebo daily for 12 weeks.	MSPrebiotic® was beneficial for stimulating Bifidobacteria development and enhancing blood glucose regulation, particularly in the ELD. MSPrebiotic® does not affect glycemic blood levels, IR, or insulin concentrations. Nevertheless, in the ELD group, in which the baseline glucose level was near the upper end of the normal range, MSPrebiotic® supplementation reduced blood glucose levels after eight weeks. MSPrebiotic® also lowered blood insulin and glucose concentrations in the ELD population, along with IR, as evaluated by the HOMA-IR/QUICKI-IR tests. While MSPrebiotic® showed a slight effect on cholesterol metabolism, more research in dyslipidemic people is necessary to thoroughly assess these measurements' effect(s). MSPrebiotic® consumption for three months did not reduce the ELD group's elevated CRP and TNF- levels, implying that formerly used therapies could be utilized in the aversion of gut barrier destruction or that these inflammatory biomarkers are based on other contributing causes like vascular comorbidities	[68] (prebiotic)
B. breve, B. longum, B. bifidum, B. pseudocatenulatum, B. animalis, B. dentium, B. xylanisolvens and *B. ovatus, B. adolescentis*	Type 2 diabetics and healthy people's sequencing data were classified into disease states using data from a metagenome-wide association analysis.	Here, 15 often-picked criteria were identified that significantly reduce the bacteria used to diagnose Type 2 diabetes, saving time and money. Furthermore, several species linked to T2D development pathways were identified during biological validation, including other species as possible biomarkers. They included *Bacteroides vulgatus*, which was primarily found in healthy subgroups. Still, in lower quantities in Patients with t2dm, *Eggerthella lenta*, which was found in lower numbers in control clusters, in comparison to patients with T2DM, *Bacteroides stercoris*, which was found in lower numbers in three healthy groups in comparison to most significant subgroup of Patients with t2dm, and *Subdoligranulum*, which	[50]

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		was found in lower numbers in three, In addition to these taxa, *B. xylanisolvens* and *B. ovatus* were discovered as two key associated with type 2 diabetes taxonomic biomarkers. Numerous *Bifidobacterium* taxa (including *B. breve*, *B. longum*, *B. bifidum*, *B. pseudocatenulatum*, *B. animalis*, *B. dentium*, *and B. adolescentis*) are also recognized as crucial characteristics in the leading hundred profiles of each analyzed four investigation approaches. Similarly, numerous Ruminococcus and Blautia species, especially *Blautia hansenii*, *Blautia sp-KLE-1732*, and *Blautia producta*, were identified as important phyla in each of the four classification techniques examined.	
Romboutsia, *Terrisporobacter*, *Peptostreptococcaceae*, *Intestinibacter bartlettii*, *Escherichia/Shigella*, *Intestinibacter bartlettii*, *Terrisporobacter*, *Peptostreptococcaceae*, *Clostridium sensustricto*	Residents of Amsterdam, the Netherlands, aged 18 to 70. Participants were chosen at random from the municipal registration center and classified as per their ethnic background: African Surinamese, South Asian Surinamese, Dutch, Turkish, Ghanaian, and Moroccan	Compared to the microbial community of African Surinamese, their microbiota communities showed more significant differences between the controls and T2D-administered metformin cases, as shown by decreased measures of the alpha diversity group and more dramatically divergent abundance in ASVs and pathways. *Romboutsia* was a valid biomarker of the connection between the gut flora and T2D-administered metformin cases in both ethnic groups. After all adjustments, Met-T2D profoundly influenced *Terrisporobacter*, *Peptostreptococcaceae*, *Intestinibacter bartlettii*, *Escherichia/Shigella*, and *Clostridium sensustricto* abundances in African Surinamese. In South-Asian Surinamese, those significant effects subsided after factoring in the effect of other T2DM pharmaceuticals. While significant ethnicity interactions with T2DM patients on metformin medications were observed for *Intestinibacter bartlettii*, *Terrisporobacter*, and *Peptostreptococcaceae*, they were not insignificant for *Escherichia/Shigella* and *Clostridium*, implying the impossibility of ruling out ASVs in South-Asian Surinamese. T2DM patients in South-Asian Surinamese on metformin, on the other hand, had a much greater prevalence of *Lachnoclostridium*. No clinically essential biological indicators were detected when comparing treatment-naive patients of both ethnicities with their controls. However, compared to their controls, significant differences in microbial community functions and compositions were reported in patients with T2D on metformin. Furthermore, in both ethnicities, ASVs with the most crucial relationship were assigned to *Romboutsia*, and it was consistently less abundant in patients with T2D on metformin than in the healthy subjects.	[74]
Faecalibacterium, *Lachnospiracea incertae sedis*, *Gemmiger*, *Roseburia*, *Coprococcus*, *Bacteroides*, *Rumi nococcus*, *Gemmiger*, *Ruminococcus*, *Bacteroides*, *Dialister*, *Escherichia*/*Shigella*, *Klebsiella*, *Streptococcus*, *Lactobacillus*, *Bacteroides*, *Dialister*, *Parabacteroides*, *Alistipes*	Of the understudied research population, 1992 subjects were used to define 20 microbial categories. Data for this research were derived from the KORA 2013/2014 study (FF4) and the subsequent follow-up polls to the initial KORA 1999/2001 study S4). KORA S4 comprised 4,261 individuals from two southern Germany adjacent counties in Augsburg (this county inclusive). However, KORA 2013/2014 included 2,279 people aged 38 to 88 who were part of the original S4 study.	*Roseburia*, *Gemmiger*, *Lachnospiracea incertae sedis*, *Coprococcus*, *Ruminococcus Bacteroides*, *and Gemmiger*, *Bacteroides*, *Ruminococcus*, to a slighter degree, showed the most robust/most prevalent connections with food. Arrhythmic OTUs were identified in significantly higher numbers in *Streptococcus*, *Escherichia/Shigella*, *Parabacteroides*, *Klebsiella*, *Lactobacillus*, *Bacteroides*, *Dialister*, and *Alistipes* than in the other bacteria. The remaining categories had a percentage of arrhythmic OTU ranging from 5% to 17%. Another subgroup showed the highest number of diabetes-specific arrhythmic OTUs among the 14 OTUs utterly arrhythmic in diabetics, accounting for 42 percent of the subgroup (all other subgroups comprised between 0 and 7 percent) Closer conformity to Mediterranean meals was also linked to a higher *Faecalibacterium* susceptibility, which was inversely interconnected to T2DM patient prevalence. After adjusting for Bonferroni's correction, *Faecalibacterium*, *Coprococcus*, *Ruminococcus*, *Bacteroides*, and *Ruminococcus* were substantially and favorably linked to whole grains, fruit, total insoluble/soluble fiber ingestion, and they were inversely correlated with cheese and red beef. These links to subdivision 14 seemed coherent, given that the *Coprococcus* taxa ferment fiber and produce butyrate, linking their incidence to health improvements.	[52]

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		Bacteroides, Parabacteroides, Bacteroides, Dialister, and Alistipes made up 74.76 percent of the genus Bacteroides, and they were all connected with BMI substantially and positively. However, subgroup 13 was no longer substantially related to dietary items or nutrients once multiple testing was adjusted, implying that another factor is the primary driver. Dietary factors did not affect *Streptococcus, Escherichia/Shigella, Klebsiella, or Lactobacillus.* However, there was a substantial positive correlation between this subgroup and prevalent T2D. Hence, it is considered that the drug metformin, which is commonly used to treat T2DM, accounts for this link.	
Collinsella, Lactobacillus, Ruminococcus, and *Streptococcus*	56 Italians	The impact of fiber-rich macrobiotic (Ma-Pi 2) over-controlled diets in supporting the recovery of gut microbiota host mutualism was investigated. This diet promoted metabolic regulation in patients with type 2 diabetes by restoring fibrolytic SCFA-producing gut bacteria constituents.	[47]
The Christensenellaceae R7 group, *C sensustricto* 1, Ruminococcaceae UCG005, UCG008, UCG010, and NK4A214 *Marvinbryantia*, Clostridiaceae 1, Peptostreptococcaceae, *Romboutsia*, *Intestinibacter*	The Rotterdam Study and LifeLine-DEEP studies investigated 2166 individuals from two Dutch population-based prospective cohorts.	There were twelve bacterial groups linked to HOMA-IR/T2DM in this study. More significant abundances of butyrate-producing microbes were linked to poorer T2DM susceptibility. In people without diabetic conditions, a more diverse microbiome and butyrate-producing gut flora communities were correlated with a declined susceptibility to T2DM and insulin resistance.	[89]
Bacteroidetes, Verrucomicrobia, Actinobacteria, Proteobacteria, Firmicutes, Actinobacteria, Tenericutes, Lentisphaerae, Euryarchaeota, Cyanobacteria, Elusimicrobia, TM7, and *Synergistetes*	Thirty healthy controls (HC) (13 females and 17 males), 25 patients with type 2 diabetes without DR (14 males and 11 females), and 28 people with DR and T2DM (7 females and 21 males) were recruited as three separate cohorts, making 83 south Indian individuals.	In diabetic patients, compared to DR patients, the prevalence of *Actinobacteria* was significantly lower. Ten of the 11 minor phyla varied considerably between the three cohorts. DR and cT2DM subjects experienced increased abundances of 8 and 11 genera, respectively, compared to HC, and three genera (*Escherichia*, *Enterobacter,* and *Acidaminococcus*) were prevalent throughout. Although anti-inflammatory bacteria (*Roseburia, Coprococcus, Lachnospira, Phascolarctobacterium, Anaerostipes,* and *Blautia*) were less prevalent in T2DM than HC, pro-inflammatory bacteria (*Enterobacter, Escherichia, Methanobrevibacter,* and *Treponema*) were identified to be more prevalent. The findings suggest a healthy mix of anti- and pro-inflammatory microorganisms is essential for HC. Apart from *Roseburia, Lachnospira,* and *Blautia,* various anti-inflammatory taxa such as *Mitsuokella, Bifidobacterium, Streptococcus, Ruminococcus, Lactobacillus, Faecalibacterium, Butyrivibrio* were reduced in DR. Furthermore, compared to T2DM and HC, one pro-inflammatory microbe, *Shigella*, showed an increase in DR. We observed a drop in two probiotic bacteria, *Lactobacillus* and *Bifidobacterium*, in persons with DR, along with a rise or decline in anti-inflammation processes and/or potential pathogenic bacterial communities. The modification was assumed to function because there were fewer anti-inflammatory genera, probiotic bacteria, and more bacteria from the DR functional interactions.	[26]
Firmicutes, Actinobacteria, and *Bacteroidetes*	18/United Arab Emirate	The gut flora profiles of controls and diabetics did not significantly alter when fed different diets. However, type 2 diabetics had higher abundances of bacterial microbes essential for the metabolic pathway of Vitamin K2 (menaquinone) super pathway production than healthy individuals. As a result, a mechanism for discovering and developing newer biomarkers and more suitable Type 2 diabetes mellitus management regimens has been established.	[23]
Clostridiaceae_1 and *Peptostreptococcaceae* and four	Eighteen healthy Caucasian participants	Particularly after the first two or three doses of metformin, the inner diversity of the gut flora was drastically reduced. It was also observed	[75]

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genera within these families: *Clostridiaceae_1*, *Peptostreptococcaceae*_unclassified (family *Peptostreptococcaceae*), and *Peptostreptococcaceae*, *Enterobacteriaceae*, *Escherichia-Shigella*.		that even though the inner assortment of the gut flora in research participants rose marginally after seven days of metformin prescription, it remained considerably lesser than *via* metformin intake. Escherichia spp. were found in high numbers in specimens ingested before metformin therapy from persons who subsequently experienced tri*via*l or damaging adverse effects. No significant changes were observed in taxa representation at the phylum level at any contrast between the M0/M24h/M7d specimens. However, weekly metformin treatment was linked to increased reductions in *Clostridiaceae* 1 and *Peptostreptococcaceae*, along with four taxonomic classifications among these families: unclassified *Peptostreptococcaceae* and *Asaccharospora Clostridiaceae*. In addition, compared M24h/M7d specimens revealed a considerable rise in the orders *Enterobacteriales* and *Enterobacteriaceae*, comprising the genera *Escherichia-Shigella*.	
Clostridium bartlettii, Barnesiella intestinihominis, Parabacteroides, Enterococcus faecium, Odoribacter, Lactococcus lactis, and *Dialister*		Although metformin failed to reduce microbiome alpha diversity in the healthy cohort, the microbiota was reduced in the T2DM cluster. A decrease in *Barnesiella intestinihominis* and *Clostridium bartlettii* abundance and a rise in Oscillibacter and Parabacteroides distasonis abundance were unclassified and overlapped between both research groups at the species level. Furthermore, a higher *Prevotella copri* predominance in the non-responders subcategory and predominance of *Lactococcus lactis, Dialister, Enterococcus faecium*, and *Odoribacter* at baseline were also found.	90
Prevotella, Megasphaera, Akkermansia, Escherichia, Sutterella, Lactobacillus, Acidaminococcus, Blautia, and *Ruminococcus*	102 Indians	The difference in the abundance of gut microbiomes serves as biomarkers when compared between healthy, newly diagnosed type 2 diabetes and treated groups.	49
L. delbrueckii, *L. ruminis* and *L. case*	6154 Europeans, Asians, Africans, South, and North Americans, Oceania	The prevalence of gut lactobacilli is modulated by nutrition, contact, and geography, in addition to the microbiota populations understudied. According to a study that used Lactobacillus clusters to show unique global abundance characteristics, it has significant associations with diseases linked to a western lifestyle.	91
g_butyrivibrio, c_deltaproteobacteria, g_megamonas, c_alphaproteobacteria, o_lactobacillales, g_mogibacteriaceae spp, f_comamonadaceae, g_clostridiaceae spp, f_mogibacteriaceae, s_dispar, and *g_dorea*,	1832 Chinese	Gut microbes linked to type 2 diabetes were discovered using an interpretable computer language. In addition, the researchers created a new microbiome risk score (MRS) that correlates with little blood factors from the gut flora. Finally, the fecal flora transition investigation further verified the impact of the detected microbe combinations on T2DM development, including that adipose tissue distribution could alter the MRS-T2D association.	35
Verrucomicrobia, Firmicutes, Actinobacteria, Proteobacteria, and *Bacteroidetes*	6 Germans	Modifications in inflammatory and metabolic markers were linked to changes in microbiome gene and composition function. This alteration is proposed to facilitate the achievement of novel therapeutic and diagnostic techniques focusing on individual got microbial community metagenomic sequencing.	33
L. brevis	The study involved 26 diabesity subjects administered a daily multispecies prebiotic (or a placebo) and probiotic ration for six months.	According to microbiome analysis, there were no substantial variations in taxonomic content/alpha or beta fecal microbiome variabilities across categories or between starting and the end interventions in any of the groups. In the synbiotics group, the *L. brevis* richness had the utmostly significant variation in pre-/post-treatment flora communities. Compared to the placebo cluster, there was no substantial difference in glucose metabolic processes in the synbiotics cluster. Furthermore,	92

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		either group's lipid profile and insulin resistance remained unchanged due to the MTT reactions.	
Bifidobacterium and *Lactobacillus*, *Faecalibacterium*, *BlautiaClostridium*, *Eubacterium_hallii_group*, *Streptococcaceae*, *Tannerellaceae*, *Pasteurellaceae*, *Oscillospiraceae*, *Christensenellaceae*, *Acidaminococcaceae*, *Anaerovoracaceae*, *Peptostreptococcaceae*, *Clostridiaceae*, *Eggerthellaceae*, *norank_o_Clostridia_UCG-014*, *Escherichia-Shigella*, *Butyricicoccaceae*, *Erysipelotrichaceae*, *Eubacterium_coprostanoligenes_group*, and *Monoglobaceae*	25 DM individuals with retinopathy (DR), 25 healthy controls provided fecal samples (HC), and 25 patients with diabetes without retinopathy (DM).	The three categories had diverse microbial compositions and structures: β and α differences in the DR and DM groups were lower than in the HC group, with the Blautia genus being the most prominent in the DM cluster. Compared to the HC group, the DR and DM groups also had greater concentrations of *Lactobacillus* and *Bifidobacterium* but lower amounts of *Clostridium genera*, *Faecalibacterium*, *Escherichia-Shigella*, and the *Eubacterium hallii* group. Since the *Eubacterium hallii* group, *Clostridium*, and *Faecalibacterium* are renowned human gut pioneers and butyrate makers, they are strongly discriminated from T2DM among the genera with decreasing abundance. As a result, it is considered that a drop in these helpful bacterial communities was associated with the development of diabetes and retinopathy. *Bacteroidota*, *Actinobacteriota*, *Proteobacteria*, and *Firmutes* outnumbered other phyla from each category when the concentration of microbial composition was evaluated at the genus and phylum levels. Results also showed that 30 major genera were dispersed with variable abundance and diversity in the three groups using circos analysis. Bacteroidetes, Desulfobacterota, and Firmicutes phylum disturbances were also linked to DM and DR. As a result, bacteria belonging to Desulfobacterota and Bacteroidetes phyla could release LPS, resulting in inflammatory damages or accelerated energy metabolism problems, which are both pathological characteristics of diabetes.	34
Bacteroides, *Faecalibacterium*, *Proteobacteria* and *Bifidobacterium*	243 Chinese	Dysbiosis of the gut flora served as a prospective gene marker for the emergence of T2D due to obesity. Lack of SCFA generation due to gut-microbe sugar metabolism malfunction also potentially resulted in suppressed inflammation in the gut. The gut bacteria's low sugar utilization efficiency placed immense pressure on the human host to ingest and metabolize residual sugar.	39
Firmicutes and Bacteroidetes	12 Germans	Short-term dietary constraints of branched-chain amino acids (BCAA) enhance postprandial insulin sensitivity/white adipose tissue mitochondrial effectiveness and reduce meal-induced insulin production. A one-week reduction in dietary BCAAs has little or no effect on insulin sensitivity. However, it did not raise circulating fibroblast-growth factor-21 concentrations and intestine Bacteroidetes density.	38
Bacteroidetes dominated, with *Firmicutes*, *Actinobacteria*, and *Proteobacteria* following closely behind.	58 diabetic patients (21 controls, 37 cases)	After genome sequencing into seventeen distinct phyla, this study determined the distribution of various gut microbiomes. Most sequences belonged to four phyla. Bacteroidetes dominated, with *Proteobacteria*, *Actinobacteria*, and *Firmicutes* following closely behind. In addition, the B/F ratio was higher in cases than in controls from univariate analysis (cases, 1.45; controls, 0.94; $P = 0.049$). Therefore, increased gut bacteria B/F ratio might be a biomarker for T2DM individuals developing sight-threatening diabetic retinopathy.	37
Fusobacteria, *Proteobacteria*, *Lactobacillus*, *Enterobacter*, *Eubacterium*, *Erysipelatoclostridium*, *Alistipes*, *Parabacteroides*, *Blautia*, *Bacteroides*, *Faecalibacterium*,	Ten people took part in this study. Subjects were between 19 and 45 years and in excellent health.	Individuals' phyla level predominance was observed, with Bacteroidetes and Firmicutes predominating at baseline and postmetformin. Proteobacteria and Fusobacteria increased more in the post-metformin + vancomycin and postvancomycin periods than in the previous periods. Vancomycin injection lowered the predominance of Bacteroidetes and Actinobacteria at the phyla stage. However, it raised the predominance of Proteobacteria compared with the controls. Lactobacillus and Enterobacter genus' relative abundance increased, while *Eubacterium*, *Bacteroides*, *Parabacteroides*, *Blautia*, *Alistipes*, *Faecalibacterium*, *and Erysipelatoclostridium* genus relative abundance	40

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		declined. In addition, when contrasted with the baseline, the relative abundance of E. coli rose after vancomycin treatment. Compared with the control group, the wide phylum Proteobacteria availability improved while that of Bacteroidetes declined. Moreover, while the predominance of the genus Escherichia expanded, that of Parabacteroides diminished. No species changed between the postvancomycin and postmetformin + vancomycin timeframes at the phyla/genera level. The interaction amid this impact and genus with altered relative abundances before and following vancomycin medication due to a significant variation in the antihyperglycemic impact was also evaluated before and following vancomycin ingestion. A link was found between the relative abundance of *E. coli* in the vancomycin + post-metformin period and the antihyperglycemic impact. This antihyperglycemic impact was, however, adversely linked with the relative presence of *Enterobacter* and *Faecalibacterium* in postmetformin samples. An association between genus predominance and antihyperglycemic properties was examined. It was concluded that the relative predominance of *Erysipelatoclostridium* and *Escherichia* was favorably connected with antihyperglycemic effects, and *Faecalibacterium/Enterobacter* predominances were unfavorably linked to these variables.	
Bacteroidetes Proteobacteria Verrucomicrobia Bacteroidetes, and *Firmicutes*.	37 Mexican-American	The prevalence of specific bacterial taxa differed significantly between type 2 diabetics and non-diabetics. In type 2 diabetes, *Firmicutes*, *Proteobacteria*, and *Verrucomicrobia's* percentage abundances were more significant. In comparison to the non-T2DM group, *Bacteroidetes* were less abundant.	[32]
Lachospiraceae, Clostridiaceae, Erysipelotrichaceae, Ruminococcaceae	Accessions to the NCBI SRA database were used to retrieve the datasets SRP002427, #ERP000108 (MetaHIT), SRP015779, SRP011011, SRP002423, and SRP000319.	In patients with T2DM and UC, although lacking in patients with CD, abundance investigation in phyla revealed a substantial drop in Firmicute-derived bsh compared to healthy individuals. Compared to these healthy patients, T2DM and UC patients had lower rates of adh and hsdh genes, while CD patients had higher levels. Further investigations of *bsh* also revealed noteworthy discrepancies between the various Firmicutes taxa and illness/healthy populations. From this observation, BSH protein sequences were analyzed, identifying Firmicute *bsh* as the most abundant strain. In all T2DM patients, *bsh* predominance, corresponding to these protein groups, was considerably lower than in healthy subjects. Bsh genes from the Ruminococcaceae and Clostridiaceae, Lachospiraceae, and Erysipelotrichaceae families were detected in this cluster.	[93]
Actinobacteria Bacteroidetes, Proteobacteria, Firmicutes, and Verrucomicrobia.	For this study, 49 people were enlisted: 20 pre-diabetics, 14 Type 2 diabetics, and 15 controls	*Actinobacteria*, *Proteobacteria*, *Bacteroidetes*, *Firmicutes*, and *Verrucomicrobia* were the top five phyla discovered. However, the phylum *Synergistetes* was considerably diminished in controls than in T2DM patients, with uncharacterized taxa from the *Pseudonocardiaceaes* being considerably higher in preDM clusters (p = 0.04). In addition, while *Chloracidobacteria* was abundant in the non-diabetic over preDM group, class *Saprospirae* was suppressed in the pre-diabetic *vs* diabetic group (p = 0.04). Also, compared with other categories, the Prediabetic cluster was considerably higher in an unknown genus from the *Pseudonocardiaceae* family. Type 2 diabetics, however, had significantly higher *Collinsella* and an unknown genus from the family *Enterobacteriaceae* (Enterobacteriaceae genus, p = 0.02; *Collinsella*, p = 0.03).	[29]
Intestinibacter, Clostridium, Romboutsia	20 healthy Koreans were recruited	We looked at variations in gut microbiota abundances at the genetic levels between pre-metformin treatment and post-metformin medication (after the last metformin administration). The relationship between metformin's PD parameters and the microbiota was investigated to see if metformin's hypoglycemic effect was linked to the microbiota. Firmicutes were found to have a negative correlation with Gmax and	[76]

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		AUGC values. We also looked at relationships at the genus levels and discovered that AUGC and Gmax values were favorably associated with *Escherichia. Intestinibacter*, *Romboutsia*, and *Clostridium*, on the other hand, were found to be inversely related to the PD parameters.	
Firmicutes, *Proteobacteria*, and *Verrucomicrobia*	6627 Chinese	A stratified cluster sampling approach estimated the relationships between air pollution, gut microbial diversity, and diabetes. Long-term particulate matter exposure may raise the risk of T2DM and impair gut bacteria diversity. Particle matter relationships with diabetes risk were also partially attributed to gut microbiome modifications.	[36]
Faecalibacterium, *Bifidobacterium*, and *Akkermansia* genera	60 Chinese	The microbial community makeup in people with T2D was investigated. Here, researchers used a hybrid of supervised classification techniques and univariate analysis approaches. The findings revealed a link between microbial tyrosine gut metabolism and diabetes.	[94]
Clostridiales and *Akkermansia*	25 Patients	The gut microbial community was analyzed to identify their alpha, beta, and microbiome diversity. Although the *Akkermansia* genus increased in abundance, *Clostridiales* were found in lesser quantity in patients with T2D.	[76]
Bifidobacterium, *Phascolarctobacterium*, *Ruminococcus*	Thirty-six Chinese individuals, male and female, range in age from 18 to 65 years.	The effects of galactooligosaccharides (GOS) and fructooligosaccharides (FOS) on glycemic indices and intestinal microbiota during an oral glucose tolerance test (OGTT) were investigated. Relatively brief use of high-dose prebiotics negatively affected glycolysis, evidenced by fasting glucose after GOS intervention and OGTT after FOS intervention. Furthermore, although Bifidobacterium's relative abundance increased significantly in both the GOS and FOS groups, bacteria that produce butyrate: *Ruminococcus* (GOS group) and *Phascolarctobacterium* (FOS group), dropped. Hence, although GOS and FOS enhanced *Bifidobacterium*, they negatively impacted glycolysis by lowering butyrate-producing microorganisms.	[95]
Among the metabolites that predicted greater microbiome diversity were indolepropionate, cinnamoylglycine, 3-phenylpropionate(hydrocinnamate), and 5-alpha-pregnan-3beta, 20alpha-diol monosulfate, comprising phenylpropionate/ indolepropionate also have a link to lower T2DM incidences	United Kingdom (1018)	Microbial metabolites, which may be altered by food, largely regulate gut microbiome biodiversity on T2D. Hence the availability of specific microbial metabolites correlates with the diversity of microbiomes.	[96]
Lactobacillus spp., *Bifidobacterium spp.*, *Streptococcus spp.* *Saccharomyces*	60 Australians	Systematic alteration of gut microbial populations using placebo and probiotics capsules as therapeutic strategies for treating and preventing T2DM and related metabolic abnormalities was recorded.	[84]
Agathobacter, Collinsella, Dorea, *Lachnoclostridium, Faecalibacterium, Blautia, Roseburia, Subdoligranulumt, Megasphaera, Lactobacillus*, *Parabacteroides*, and *Alistipes*	India (278) and Denmark (259)	According to phenotypic data and inflammatory cytokine levels, the function of the gut flora populations in the pathophysiology of prediabetes in Indian people differed from that of Europeans. Microbial dominance patterns and varying amounts of markers of inflammation also discovered significant sub-clinical biomarkers of prediabetes, along with potential early indicators for people susceptible to dysglycemia	[97]
We detected 19 with more than 1% per sample within each treatment level, mainly belonging to the Firmicutes phylum (*Akkermanalaceae*,	47 Egyptian participants: 22 TID, seven healthy controls, and 18 TIID. The diabetic individuals were divided into seven groups based on	No substantial alterations between the types I/II and healthy individuals. However, *Lachnospiraceae, Howardella*, and *Pseudomonas* were shown to be more critical in TIIND than the control group, which had a large rise in Lactobacillus, *Lachnospiraceae, Howardella*, and *Veillonellaceae* were more prevalent in the TIINN, and	[42]

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Ruminococcaceae, Clostridiaceae, Christensenellaceae, Listeraceae, Leuconostocaceae, Streptococcaceae, Lactobacillaceae, Peptostreptococcaceae, Lachnospiraceae, Veillonellaceae, Eryslipelotrichaceae, Bifidobacteriaceae, and the Gram-negative *Acidaminococcaceae*).	whether they were treated (uncontrolled *vs* controlled diabetes symptoms).	*Ruminococcaceae*/*Christensenellaceae* were substantially additional in healthy individuals. Alternatively, *Veillonellaceae* and *Pseudomonas* were found in greater quantity in TIIC. For *Howardella* and *Lachnospiraceae*, TIIND was more abundant than TIND, while for TINN and TIINN, *Gemella* and *Christensenellaceae* were more prevalent in TINN. The TIIC therapy predominantly caused a shift towards the phylum Firmicutes (*Acidaminococcus* and *Ruminococcaceae*). All diabetes groups had a substantial upsurge in the predominance of Gram-negative, possibly opportunistic pathogenic bacterial communities (*Prevotella, Pseudomonas*) compared to the control group. Furthermore, a gram-positive *Gemella*, which has been linked to an elevated risk of diabetes, and compared to the control group, considerably rose in all T2DM categories. Alternatively, *Terrisporobacter*, *Clostridium* (highly fermenting bacteria), and *Turicibacter* remained additionally numerous in the control group than TID. According to the microbiological signatures in TIID, the healthy subjects also had more genuinely useful microbiological species such as *Turicibacter*, *Lactobacillus*, and *Terrisporobacter*.	
Akkermansia, *Bacteroides*, *Bifido bacterium*, *Blautia*, *Clostridium*, *Coprococcus*, *Dorea*, *Prevotella*, *Roseburia*, and *Ruminococcus*	KORA is a prospective study group in Augsburg (Germany) used to investigate the role of lifestyle, environmental and genomic variables in illness advancement, particularly metabolic diseases.	In this study, 87 OTUs were shown to oscillate in controls but not in T2D patients. *Clostridium, Bacteroides, Akkermansia, Bifidobacterium, Blautia, Coprococcus, Dorea, Prevotella, Ruminococcus,* and *Roseburia* were among them. The 14 selected rfOTUs, on the other hand, made no distinction by obesity, confirming that obesity and T2D influence microbiota profiles differently. Individual microbiota compositions were also compared, revealing that the two primary phyla, Bacteroidetes and Firmicutes, dominated the ecosystems. Participants in C1 exhibited the least diverse microbiotas and had vastly higher relative Bacteroides abundances. However, *Ruminococcus* species dominated far more diversified clusters, C2 (the highest number of individuals), and *Prevotella* dominated C3. Since the relative abundances of particular OTUs showed the loss of daily oscillations in diabetes patients, the fraction of rOTUs in prediabetes was lowered from 10.4 percent to 7.6 percent. JTK CYCLE or harmonic cosine-wave regression yielded similar results, indicating the findings' reliability.	[28]
Intestinibacter bartlettii, Akkermansia muciniphila, and *Subdoligranulum variabile*	Sweden	The dysbiotic gut community understudied caused by metformin ingestion by people with diabetes increased nutritional disparities due to depleting *I. bartletti*, a major *Firmicutes bacteria, Escherichia spp., S. variabile*. Since these four microorganisms have widely divergent growth medium needs and metabolic reactions to environmental and nutritional changes, they supplied and struggled for gut-based nutrients in diverse ways due to their metabolic activities, comprising amino acids, gasses, and SCFAs. Potential commensal interaction was also observed. Some of these chemicals were produced by *S. variabile* and *A. muciniphila* (e.g., glycine and threonine), while *I. bartlettii* and *Escherichia sp* ingested them. Thus, the gut flora metabolic processes delivered to the body as prebiotics, postbiotics, and probiotics for synthesizing amino acids and SCFAs can serve as potential treatments for T2DM management.	[62]
Phylum: Firmicutes, *Bacteroides, Actinobacteria.*	Stool-based human microbiome project (HMP)	No substantial alterations in the gut microbial community linked with age, gender, illness state, or any other available metric were observed.	[22]

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Family: Lachnospiraceae, Veillonellaceae, Coriobacteriaceae, Ruminococcaceae, Prevotellaceae, Bacteroideaceae, Rikenellaceae Genus: Prevotella, Collinsella, Roseburia, Streptococcus, Dialister, Bacteroides, Alistipes, Parabacteroides	data reference and Cameron County Hispanic Cohort (CCHC).	Microbial network interactions were discovered between three additional datasets and operational taxonomic units (OTUs). A group of seven species also constituted tightly coupled networks in all four datasets tested, characterized by butyrate producers, which were typically enhanced in obese people but depleted in diabetic subjects.	
Bacteroidetes, Proteobacteria, Fusobacteria, Verrucomicrobia, Porphyromonadaceae, Prevotellaceae, Paraprevotellaceae, Flavobacterium, and Flavobacteriaceae	Patients with chronic kidney disease (T2DM-CKD) and T2DM were compared to healthy persons to see if there was a link between Gram-negative bacteria dysbiosis and LPS in gut flora communities.	The gut microbiomes of the T2DM-CKD and control groups contained four Gram-negative phylum (*Proteobacteria, Bacteroidetes, Verrucomicrobia*, and *Fusobacteria*). Patients with T2DM-CKD had significantly higher relative abundances of *Verrucomicrobia,* Fusobacteria, and Proteobacteria than controls. However, Actinobacteria and Firmicutes were found among the Gram-positive phyla. In addition, *Bacteroidaceae, Porphyromonadaceae, Prevotellaceae, Paraprevotellaceae,* and *Flavobacteriaceae* were found in the human gut five genera (*Porphyromonas, Bacteroides, Paraprevotella, Flavobacterium,* and *Prevotella*). In particular, the phylum Bacteroidetes' Weeksellaceae family showed an alteration in the gut microbial community in individuals with T2DM-CKD, with increasing distribution and abundance of Gram-negative bacteria.	30
N/A	Genome-wide genotyping, gut metagenomic sequencing, and SCFA levels were jointly used to examine 952 controls	While host genetic pathways increased the SCFA butyrate gut production, they also enriched insulin sensitivity following an OGT. Aberrations in the absorption or synthesis of other SCFAs, like propionate, were also linked to higher T2DM susceptibility. (P = 0.004), according to bidirectional Mendelian Randomization (MR) analyses.	63
f_Streptococcaceae, f_Enterobacteriaceae, g_Rothia, f_Lachnospiraceae, and *f_Rumino-coccaceae*	14 Chinese	Findings showed a relationship between intestinal microbial changes, insulin resistance, and circulating endotoxemia, implying the altered gut microbiota as the mechanistic explanation of the protective role of Roux-en-Y gastric bypass intervention in obesity-related T2DM.	98
Enterobacter, Romboutsia, Lachnospiraceae Clostridium sensu stricto	101 Koreans	The study revealed practical treatment strategies for diseases caused by metabolic disorders using specific bacterial signatures associated with T2D and NAFLD.	99
Bifidobacterium, Eubacterium, Akkermansia, Subdoligranulum, Faecalibacterium, Lactobacillus, and *Bacteroides*	80 Japanese	Based on gut microbiome trend changes, hierarchical clustering of typical food habits was undertaken, and three unique groups were identified. Sucrose was in Cluster I, lipid intake was in Cluster II, and carbohydrate intake was in Cluster III. Results showed that the alteration degree in *Faecalibacterium* was positively and significantly associated with rice consumption but inversely correlated with bread consumption. Furthermore, the magnitude of change in *Subdoligranulum* and *Akkermansia* was inversely proportional to potato consumption. In Japanese T2D patients, acarbose also changed the gut microbiome composition, linked to food choices.	100
Prevotella, Eubacterium, Roseburia, Clostridium, Bacteroides, Ruminococcus, Lactobacillus, Faecalibacterium, Parabacteroides, Blautia, Dialister, Butyricicoccus, Acetivibrio, Butyrivibrio, and *Collinsella*.	81 Indians	The biomarker potentials of gut microbiota, pronounced as butyrate-producing bacteria, were predominantly abundant in healthy Indians but reduced in type 2 diabetes. Butyrate notably stimulated colonic T-regulatory cellular factors, reduced pro-inflammatory macrophage manufacture, and enhanced gut membrane reliability, leading to a proinflammatory gut condition.	51

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Bacteroides, Prevotella, and *Romboutsia*	75 Indonesians	The decrease in conjugated bile acids, which had a diabetic effect, was greatly linked with Bacteroides in the understudied Indonesian diabetics. This shift was, however, restored in participants using metformin.	73
Ruminococcus	550 Americans	The significance of microbiota genetic expression on the postprandial glycemic index was discovered in this investigation. It was the first time the gut microbiome's metatranscriptomic activity was linked to individual differences in glycemic sensitivity in adults. In addition, new microbiological properties, such as the fucose metabolism and the indole acetate synthesis pathways, were also discovered, associating molecular mechanisms with glycemic regulation.	101
Lactobacillus gasseri, Lactobacillus salivarius, S. mutans, and *Streptococcus* species		To restrict the gene list to the most *via*ble prospects, subtractive assembly was used from the differentiated transcripts that were persistently prominent in T2DM categories	102
Ruminococcaceae, Lachnospiraceae, and *Enterobacteriaceae*	40 Chinese	The gut flora of patients with controls and diabetics, including those from diverse ethnic communities in northwest China, differed substantially in this research. The findings offer new perceptions of the potential connection between gut microbiota and diabetes prevalence. In addition, data from the microbiome could also be used to develop biomarkers for Type 2 diabetes mellitus diagnosis and monitoring.	44
Roseburia intestinalis, Roseburia inulinivorans, Haemophilus (H. haemolyticus, H. parainfluenzae, H. pittmaniae, and H. influenzae), Clostridium ramosum, Eggerthella lenta, Streptococcus, and Lactobacillus	344 Chinese	Following mapping the current reference nucleotide sequence catalogs in the gut microbiota, novel models were created and built to re-examine specimens from diabetics and healthy subjects in populations from China to show the possible associations between intestinal microbial populations and type 2 diabetes pathogenesis. Different species and taxonomic proportions were observed in Haemophilus, Lactobacillus, and butyrate-producing bacteria.	45
The four major phyla constituting the P group (patients with T2DM and dampness-heat stagnating in the spleen symptoms) were Bacteroidetes (53.13%), Proteobacteria (5.55%), Firmicutes (30.46%), Actinobacteria (0.94%). Firmicutes (50.66%), on the other hand, was the most prevalent microbial phylum in the healthy participants, followed by, Proteobacteria (2.00%), Bacteroidetes (37.94%), and Actinobacteria (1.91%)	This study understudied six patients with obesity and T2DM and six healthy subjects. All people with diabetes had fasting plasma glucose (FPG) of less than 7.0 mmol/L, two-hour postprandial blood glucose (2-hPBG) of less than 11.1 mmol/L, and HbA1C of less than 6.5 percent. Diabetics were all weighty (BMI ≥ 25 kg/m2).	In patients with T2DM, the relative abundance of Firmicutes diminished while Bacteroidetes surged. Therefore, Firmicutes, Bifidobacterium, Bacteroidetes, and Phascolarctobacterium are all promising targets for T2DM therapy. In addition, Bacteroides, Paenibacillus, Oribacterium, and the order Acidaminococcales are considered T2DM biomarkers. Bacteroides (31.07 percent) was the most common genus in the P grou p, followed by Roseburia (3.39 %), Eubacterium (4.12 %), Prevotella (10.07 %), and Faecalibacterium (2.88 percent). These biomarker species differed considerably between the two groups, according to LEfSe analyses. The LDA results found 43 biomarkers th at differed significantly between the groups. The enrichment of distinct gut bacteria specific in the consumption of v arious plant polysaccharides was evidenced by the increasing abundanc e of GHs in each group. At the microsystem scale, upregulation of GHs also results in significant proportions of energy intake and, as a result, T2DM pathogenesis.	24
Veillonellaeae genera, Dialister, Megasphaera, Prevotella, Mediterraneibacte faecis, Lactobacillus, and *Bifidobacterium*	92/ Philippines	The gut microbial community was analyzed based on nutrition and metabolic conditions. Low carbohydrate diets rebuilt intestinal microbial diversity, particularly *Prevotella*, predisposing Filipinos to T2DM when consuming a high-energy diet. Low butyrate amounts were correlated to a decline in *M. faecis*.	103

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Fusobacterium, Bilophila, and *Bifidobacterium*	56 patients with T2DM	PICRUSt estimated functional metagenomes of the gut flora community within the understudied patients based on data from 16S rRNA sequencing results. According to the findings, cholecystectomy overturned the abundance of Firmicutes and Lachnospira in long-standing T2DM conditions than in T2D type-I individuals. Furthermore, the procedure restored the Fusobacteria phylum and species Bilophila/Fusobacterium predominances. Conversely, the T2DI and T2DIIC groups had more significant pattern correlations in gut flora compositions and anticipated functional metagenomics communities than the T2DII group. Bifidobacterium abundance dropped even more as diabetes progressed, contributing to improved knowledge of Bifidobacterium's significance in Type-2 diabetes. Moreover, in long-term diabetics, although cholecystectomy did not positively impact the phylum Bacteroidetes, it raised the relative richness of the *Bilophila* and *Fusobacterium* genera, resulting in opportunistic infections or intensified metabolic problems caused by high-fat diets. TSH levels were also strongly linked to the relative infusion of large *Lautropia, Parabacteroides, Leuconostoc, Enterococcus,* and *Megasphaera* quantities using correlation analysis. In summation, cholecystectomy improved the composition and function of the gut flora communities in long-term diabetics.	[27]
Bacteroides and Firmicutes	806 Chinese	Using machine language technology, gut microbiomes as biomarkers could distinguish type 2 diabetes from control non-diabetes and other diseases, with a higher level of specificity.	[104]
Coprococcus eutactus, Clostridia bacterium, Faecalibacterium sp., Alistipes *spp., Pseudoflavonifractor spp., Clostridium spp., Oscillibacter spp Flavonifractor plautii, Alistipes obesi, Eubacterium rectale,* and *Intestinimonas butyriciproducens*	484 Swedish	The human microbiome is a modifiable determinant for developing personalized medicine techniques to prevent T2DM delay, intimately linked to dietary variables. When diabetes medications are lacking, the total intestinal gut microflora fluctuates with glycemic status. Fasting glycemic indices and bacteria that produce butyrate were diminished in prediabetes and t2dm subjects, despite the variations being closely linked to glucose intolerance. Genes associated with pathogenicity were also identified in the genomes of the putative butyrate makers with increasing abundance.	[54]
Collinsella, Odoribacter, Parabacteroides, Faecalibacterium.	Fourteen native Japanese males from Japan/Hiroshima and fourteen Japanese-American men from California and Los Angeles	The gut flora of Japanese-American males differed from those of native Japanese men, with a lower prevalence of Odoribacter. Similarly, insulin resistance in Japanese-American males was higher than in native Japanese males. Researchers also discovered a genus of bacteria with different distributions in Japanese-American/native Japanese men: 16S ribosomal ribonucleic acid genetic percentages presented Collinsella in Actinobacteria communities, followed by Parabacteroides and Odoribacteria in the Actinobacteria taxonomy. Finally, Faecalibacterium, a member of the Firmicutes taxonomy, was superior to Bacteroidetes in Japanese-American males compared to native Japanese males.	[25]
Bifidobacterium longum, bacterium rectale, Faecalibacterium prausnitzii, Roseburia intestinalis, E. coli, Bacteroides plebeius, and *Prevotella copri*	36 South Koreans	Even before clinical examinations highlighted sub-clinical inflammation in adults increasingly vulnerable to T2DM, functional and compositional microbial fingerprints confirmed the existence of sub-clinical inflammation. As a result, they serve as both unique markers for early detection and a focus for precautionary treatments.	[55]
Spirochaete, Turicibacter, Bifidobacterium, Lactobacillus, and *Fusobacterium*	180 Chinese	The implications of numerous anti-diabetic drugs on the gut microbiota were understudied, and the amounts of butyrate-producing species such as *Ruminococcus* and *Faecalibacterium* were shown to be limited in non-treated Type 2 diabetes mellitus.	[48]

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Roseburia spp., Ruminococcus bromii, Faecali bacterium prausnitziian, Bifidobacterium spp	409 Chinese	A drug-naive Type-2 diabetes patient was studied in a randomized, double-blinded, placebo-controlled clinical trial. Although older people were substantially more concentrated following treatment than younger people, post-treatment relative diversity and *Lactobacillus crispatus* and *salivarius* prevalence were only significantly higher in older adults relative to their baseline. Furthermore, excluding *Bifidobacterium longum*, probiotic-containing varieties revealed a dose-response correlation with decreased HbA1c levels in elderly subjects only.	46
Proteobacteria, Prevotella, Alloprevotella, Bacteroidetes, Firmicutes, Proteo bacteria, Negativicutes, Actinomycetes, and *Fusobacteria*	For this study, 180 people were enlisted: 60 with PreDM, 60 with T2DM, and 60 non-diabetics (controls)	Between T2DM, PreDM, and healthy control groups, substantial variations in the proportion of microorganisms were observed. Specifically, while the PreDM group had considerably more proteobacteria than the control group, relative predominances of Alloprevotella and Prevotella were considerably increased in the T2DM compared to the control clusters. Additionally, paraprevotella's relative predominance was lower in the PreDM and T2DM ($P = 0.011$, $P = 0.045$) than in the control groups. Moreover, Bacteroides' relative predominance in the T2DM cluster was considerably diminished than in the PreDM and control groups. *Firmicutes, Actinomycetes, Bacteroidetes, Proteobacteria,* and *Fusobacteria,* were the five most common phyla discovered among the 180 samples investigated. Results also showed that while the prevalence of the phylum Proteobacteria was considerably poorer in the preDM compared to the control clusters, the T2DM cluster insignificantly possessed more *proteobacteria* concentrations than the control cluster ($P > 0.05$). Nonetheless, at the phyla stage, no statistically noteworthy dissimilarities were detected in the three classes except for *Proteobacteria*. Among the 27 classes, only the T2DM category *Negativicutes* were increasingly prevalent than other class levels.	105
A. muciniphila, Bacteroides, Proteobacteria, Firmicutes	With and without recently diagnosed T2D, 182 abdominally and lean obese individuals were studied.	Even though the prevalence of *A. muciniphila* was markedly smaller in lean people with T2D compared to participants undiagnosed with Type 2 diabetes mellitus, it was not lower in obese people with T2D. *Bacteroides, Proteobacteria, and Firmicutes* were the most predominant phyla in the healthy population and those with newly diagnosed T2D and/or abdominal obesity. On average, the T2DNO group demonstrated a significantly greater frequency of the *Firmicute* (30%) and a diminished predominance of *Bacteroidetes* (62%) than the other three groups. However, no substantial disparities between the four groupings were discovered at the phylum level.	21
Acidovoraxcitrulli, Acinetobacter baumannii, E. coli, Leptospira species, Helicobacter hepaticus, Burkholderia glumae, and *Koribacter versatilis*	352/Denmark	Patients with T2D were distinguished from controls KO annotations and eggNOG of the gut microbiome using two optimum support vector machine (SVM) classifiers (9 Max-Relevance and Min-Redundancy). The traits used in such classifiers could be prospective biomarkers for differentiating Type 2 diabetes patients from healthy subjects at the microbial community level.	56
Proteobacteria, Bacteroidetes, Firmicutes, Megamonas, Bacteroides, Prevotella, Fusobacterium, Dialister, Ruminococcus, Subdoligranulum, Alistipes, Faecalibacterium, Bifidobacterium, Escherichia-Shigella, Lachnoclostridium, Lachnospiraceae, Ruminococcaceae, Veillonellaceae, Anaerostipes, Pseudobutyrivibrio,	There were 65 T2D patients in total, 49 with diabetes complications and 16 without, as well as 35 healthy controls.	The discrepancies in gut microbial composition between the T2DM cluster and other clusters were studied using the Welch t-test. The most prevalent microbial taxa in the three categories were *Proteobacteria, Bacteroidetes,* and *Firmicutes* at the phylum level. However, at the genus level, *Megamonas, Bacteroides, Prevotella, Fusobacterium, Dialister, Ruminococcus, Subdoligranulum, Alistipes, Faecalibacterium, Bifidobacterium, Escherichia-Shigella,* and *Lachnoclostridium* were the most prevalent microbial taxa. Additionally, although the prevalence of Proteobacteria and Firmicutes in people with diabetes was substantially higher than in the healthy participants, Bacteroidetes were reduced, and the Firmicute/Bacteroidetes ratio (F/B ratio) was greater in T2D/T2D+ clusters than in the healthy category.	65

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Streptococcus, Butyricicoccus, Veillonella		While only the genera [Eubacterium] hallii and Blautia were considerably more significant in the T2D category than controls, the Proteobacteria genus Parasutterella was only considerably higher in T2DM than in the healthy group. Also, when comparing the T2DM and T2D groups, the Firmicute/Bacteroidetes ratio rose, but the Firmicutes phylum declined. Proteobacteria, on the other hand, increased in the T2D group, as evidenced by the species *Blautia*, *Parasutterella [Eubacterium] hallii*, and *Coprococcus* Acetate, propionate, and butyrate levels were considerably poorer in the T2D+ group than in the T2D group. In contrast, the *Bacteroidetes:Firmicutes* ratio was increased in Type 2 diabetes mellitus than in controls. The genera *Prevotella* and *Bacteroides* were thus shown as key contributors to the phylum Bacteroidetes' considerable decline in Type 2 diabetic patients.	
Bacteroides, Subdoligranulum, Prevotella, Lachnospiraceae_incertae_sedis., Enterococcus Escherichia-Shigella, and *Akkermansia.*	316 Chinese	The gut flora makeup and functionality in T2DM patients were significant biomarkers to distinguish diabetic from healthy individuals.	[31]
Faecalibacterium prausnitzii, Streptococcus salivarius, Escherichia coli, Eggerthella sp., Akkermansia muciniphila, Clostridium bartlettii, Bacteroides caccae, Bacteroides finegoldii, and *Collinsella intestinalis*	254 Chinese adult stool samples from untreated pre-diabetic (PreDM, 80), diabetic (TN-T2D, 77), and control (97) subjects.	The KW test detected statistically significant variations in MLG's relative abundances across Pre-DM, NGT, and TN-T2D patients. PreDM persons had diminished levels of *Faecalibacterium prausnitzii* that produce butyrate than TN-T2D and NGT individuals. However, when compared to NGT individuals, MLGs associated with *Eggerthella sp., Streptococcus salivarius* (MLG-6991), and *E. coli* were considerably enriched in Pre-DM. In addition, in comparison with TN-T2D individuals, PreDM persons substantially increased E. coli richness. Furthermore, TN-T2D patients had diminished Clostridium bartlettii and A. muciniphila and enriched predominances of *Bacteroides caccae, Bacteroides finegoldii,* and *Collinsella intestinalis* when compared to Pre-DM and NGT. While numerous Pre-DM and NGT unswerving signatures contrasted with TN-T2D were detected, including an elevated *Akkermansia muciniphila* and a reduced availability of *Bacteroides spp,* the predominance of numerous Firmicutes species that produce butyrate, was significantly smaller in TN-T2D and PreDM likened to NGT.	[43]

Future Perspectives

Due to the roles of genetic factors in several diseases associated with a dysbiotic microbial community, dual treatment approaches (e.g., amalgamating microbiota-targeted and immunotherapy) have been recommended to re-establish the microbiome environment for practical therapeutic communications strategies between the targeted microbial population and the host. To this end, the knowledge of host-microbiota interaction mechanisms at biochemical and molecular levels is critical to the success of these initiatives, showing the need for more outstanding research into microbial community functions. Notably, since these investigations can provide additional information about the host-microbiome interactions that affect normal health, they have been hypothesized to eventually lead to medications targeting microbial communities that can preserve health and manage various conditions.

Considering that T2DM patients are often on numerous prescribed drugs and have other unrelated/related comorbidities, a more rigorous effort is necessary to unravel 'universal' microbiome profiles. This microbiological profile could represent a specific community or several gut microbe populations. Establishing a standard profile for microbiota-targeted therapies creates a substantial metabolic impact-proof host-microbiome intermediary to identify the 'at-risk' vulnerable group(s).

While synbiotics, prebiotics, probiotics, and facilitated microbiota transfer (FMT) have been discovered as treatment regimens that need thorough assessments,[85,86] providing early intervention to susceptible populations, a recent study has also revealed that microbiome transplantation is an effective diabetes prevention measure, showing the need for future studies along this line as well.[87]

Conclusion

Based on the symbiotic relationship between the host and gut microbiota, a deviation from the typical microbiota composition (dysbiosis) in a broad range of ailments, from chronic gastrointestinal to neurodevelopmental disorders, is unsurprising. Hence, developing microbial modulators (e.g., diet, antimicrobials, probiotics, or prebiotics) or microbiota-based remedies can alter the host-microbiome's makeup and substitute a few dysfunctional microbes, depending on the ailment stage and type. Also, investigating whether dysbiosis of the microbiota is a result or a cause of identified diseases, especially T2DM, can change the tactics required to restore symbiosis.

Conflict of Interest

The authors declare no conflict of interest.

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Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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