Chemical Mechanisms and Strategies for the Regulation of Integral Gut Metabolites and Possible Treatments

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Abstract

The production of microbial metabolites, facilitated by the gut microbiome, influences immune function and host physiology. In conditions like inflammatory bowel disease (IBD) and colorectal cancer, such metabolites offer potential therapeutic strategies. This review analyzes the chemical transformations of notable microbial metabolites and their roles as drivers in chemical modulation and enzyme activity. Research into bile salt hydrolases (BSHs) in tandem with 7α-hydroxylase - enzymes that specifically promote the metabolism of bile acids through the catalyzation of reactions that involve primary and secondary bile acids - has led to advancements in current comprehension of the complexities of pathways within the gut microbiome. Recent developments in synthetic bioengineering are given attention, as are the challenges in translating such advancements into clinical approaches. Recent technologies akin to metagenomics and metabolomics have emerged in addition to the identification of metabolites that can be inhibited to further advance clinical practices. Using an understanding of microbial chemistry, current gaps in knowledge are addressed in order to suggest future research to modulate the gut microbiome.

Introduction

Playing a significant role in pathogenesis and host health, the gut microbiome is a conglomeration of microorganisms that reside in the human gastrointestinal tract. Microbial metabolites, which are small molecules that are synthesized by gut bacteria, mediate interactions between the microbiome and the host. Including cellular signaling and regulation of immunity, such metabolites are implicit in host health. Short-chain fatty acids (SCFAs) and bile acids are among the most studied metabolites due to their involvement with many prevalent conditions. A comprehension of the specific mechanisms that involve the gut biome allocates for the expansion of potential therapies to treat metabolic conditions.

However, due to the number of microbial species found in the human microbiome—a strong majority of them being uncharacterized—there are many interdependent mechanisms. Therefore, it is difficult to assess which specific, isolated mechanisms are drivers of each respective process. Because of this complexity, therapeutic approaches that target certain mechanisms may inadvertently affect others. Variations in environmental factors, including diet, and microbial composition also make it difficult to synthesize a universal solution.

Key Gut Microbial Metabolites

A process that predominantly occurs in the liver - the biosynthesis of bile acids is composed of two major enzymatic pathways: the acidic (alternative) and the neutral (classical) pathways. Converting cholesterol into bile acids is the primary objective of these mechanisms. The rate-limiting step is catalyzed by cholesterol 7α-hydroxylase (CYP7A1) as part of the classical pathway; this pathway is credited with a majority of bile acid production (L. Liu et al.). Notable enzymes, including 3β-hydroxysteroid dehydrogenase (3β-HSD) and 7α-hydroxy-4-cholesten-3-one (CYP8B1), have cascading reactions that involve 7α-hydroxycholesterol. This is later transformed from cholesterol by 7α-hydroxylase from the classical pathway. The process of transformation leads to the synthesis of cholic acid (CA) and chenodeoxycholic acid (CDCA) as well as other primary bile acids (L. Liu et al.). Occurring less frequently, the alternative pathway aids the conversion of cholesterol to 27-hydroxycholesterol via sterol 27-hydroxylase (CYP27A1) to formulate CDCA (L. Xiao-Rong et al.). Subsequent bile acid diversity overall has increased.

The maintenance of a steady bile acid pool within the host is ensured by 95% of bile acids being reabsorbed through the enterohepatic circulation after synthesis (L. Liu et al.). However, upon reaching the intestine, their function and composition undergo significant modification. The bile acids are then converted from primary bile acids into secondary bile acids by gut bacteria and the utilization of bacterial enzymes. Removing amino acids such as glycine and taurine allows for the deconjugation of bile acids through bile salt hydrolases (BSH). Furthermore, the respective

conversion of CA and CDCA into deoxycholic acid (DCA) and lithocholic acid (LCA) is facilitated by enzymes like 7α-dehydroxylases (L. Liu et al.). The combination of these chemical transformations plays a role in host metabolism and is impacted by the gut microbiome.

Dysbiosis is a variant of alterations in gut microbiota that corresponds to the imbalance of microbial populations that is correlated with non-alcoholic fatty liver disease (NAFLD) and cholestasis (S. Cao et al.). Studies highlight that particular bacterial populations like Firmicutes and Bacteroidetes phyla are associated with increased levels of DCA and LCA, secondary bile acids that have an impact on host physiology (L. Liu et al.). The efficiency of the enterohepatic recycling process showcases that the overall bile acid pool in humans is estimated to be 3 to 5 grams, with about 0.5 to 1 grams being excreted in feces daily (S. Cao et al.).

The lipid and glucose metabolism pathways are influenced by the biosynthesis of bile acids; bile acids affect metabolic mechanisms through the engagement of nuclear receptors like membrane-bound receptors, including TGR5, and the farnesoid X receptor (FXR). Energy homeostasis and inflammation are further influenced by bile acids (L. Liu et al.).

Cholic acid is a notable factor and primary bile acid—synthesized via the classical pathway—in the emulsification of dietary fats and the facilitation of the absorbance of such fats into the intestine (L. Liu et al.). Beyond digestion, the resultant modulation of lipid metabolism via cholic acid through the activation of FXR allocates gene expression for cholesterol and glucose metabolism. Research demonstrates that in one sample, 50% of the bile acid pool is colic acid, which shows its strong influence on bile acid physiology (L. Liu et al.).
Another primary bile acid is chenodeoxycholic acid (CDCA); this substance activates FXR to modulate lipid and glucose metabolism. One study showed in animal models that this influence of CDCA on metabolism pathways, which account for approximately 30% of the bile acid pool, improves insulin sensitivity (L. Xiao-Rong et al.).

Among secondary bile acids, deoxycholic acid (DCA) is produced via cholic acid's bacterial metabolism. DCA influences the composition of the gut microbiota and regulates energy expenditure. Energy metabolism and glucose homeostasis are impacted by DCA and its activation of TGR5. An emphasis on the role of dysregulated metabolism for DCA can be seen by its elevated levels being correlated with metabolic disorders (S. Cao et al.).

Moreover, lithocholic acid (LCA) is another secondary bile acid—possessing anti-inflammatory properties—that is derived from CDCA. Similarly - while in minor amounts - LCA can increase the activation of FXR, which regulates bile acid synthesis and lipid metabolism. Suggesting a link between bile acid metabolism and liver health, metabolic conditions such as NAFLD are associated with elevated levels of LCA (L. Liu et al.).

Finally, ursodeoxycholic acid (UDCA) is a bile acid with therapeutic implications for the treatment of cholestatic liver diseases (L. Liu et al.). Clinical studies highlight that over 40% of patients treated with UDCA report high efficacy for liver function. This exemplifies how UDCA improves bile flow and reduces hepatotoxicity (L. Liu et al.).

DNA-Interacting Compounds

Colibactin is a microbial metabolite that interacts with DNA. Its synthesis involves microbial interactions and enzymatic pathways: colibactin is produced by particular strains of Escherichia coli, which carries the pks genomic island—a gene cluster encoding approximately 54 genes and the genetic basis for colibactin biosynthesis. Colibactin holds genotoxic properties and correlates with colorectal cancer (L. Xiao-Rong et al.). The mechanisms of colibactin synthesis include cyclization and tailoring reactions prior to the initial condensation of amino acids and fatty acids (L. Xiao-Rong et al.). These mechanisms are facilitated by enzymes, including ClbC, that catalyze the loading of a starter unit onto a polyketide synthase (PKS) and are encoded within the PKS island. Genotoxic effects—through the formation of DNA adducts—are enabled by the final colibacin structure and its intercalation with DNA.

The role of carcinogenesis stems from the ability of colibactin to induce DNA damage as the metabolite interacts with DNA by promoting the breakage of double bonds and interrupting typical replication and repair processes. Furthermore, mutations and corresponding increases in the risk of colorectal cancer are caused by genotoxicity from colibactin. Epidemiological studies showed that 15 to 20% of strains of E. coli among the human gut microbiota possess the pks island and are capable of producing colibactin (L. Liu et al.). Furthermore. Tumor formation has been linked to E. coli which produces colibactan and holds carcinogenic potential (L. Xiao-Rong et al.).

Beyond the genotoxic effects of colibactin synthesis, colibactin biosynthesis has enabled advances in the profiling of other microbial metabolites to monitor their roles in homeostasis and disease progression. These new insights have led to new therapies being developed to minimize the abundance of colibactin-producing strains through the administration of probiotics and inhibitors to target their biosynthetic pathway (L. Xiao-Rong et al.).

Chemical Mechanisms of Microbial Metabolite Transformation

Governed by specific enzymes, the transformation of compounds that interact with DNA and bile acids is regulated by those same enzymes, which regulate the bioavailability and activity of the metabolites. Bile salt hydrolases (BSHs) are one variety of bacterial enzymes that specifically oversee bile acid metabolism through the catalyzation for the deconjugation of the bile acids. Involving the removal of amino acids, like glycine or taurine, from bile acids, the bile acid

transformation produces more hydrophobic free bile acids that are capable of greater microbial modifications (Guzior and Quinn). Another enzyme, 7α-dehydroxylases, converts primary bile acids into secondary bile acids to alter their biological roles. This is driven by hydroxysteroid dehydrogenases and involves the inversion of stereochemistry at specific hydroxyl groups on bile acids (Guzior and Quinn). Moreover, epimerases catalyze the epimerization of hydroxyl groups to further modify bile acid molecules (Guzior and Quinn).

For compounds that are involved with mechanisms that alter DNA, gut bacteria and enzymes like glucuronosyltransferases (UGTs) and cytochrome P450s facilitate conjugation and oxidative metabolism, respectively. Glucuronosyltransferases both promote the extraction of compounds that interact directly with DNA by enhancing the water solubility of the compounds and also increase their bioavailability and biological activity (Guzior and Quinn). Conversely, the activation of DNA-interacting compounds is monitored by Cytochrome P450 enzymes that facilitate oxidative reactions and hydroxylate substrates (K. Hou et al.). However, gut bacteria instead hydrolyze glucuronide by expressing β-glucuronidase to increase the concentration of active forms of DNA-interacting compounds (Guzior and Quinn).

Since the activity of enzymes—such as BSHs and 7α-dehydroxylases—and bacteria vary between individuals, a human can have significant differences in their bile acid profile relative to another human (Guzior and Quinn). Another instance is the concentration of Eubacterium lentum, which can influence the metabolism of compounds like digoxin and other cardiac glycosides. This was demonstrated by a 200% increase in serum levels in the presence of these bacteria (K. Hou et al.). This variation therefore can influence disease progression through influences like NAFLD and cholestasis.

Certain bacterial enzymes can mediate the chemical transformations that are administered by gut microbiota; oxidative and reductive reactions are notable examples of such mechanisms that are integral to bile acid metabolism. Gut bacteria like Clostridium cinders promote oxidation reactions that involve hydroxyl groups on bile acids to convert primary bile acids to secondary bile acids (Guzior and Quinn). Contrarily, the facilitation of the transition between different bile acid species is seen through the NADH-dependent reduction of 3-oxo deoxycholic acid catalyzed by BaiO (Guzior and Quinn).

Conjugation reactions between bile acids and amino acids occur within the gut as well; a recent study highlighted that phenylalanine and tyrosine—variants of amino acids—undergo conjugation with bile acids to form a new class of metabolites known as microbially conjugated bile acids (MCBAs). Suggesting implications for host physiology, the modifications influence receptor activation and bile acid solubility (Guzior and Quinn). What all these types of reactions have in common is their influence on the properties of bile acids. For instance, a marked increase in hydrophobicity can be seen by the reduction of colic acid to deoxycholic acid, which leads to

an increase in its partition coefficient. From metabolic disorders to liver diseases, these chemical modifications can change the biological function of compounds and alter their involvement in conditions.

The production and subsequent transformation of metabolites, such as bile acids and neurotransmitters, is influenced by the interactions between different microbial metabolic pathways. For example, signaling pathways that relate to metabolism and inflammation as well as the innate chemical properties are affected by the deconjugation and dehydroxylation of bile acids by gut bacteria. Deoxycholic acid and other bile acids activate the NF-κB pathway to play a role in inflammatory responses and liver disease progression (K. Hou et al.). Epimerization by gut bacteria can further disrupt pathways with host nuclear receptors such as FXR and TGR5 through the conversion of cholic acid to ursodeoxycholic acid (Guzior and Quinn).

The synthesis of neurotransmitters is a process that is influenced by gut microbes as species like bacteria produce gamma-aminobutyric acid (GABA). GABA is a notable neurotransmitter that is involved in pathways that modulate mood and anxiety (Y. Chen et al.). Another neurotransmitter that influences serotonin synthesis in the brain is tryptophan, which is modulated by bacterial strains that include Lactobacillus and Escherichia coli. Therefore, cognitive function and mental health can be impacted by microbial composition, as they can alter neurotransmitter levels (K. Hou et al.).

Since bile acids are able to constitute signaling molecules to influence drug metabolism, the gut-liver axis exemplifies the interaction between microbial mechanisms: gut bacteria adjust the ability of bile acids produced in the liver to regulate nuclear receptors, controlling the expression of enzymes that stabilize drugs. One study showed that the metabolism of pharmaceuticals like tacrolimus is reduced in efficacy as gut bacteria will produce reduction products (S. Tsunoda et al.).

The task of modulation of host metabolism and immune responses can befall microbial metabolites like microbial short-chain fatty acids (SCFAs). Produced via gut bacteria fermenting dietary fibers, SCFAs like butyrate exert anti-inflammatory benefits and enhance intestinal barrier function (K. Hou et al.). Consequently, SCFAs have been linked to the reduction of risk for conditions like inflammatory bowel disease (IBD). This underscores the role that microbial metabolites play in the maintenance of gut health.

Chemical Strategies for Modulating Microbial Metabolism

Inhibitors can influence the production of undesirable metabolites by selectively regulating the activity of enzymes in the gut microbiome, which allocates therapeutic potential for such inhibitors. For instance, trimethylamine-N-oxide (TMAO), a metabolite implicated in

cardiovascular diseases, can be reduced by the inhibition of a microbe known as TMA lysase. This blockage of TMA production can be overseen by 3,3-dimethyl-1-butanol (DMB), an analog of choline. DMB also has the added benefit of preventing damage to the bacteria responsible for its synthesis. Research showed that attenuation of atherosclerotic lesions and subsequent reductions in plasm TMAO levels stem from a murine model treated with DMB. This highlights the ability of such inhibitors to modulate cardiovascular risk factors (Sharpton et al.).

To reduce toxicity levels that correlate with chemotherapy, bacterial β-glucuronidase—an enzyme that is key for the conversion of the chemotherapy prodrug irinotecan (CPT-11) into its toxic form, SN-38—should be targeted as well. This will preserve the efficacy of cancer treatments that involve chemotherapy while simultaneously promoting gut health. Inhibitors that can target β-glucuronidase without affecting other enzymes have been identified through the use of high-throughput screening; thus, the ramifications of irinotecan were reduced in animal models (N. Aggarwal et al.). Similar efforts to inhibit glycosyltransferases led to the development of compounds with the ability to disrupt microbial cell wall synthesis due to the glycosyltransferases' involvement in bacterial glycan biosynthesis. One such variety of glycosyltransferases, UgtP, was inhibited in Staphylococcus aureus in order to resensitize methicillin-resistant strains (MRSA) to antibiotics (Calles-Garcia and Dube).

Engineered Bacteria Producing Beneficial Metabolites

Synthetic biology offers another approach to utilizing chemical strategies to affect these mechanisms. Bacteroides species that were originally tasked with producing indole, a microbial metabolite linked to the progression of chronic kidney disease, were engineered to prevent the synthesis of indoles. Mouse models of kidney disease that were administered these synthetic Bacteroides saw reduced levels of the toxic metabolite indoxyl sulfate. Therefore, new therapeutics for managing metabolic disorders can be implemented through the control of enzyme inhibition and microbial metabolite production. However, beneficial metabolites can also be produced through the utilization of synthetic biology: optimization of the production of butyrate via metabolic models at the genome-scale resulted in the successful synthesis of the SCFA after prior failures to engineer Bacteroides thetaiotaomicron to produce butyrate (J. Arnold et al.) In order to treat diseases that display metabolite imbalances in pathogenesis, modifying metabolites through synthetic biology should be explored.

Coli strains can also be engineered to facilitate the chemical modulation of microbes; the E. coli strain SYNB1618 was engineered to treat phenylketonuria (PKU) through the metabolism of phenylalanine. Clinical trials underscored the safety and practicality of this potential therapeutic through incremental increases in downstream strain-specific metabolites to provide proof of mechanism for therapeutic use (J. Arnold et al.). While not constituting E. coli strains, engineered Lactobacillus lactis and Bifidobacterium longum have also shown potential to

modulate microbial metabolism. In mouse models of colitis, interleukin-10 (IL-10)—an anti-inflammatory cytokine—was produced through these two engineered probiotics to significantly reduce inflammation. (M. Charbonneau et al.); (J. Arnold et al.).

For cancer therapies, the expression of immune-modulating molecules, including PD-1 antibodies' ectodomain, can be facilitated by the engineering of bacterial extracellular vesicles (BEVs). Since the ectodomain of the antibodies will bind to the PD-L1 on tumor cells, the approach will be able to regulate the tumor microenvironment to increase antitumor efficacy (M. Charbonneau et al.).

Therapeutic Potential and Challenges

Inflammatory bowel disease (IBD) can be addressed through therapies that involve SCFAs that promote properties that deter inflammation, which is optimal when regulating immune responses. In particular, SCFAs were seen to significantly reduce pro-inflammatory cytokines and chemokines in clinical trials involving IBD. Butyrate impacts these inflammatory pathways by inhibiting IL-1β-induced IL-6 and IL-8 mRNA levels in human enterocytes (N. Alsharairi). A combination of supplementation and microbiota modulation to enhance SCFA production is suggested to be a beneficial tactic, as SCFA levels in IBD patients are often decreased (N. Alsharairi).

SCFAs can further be implemented as a therapeutic for colorectal cancer, as the fatty acids are associated with modulating cell proliferation and apoptosis. Acting as an epigenetic modifier, butyrate inhibits tumor growth and inflammation through gene expression. A study that administered butyrate to colorectal cancer cells successfully induced apoptosis, suggesting the potential of butyrate for efficient cancer treatment. Furthermore, increasing butyrate can increase CD8+ T cell activity to promote the suppression of tumors: in mice models that had tumors, organisms that were treated with butyrate suggested a complement cancer therapy could be used with SCFAs, as the models saw a reduction in tumor size compared to controls (Y. He et al.).

The use of fecal microbiota transplantation (FMT) in the treatment of IBD and colorectal cancer has been explored in clinical trials. FMT saw a high clinical success rate when treating recurrent Clostridioides difficile infections (A. Gupta et al.) This underscores its ability to modulate gut microbiota and restore optimal health. Furthermore, prootics in IBD treatment only were explored in a meta-analysis to highlight the reduction of relapse rates in ulcerative colitis after administration of probiotics to further underscore the potential efficacy of microbiota modulation as a therapeutic approach (T. Hitch et al.).

Beyond butyrate, propionate—another SCFA—can regulate lipid metabolism and insulin sensitivity. Specifically, propionate promotes population growth regulatory T cells (Tregs) to

improve metabolic outcomes and reduce systemic inflammation. This can be particularly useful for conditions like obesity and metabolic syndrome (T. Hitch et al.). Improvements in insulin sensitivity and metabolic profiles were seen in clinical trials that involved the administration of higher levels of SCFAs. High-fiber diets in clinical trials were further explored, as one study saw participants who were given a high-fiber diet have a reduction in insulin resistance. The use of probiotics as supplements was also used as a potential weight management and metabolic health treatment; a randomized controlled trial saw that after 12 weeks of usage of probiotics, participants experienced reductions in BMI and waist circumference.

While these developments remain promising, the issue of the complexity of the gut microbiome itself must still be addressed. Since there are a significantly large number of microbiota found within the gut and the interactions between microbial species and their metabolites are highly intricate, disruptions in one pathway through a therapeutic may lead to inadvertent ramifications on other mechanisms. A single microbial species will produce different metabolites depending on the diet of the host organisms and the overall microbiome composition. Therefore, predicting therapeutic outcomes targeting a specific bacteria can become difficult (T. Hitch et al.). Furthermore, while there is abundant evidence supporting a correlation between metabolites and modulating inflammation or immune responses, the precise pathways that carry out these benefits are not yet fully understood. For example, butyrate's role in enhancing Treg populations is still relatively recent in innovation, so more research is required to fully develop high efficacy for human therapies (Y. He et al.).

In terms of practice, there are regulatory barriers such as approval for microbiome-based therapies (FMT, or engineered probiotics) that are still underdeveloped. Further clinical studies must be enacted to ensure safety for administration. On an international scale, variances in classification among regulatory agencies for respective nations of microbial metabolites and probiotics may lead to unequal distribution and approval of treatments. Variations in strain selection and formulation also make standardization of microbial products difficult. Quality control standards in therapeutic manufacturing should be established to ensure uniform efficacy.

While most of the onus of microbial therapeutics is on the healthcare sector, patient compliance could prove difficult as well: requiring long-term dietary changes and probiotic supplementation, alterations in the gut microbiome can be impractical to expect patients to fully maintain. Moreover, changes in food selection may not be accessible for all patients due to cost or locational accessibility.

Potential Side Effects and Resistance Development

Significant modulations in the gut microbiome may cause unintended side effects. For example, symptoms of gastrointestinal symptoms—diarrhea and bloating—can be caused by the

administration of FMT, even with its efficacy in treating C. difficile infections. Moreover, the transference of pathogenic microbes or unknown metabolic disturbances makes the long-term effectiveness of the treatment difficult to assess (A. Gupta et al.).

Some hosts may also be immunocompromised, which makes infections particularly concerning. While beneficial in most cases, bacterial strains like Lactobacillus are associated with bacteremia in significantly vulnerable patients (T. Hitch et al.). During the initial stages of probiotic supplementation, gastrointestinal side effects are also common (T. Hitch et al.).

Resistance may also be developed as antibiotic treatment can disrupt the gut microbiome and reduce its microbial diversity. Subsequent growth of resistant strains of bacteria could then arise, making effective treatment more arduous. Similarly, the gut microbiome can become resistant to interventions to modify its composition; probiotic supplementation or dietary changes can develop resistance in certain microbial taxa and reduce the intervention's overall efficacy in the patient.

Future Directions

Building on the lack of full understanding of the entirety of metabolic pathways found within the gut microbiome, there is a lack of comprehensive metabolite characterization: only a small portion of the 50,000 microbial metabolites have been studied in detail (S. Ghosh et al.). Tools like CRISPR-Cas9 for gene editing and high-throughput screening should be employed in future research in order to uncover these mechanisms.

Dependent reactions where one microbe’s metabolic byproducts are used to synthesize another product via a separate microbe must be explored as well to better comprehend and analyze the interdependencies that lie within the gut microme. New insights for microbial communities that affect host health could be uncovered by the use of co-culture experiments, while longitudinal studies relating to the disease progression and diet of a host can also track the changes in microbiota over time. Coupling these approaches with multi-omics could yield a new perspective on how to establish practical therapeutics.

The gut-brain axis that links microbiota in the gut to brain function could be explored further by establishing connections between particular microbial metabolites and their cognitive and behavioral effects. SCFAs have been shown to influence cognitive function and mood, and this understanding could lead to treatments being developed for neurological disorders like depression and anxiety utilizing microbial metabolites—not just limited to SCFA but other compounds as well (Y. Liu et al.). Moreover, environmental factors like pollution and urbanization and their influence on gut flora can lead to innovations in environmental microbiology as such data that can be utilized for public health strategies (A. Mayorgas et al.).

Revealing the diversity of the gut microbiome, metagenomics allocates the sequencing of whole microbial communities without necessitating cultures. This allows for the discovery of new microbial species and metabolic pathways in order to synthesize bioactive metabolites (S. Ghosh et al.). The use of techniques such as mass spectrometry (MS) and nuclear magnetic resonance (NMR) in metabolomics has also led to the profiling of microbial metabolites and their roles in host health. With advancements in machine learning and artificial intelligence, large multi-omics datasets can be analyzed at a much higher rate to assess the capability of the metabolites as biomarkers for disease (Lavele and Sokol). In order to determine the biological activity of the metabolites, the usage of more sophisticated versions of high-throughput screening can foster the discovery of microbial metabolites that could serve as therapeutic agents for treating conditions like metabolic disorders and cancer. (Y. Liu et al.).

Conclusion

With implications in the pathogenesis of many variations of disease, utilizing chemical strategies to modulate gut microbial metabolites can significantly influence host health; new therapeutic approaches that incorporate disruptions of mechanisms that lead to pathogenesis can include chemical inhibition of the microbial enzymes or engineered organisms. However, these new approaches also must address challenges, including the variability in individual responses. The usage of high-throughput screening and bioinformatics will aid in the identification of target microbial metabolites and mechanisms; this allocates future progress toward personalized therapies based on the specific composition of each patient's gut microbiome.

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