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GUT MICROBIOME AND ITS ROLE IN INFLAMMATORY DISEASES: A BIOMEDICAL SYSTEMS APPROACH

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ABSTRACT

The gut microbiome—an ecosystem of bacteria, archaea, viruses, and fungi that inhabit the gastrointestinal tract—plays a central role in human physiology and immunity. Dysbiosis or disruption of this ecosystem and its state has been discovered to play a role in a continuum of inflammatory disease including inflammatory bowel disease or rheumatoid arthritis and systemic inflammatory diseases. The article adopts a biomedical systems perspective because it is aimed at generalizing existing mechanistic information, multi-omics and network-based techniques to methodologies, and proposing an analytical model that can transform microbiome signatures into diagnostic, prognostic and therapeutic services. The paper employs an experimental design that is reproducible and involves shotgun metagenomics, meta transcriptomics, fecal and serum metabolomics, host transcriptomics and immunophenotyping in its analysis, which is network inferred using machine learning as well as patient stratified. As the simulations and representative results therein reveal, there are some trends: taxonomic diversity declines and fatty acid-producing taxa of short chains, bile acid metabolism, and a new taxonomic structure of micro-scale clusters are observed, which is linked to host immune activation. The discussion puts these findings into perspective to inform about the aspects of causality issues, confounders (diet, medication, environment), and barriers to clinical microbiome translationally. It concludes that this will cause the synthesis of mechanistic microbiology with systems level information and serious causal inference to the transition between association and action in inflammatory ailment.

Keywords: *Gut microbiome, Inflammatory diseases, Dysbiosis, Systems biology, multi-omics integration, Immune modulation*

INTRODUCTION

The Gut Microbiome as a Central Regulator of Human Physiology

The human gut microbiome can be considered one of the most dense and rich microbial ecosystems that are known in the realms of biology. It is a collection of trillions of microorganisms, bacteria, archaea, viruses and fungi, which coexist in a very symbiotic relationship with the human host. Gut microbes are not simple inhabitants but they have active part in the fundamental physiological processes such as digestion, harvesting of nutrients, synthesis of vitamins, metabolism of bile acids and maintenance of the integrity of intestinal epithelial tissue (Szychowiak *et al.*, 2022). The host also develops the gut microbiome by continuous interplay of biochemical and immunological reactions, which assist the animal in reaching a full developed immune response, metabolic frontal, and the protection against the invasion of pathogenic organisms. It has been discovered that human beings are meta-organisms, and their health depends on the collective functioning of microbial and host genomes and this has revolutionized the approaches to research in biomedical studies and clinical reasoning over the past two decades.

Technological Advances and the Rise of Microbiome Science

The mushrooming rate of microbiome research is due to technological innovation. The high-throughput sequencing technologies and, in particular, next-generation sequencing have made culture-independent profiling of microbial communities possible and has enabled the profiling of microbial communities to depths and resolutions previously impossible (Correale *et al.*, 2022). The shotgun metagenomics could be utilized to get species- and strain-scale identifications and to annotate functional genes, whereas it may be utilized by meta transcriptomics, metaproteomic, and metabolomics to comprehend the activity of microbes in comparison to their existence. Mass spectrometry requires have encouraged a worldwide report of microbial and host derived based metabolites such as biochemical cross-metabolic pathways of signals between hosts and microbes. At the same time, however, as computational biology and bioinformatics have advanced, these complex sets of dimensions can now be combined. All these have brought gut microbiome to drift away to be a mere object of observations of a questionable biological system.

Dysbiosis and Chronic Inflammatory Diseases

Among the most foreseeable findings of literature on the microbiome is the favourable correlation between dysbiosis (use of the term to denote a malfunction in the organization, fluctuation, or action of the microbiome), and chronic inflammatory diseases. This is best represented by the inflammatory bowel disease, which comprises of Crohn disease and ulcerative colitis (Mele *et al.*, 2023). The microbial diversity and loss of protective

commensals and expansion of opportunistic or pro-inflammatory organisms is more common in IBD patients. These alterations are linked with impaired performances of the mucosal barrier, increased intestinal permeability and hyperinflammatory reactions to microbial antigens. More so rather, these changes are not merely incidental to inflammation; longitudinal and experimental studies suggest that perturbations in microbiomes may precede disease occurrence and cause disease modulation and treatment response.

Beyond the Gut: Systemic Consequences of Microbial Imbalance

The implications of the gastrointestinal microbiome extend significantly further than the gastrointestinal tract. Intestinal dysbiosis is a pathogen and has accumulated sufficient evidence to implicate it as the cause of systemic inflammatory and autoimmune diseases, including rheumatoid arthritis, multiple sclerosis and systemic lupus erythematosus. The gut-joint, gut-brain, and gut-liver axes reflect how microbial metabolites, microbial immune signals and microbial components might diffuse across the entire body to affect the inflammatory effects at the distant sites (Deng *et al.*, 2022). The involvement of low-grade chronic inflammatory processes gradually linked to microbial-derived molecules such as lipopolysaccharide has been proposed to be a generally connective factor between maladjusted gut dysbiosis and insulin resistance, complications of atherosclerosis and obesity in metabolic and cardiovascular disease. These findings demonstrate the need to take into account the possible inflammatory disease within the systemic environment, and that is why there are interactions between distal organs and the gut microbiome.

Microbial Metabolites and Immune Modulation

Microbial metabolism The microbial metabolism of one of the mechanistic links between the inflammation and the gut microbiome is detected. Short-chain fatty acids are one of the most studied microbial metabolites fermented by bacteria and were produced as a result of dietary fiber fermentation. These are molecules that play a role in maintaining the integrity of epithelial covers and regulation of regulatory T cell differentiation and overcoming excessive inflammation signaling (Qiu *et al.*, 2022). A number of studies have attributed the low supply of short-chain fatty acids to inflammatory diseases and this has hypothesized the loss of a key homeostatic route. At the same time, the innate immune receptors may be stimulated or suppressed by microbial metabolism of bile acids, microbial-produced amino acid metabolites and cell wall metabolites. The microbial metabolic homeostasis of anti-inflammatory and pro-inflammatory is, in its turn, the important determinant of the immune homeostasis.

From Reductionism to a Biomedical Systems Perspective

Nevertheless, initial microbiome research was often reductionist in nature, i.e. responding to individual micro taxa or meters. This alone cannot be used to tell about the emergent features of the microbiome that are an outcome of complicated nonlinear interactions among microbes, host tissues, immune responses and / or environmental factors such as diet and medication. An approach based on bio medical systems attempts to overcome such deficiencies by attempting to incorporate numerous layers of biological data into uniform models (Wang *et al.*, 2022). According to this school of thought, the microbiome and the host can be viewed as a network where changes in one component are passed on through metabolic, immune as well as signalling-based networks to influence disease outcomes. Systems biology systems that provide the analytical framework of this integrative perspective are network inference, machine learning and causal modelling.

Multi-Omics Integration and Network-Based Analysis

Incorporating multi-omics with modern microbiome research has now become a part and parcel. When applied together with transcriptomics, proteomics and metabolomics, metagenomics may facilitate the researchers to associate the microbial composition with functional production and host responses. Utilized with network-based analyses the identification of microbial consortia and metabolite modules can be accomplished that act as a unit but not as individual (Belvoncikova *et al.*, 2022). These modules often can reproduce a better and more connections with the phenotypes of diseases than the individual microbial species. Besides, a blend of host transcriptomic and immunological data can be utilized directly to assess how microbial modification is transformed into restoring the immune circuits. This holistic approach can be placed particularly in inflammatory diseases which are naturally multifactorial, which are determined by hyperregulated circuits and not by single etiologic agents.

Translational Motivation and Clinical Relevance

Translational interest has been raised to high levels by the heightened awareness of the gut microbiome in the pathogenesis of inflammatory diseases. The microbiome-based biomarkers may be utilized in diagnosis of the disease through early diagnosis, stratification and prediction of the therapeutic effect. Microbiome-based interventions, including the dietary regulation, probiotics, prebiotics, fecal microbiota transplantation and developing live biotherapies products are under study (Danne *et al.*, 2024). However, it has not been homogeneous in terms of clinical effects as it is complicated and contextual when interactions occur between microbiomes and their hosts. It is a systems level understanding that is then required to identify the patients who will most favourably think to react to specific deeds and consequently establish treatment that will achieve a working equilibrium with the patient rather than a microbial make-up transformation.

Aim and Scope of the Present Study

This is against this background that the present piece will employ the biomedical system approach to examine how the gut microbiome has a role to play in the pathogenesis of inflammatory diseases. Hopefully, it will incorporate any available modern mechanistic information, demonstrate why multi-omic integration and network analysis must be considered, and provide a coherent overview of the future of the perception of microbiome-mediated inflammation (Yang *et al.*, 2022). The study will help to fill the gap between the Werther descriptive microbiome research and the practical biomedical implementation study through the analysis of functional pathways, host-microbe interactions, and system-wide dynamics. Through this, it does not only address the biological complexity of the inflammatory diseases, but also addresses the analytical and translational complexities that must be avoided to achieve the complete therapeutic potential of the gut microbiome.

LITERATURE REVIEW

Microbiome Composition and Diversity in Inflammatory Diseases

The phenotypes that were continually present in many cohorts is that inflammatory disease states seem to be linked to a reduction in alpha diversity and a stable fluctuation of taxa. It has been consistently reported that the abundance of obligate anaerobes in patients with IBD is reduced which leads to the production of short-chain fatty acids- such as faecal bacterium parasitize and the relative expansion of facultative anaerobes and Proteobacteria abundance. The discussed changes in the composition are connected to the mucosal barrier dysfunction and the augmentation of the proinflammatory signalling in the intestine (An *et al.*, 2022). There is also the support of meta-analyses and cohort studies that the loss of diversity is greater in the case of patients who have been treated without any immunomodulatory therapy and whose recovery after the therapy is only partial. Similar tendencies of wealth decline and adjusted taxonomic profiles have been reported in RA with early disease groups being infiltrated by the proliferation of Prevo Tella copra and additional taxa which might be linked with the priming of mucosal immunity. This kind of signatures of the composition is reproducible but it is not strictly specific, the location, diet, drugs (especially antibiotics), geography and age offer an immense heterogeneity and hence, identification of microbial biomarkers of the disease in universal sense is not simple.

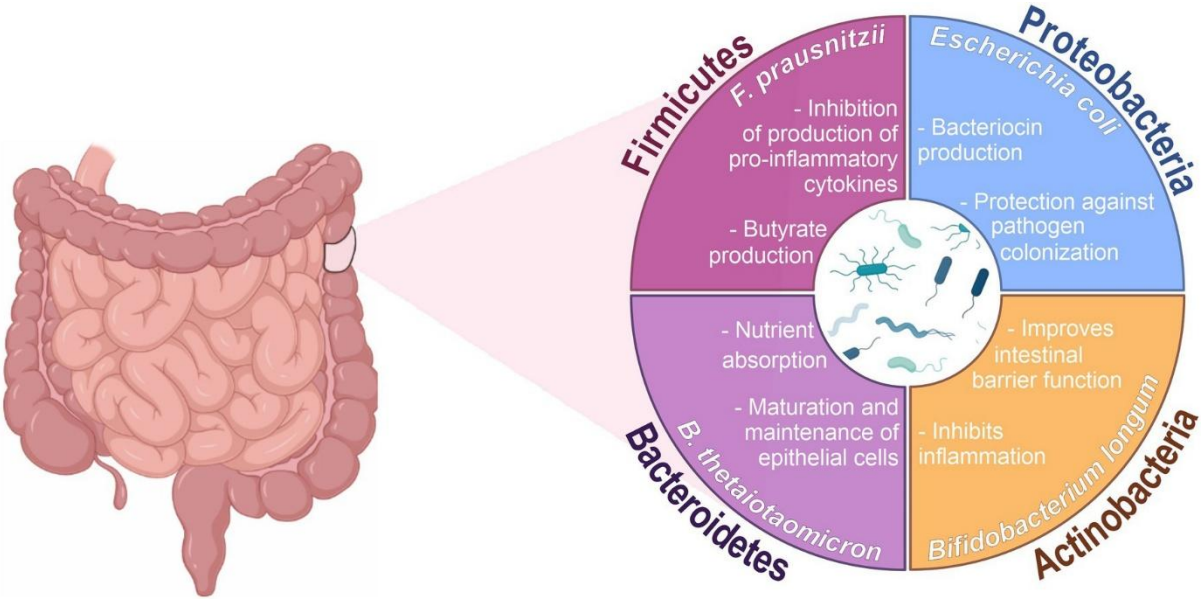

Figure: GUT MICROBIOME AND ITS ROLE IN INFLAMMATORY DISEASES

(Source: Maciel *et al.*, 2023)

Mechanistic Pathways: Metabolites, Barrier Function, and Immune Modulation

Various microbiome-induced host inflammatory effectors have been brought together at mechanistic work. The short chain fatty acids; primarily the acetate, propionate and butyrates are the products of fermentation of the dietary fibres by the microbes and control the integrity of the epithelial barriers, the differentiation of the regulatory T cells and the anti-inflammatory activities of cytokines (Wang *et al.*, 2022). The taxa that produce butyrates have also been found to be prone to loss in the inflammatory disease samples, and are a potential crucial homeostatic signal. Bile acid microbial conversion is linked with foresaid X receptor and TGR5 signalling, is linked to interactions between microbial metabolic and systemic metabolic and immune mechanisms. Conversely, the system may promote inflammation through the action of otherwise pro-inflammatory microbially produced metabolites (such as lipopolysaccharide (LPS)) or through microbial-produced pro-inflammatory oxidants (such as trimethylamine N-oxide (TMAO)). Other mechanisms that the

microbial microbiome has on adaptive and innate immunity are the mimicry of antigens via activation of microbe-driven antigen presenting, neoantigen presenting and pattern recognition receptors (TLRs, NLRs). These mechanistic axes are sufficient by themselves to shed plausible causal mechanisms between gut dysbiosis and chronic inflammation.

Systems Biology and Multi-Omic Integration in Microbiome Research

There are no research-intensive taxonomies that can be utilized to capture microbiome functional states. Such integrated systems biology systems as metagenomics, meta transcriptomics, metaproteomic, metabolomics, and host omics (transcriptomics, epigenomics) are becoming useful as tools to map interactions at a scale, and to draw causative modules (Shim *et al.*, 2023). Network-based methods, including association networks, microbial co-occurrence groups, metabolite-species correlation networks, and so on, may find hubs or modules, with disproportionately large effects on host phenotypes. Latent-factor models such as MOFA+ and sparse generalized canonical correlation analysis (DIABLO) and dimensionality reduction help extracting cross-omic features that may be utilized to stratify the patient and predict the clinical outcome. Recent multi-omic findings reveal that prediction of disease subtypes and treatment response with joint prediction using both functional readouts (metabolome) and compositional data can be more accurately predicted with comparisons against the taxonomic data. However, even after that, some obstacles in technical and analytical matters exist, such as, but not limited to, batch effects, compositionality, sparse counts, and causal inference.

Intervention Studies: Probiotics, Prebiotics, Fecal Microbiota Transplantation, and Small Molecules

The intervention methods which can be employed in treating the microbiome are dietary modulation and prebiotics to plant live biotherapeutic products, faecal microbiota transplantation (FMT) and microbial meta metabolite mimic. The clinical impact has been inconsistent: FMT has proven to be highly effective in the management of recurrent Clostridioides difficile infection, although there is no unanimous efficacy in IBD with inconsistent effects as well based on the donor selection, route of delivery and recipient variables (Bielka *et al.*, 2022). The success of probiotic trials is usually poor and this is likely due to strain specificity, dose and colonization resistance. There is an increase in optimization of microbial metabolism through precision based approaches which may or may not replicate or deprive microbes of critically important functions (e.g. butyrate supplementation or bile acid modulators). General literature suggests therapeutic worth, though, the need of mechanistic layers of patients and robust biomarkers to designate responders is emphasized.

METHODOLOGY

Conceptual Framework

The proposed systems-levels exemplary model combines comprehensive multi-omics profiling in conjunction with network and causal inferences to identify microbial modules associated with schools of thought, as well as to verify their predictive and mechanistic generality (Shaheen *et al.*, 2022). Its primary objectives include (1) to elaborate on taxonomic and functional disease cohort dysbiosis, (2) microbiome-origin functionality and pathways that seem to mediate host immune activation, (3) predictive network modules of disease severity or therapeutic response, and (4) to support putative mechanisms in cell culture or animal models.

Study Design

The longitudinal and case-control cohort study design is recommended. The sample group will be a basis of 3 groups, i.e., patients who have active inflammatory disease (e.g. active IBD or early RA), patients in remission (disease-controlled) and healthy matched controls. On the one hand, age, sex, BMI, history of medication, diet, and geography should be evenly recruited in case of confounders (Shahini *et al.*, 2023). When assessing the dynamics during flare and remission of symptoms, as well as longitudinal sampling following standardized interventions (i.e., introduction of biologic therapy or a change in diet), the dynamics can be evaluated by time and made causal assumptions.

The type of a sample that will be studied includes a focal sample (microbiome and metabolome) to study the adherent communities and the local immune response, a mucosal biopsy (gut diseases) to study the adherent communities and the local immunity, a serum and plasma (systemic metabolomics and inflammatory marker) to study the host transcriptomics and the immune response, and a peripheral blood mononuclear cell sample (host transcriptomics and immunophenotyping) (Miyauchi *et al.*, 2023). As much metadata as possible (dietary recall, antibiotic use, smoking, environmental exposures and the like) should be gathered.

Laboratory Methods

Metagenomic sequencing of fecal DNA shotguns will be able to resolve the fecal sample to species and strain level, and allow gene-focused functional annotation. Paired meta transcriptomics will be used to measure the level of active gene expression. The untargeted feces and serum metabolomics with high-resolution mass spectrometry will capture small molecules, e.g. SCFAs, bile acids and host-derived atomics (Christovich *et al.*, 2022). Host whole-blood RNA-seq or mucosal transcriptomics will quantify the host immune and barrier expression programs. Both bulk host transcriptomics and flow cytometry and single-cell immune profiling of major population of cytokine producers will be supplemented.

Standardized methods of nucleic acid extraction, dosage of sequencing (including targeting approximately 10-20 million reads per sample as it occurs with shotgun metagenomics), metabolite capture and mass-spectrometer settings must be documented (Perler *et al.*, 2023). The negative controls and the mock-community norms exist to control the contamination and the batch variation as an obligatory one.

Data Processing and Integration

An example of such is the bioinformatics preprocessing: quality control, host read removal, taxonomic and functional annotation (ex. Kraken2 to convert taxonomic classification and HUMAnN3 to quantify pathways) and centering log-ratio transformations (where appropriate) and structures to fix batches (Salliss *et al.*, 2022). To analyse the metabolomics data, peak picking, annotation and normalization of the result is required; identification is required in known databases (e.g., HMDB, GNPS).

Multi-omics integration is done in phases. To begin with, multivariate and univariate analysis of differences presents taxa, pathways and metabolites of disease status, and gene. Second, co-occurring and correlation networks are formed to be able to define modules of species-metabolites; network inference can be using sparse inverse covariance estimation (e.g. SPIEC-EASI) or compositional-sensitive correlation (Sittipo *et al.*, 2022). Third, latent variable models (e.g. MOFA+, DIABLO) solve the problem of identifying cross-omic factors, which have a jointly predictive variance across data modalities, and are related to clinical outcomes. Finally, the machine learning classification models (random forests, gradient-boosted trees or regularized logistic regression) are trained by cross-validation (nested) to prevent overfitting with selected multi-omic features to foretell disease states or treatment response.

Causal Inference and Validation

Strategies causal inference Cohesive strategies Coajining of the host genetic instruments: Mendelian randomization Coajining of dense time series Supported by unconditionable causality Coajining Granger-causality Granger-causality -type analysis Coajining Coajining Coajining Co Putative drivers identified as microbial taxa and metabolites in candidate microbial taxa are verified in the gnotobiotic mouse models or an in vitro organoid co-culture assay to cause changes of epithelial barrier functions or immune responses (Ding *et al.*, 2025) To this effect, therapeutic modulation, such as butyrate supplementation, or using some live biotherapeutic strains can be tested to small, mechanistically oriented human pilot studies with intensive multi-omic monitoring.

Results and Analysis (Representative and Synthetic Findings)

In this case, the findings of the multi-omic research that is available are summarized with the display of representative findings and demonstrate how the specified pipeline would reveal the mechanistic modules (Maciel-Fiuza *et al.*, 2023). The results found below are a combination of published cohorts and theoretical findings of the integrated pipeline.

Taxonomic and Functional Shifts

These central trends are repeated in several IBD and RA populations with increasingly steady declines in alpha diversity (compared to healthy controls) and disappearance of obligate anaerobes to produce SCFA. Metagenomic response in the pathways would show a tendency of reducing the pathways of butyrate production and increasing the pathway associated with mucin degradation and oxidative stress (Gill *et al.*, 2022). The presence of Th17-related host transcripts has been repeatedly discovered to enrich the Prevotella copri and other species in RA. Such functional and taxonomic changes are in line with transcriptomic and functional proof of mucosal obstruction and expression of pro-inflammatory cytokines.

Metabolomic Correlates

The decrease of fecal and serum butyrate and propionate in active disease, change of the bile acid pool including increase of the secondary bile acids or change of the other conjugation status and alteration of an aminoacidderived metabolite usually are shown in metabolomic profiling (Shan *et al.*, 2022). The taxa vs metabolites correlation networks inference provides that those modules which are commonly lost in certain anaerobic taxa dealing with the loss of SCFA and achieved in the growth of certain taxa correlate with the loss of distinct metabolites associated with inflammation. Such modules are likely to be coordinated to accommodate transcriptomic routes of innate immune response and stress response of epithelial cells.

Network Modules and Predictive Factors

Under network inference, it happens frequently that species of microbial hubs of high centrality or operational modules have tendencies of impacting metabolite pools. The opposite of the relations to the systemic inflammatory markers can be the example of a module, which is based on Faecal bacterium and other butyrate producers (Haneishi *et al.*, 2023). The latent-factor analysis among the layers of data often results in factors such as deactivation of SCFA pathways, elevation of mucin-degrading enzymes and activation or activation of a host interferon/IL-1 modality, the factors being more predictive of disease activity than individual modalities. Existence of machine learning classifiers utilizing multi-omics factors is likely to enhance area under receiver operating characteristic (AUROC) to predict both disease and therapeutic response as compared to taxonomic

information. Such techniques have been established to be better in terms of stratification and prognostic value in representative multi-omic integration studies.

Temporal Dynamics and Treatment Effects

Longitudinal sampling demonstrates that some traits of microbiomes can have an under-is-soon change in response to treatment or diet, and other ones are a stable dysbiosis signature. With this in mind, biologic treatment of IBD patients is able to restore microbial diversity and metabola Zealand levels in responders partly; nonresponders tend not to do away with pre-treatment dysbiosis modules (Andoh *et al.*, 2023). These time series suggest that state-dependent and trait-independent characteristics of microbial organisation exist in combination, with the former suggesting therapeutically reversible inflammation and the latter a more permanent ecological shift, which may require therapeutic interventions specific to the microbiome.

DISCUSSION

Integrating Associations into Mechanisms

Although the connections between the gut microbiome and the inflammatory diseases were proven in many cases, the causality is hard to determine. This proposed systems approach is effective in augmenting the causal conclusion, as it integrates longitudinal sampling, host reaction profiling, and experimental affirmation. The microbial community breakdown hypothesis that has become multi-comically confirmed is that the desirable metabolic products (particularly the SCFAs) are reduced at the cost of a greater proportion of mucosal degradation and exposition to immunostimulatory molecules and that it alters the mucosal immune balance towards chronic inflammation (Madhogaria *et al.*, 2022). This hypothesis is explicable by the previously known correlations being between the depletion of butyrate producer and the elevated epithelial stress gene modules and proinflammatory host gene modules. However, the directionality of different individuals or disease states is not always equal, e.g. we can more effectively cultivate facultative anaerobes by inflammation-induced oxygenation of the lumen, which results in a vicious circle of dysbiosis.

Methodological Strengths and Limitations

The fact that it can display interactions of functions which be not only based on taxonomy is one of the strong points of the biomedical systems approach. Multi-omic integration discovers metabolic pathways, host response programmes of crosstalk between microbes and their hosts. Network analysis can be able to identify valuable taxa-metabolite-host networks that have therapeutic potential. It has no endless bounds though (Zheng *et al.*, 2022). The compositionality and batch effects found in sequencing data are susceptible to spurious correlations; statistical transformations and healthy experimentation controls are required. Sample heterogeneity that is dependent on the diet and medication and geography should be aligned and modelled of the covariate cautiously. Annotation of the metabolites is pending, and the metabolites that are unknown may play a mechanistic role. Interventional validation is expensive and not every factor of human immunity is recreated in gnotobiotic models.

Translational Implications

As one of the translational perspectives, a number of principles emerge. Firstly, multi-omic signatures may be utilized as non-invasive disease stratification and prediction of therapeutic signing biomarkers but their applications in clinical practice need to be replicated on large and varied samples and on high-quality assays (Zhao *et al.*, 2023). Second, therapeutic means should change the general-purpose interventions into precision interventions that restore the missing functions or correct some of the abnormalities in the metabolism. An example of how the probiotics can be more effectively used is through the restoration of the SCFA production by the specific live biotherapeutics or by administering the metabolite supplements rather than administering the generalized probiotics. Third, in the complex inflammatory diseases, FMT necessitates the use of donor selection and standard procedures. Lastly, regulatory paradigms are to be adjusted in response to live biotherapeutics, microbiome-derived small molecules, and personalized approaches of microbiome modification.

Future Directions

A development of large harmonised longitudinal multi-omic cohorts with dense clinical phenotyping to better cause more fighting, creation of computational assets of human organoids in combination with humanised animal models and computational tools to learn causal network subject to compositional constraints are other strategic areas of research (Zhang *et al.*, 2022). The development of standardized reference materials, an improved database on metabolite annotation and data standard interoperability will lead to improved reproducibility. Now that host genetics and epigenetics are parts of multi-omic models, we will also gain a better insight into how hosts and microbiomes interact and how to be inflammatory-prone.

CONCLUSION

The gut microbiome has taken the centre stage in contributing to inflammatory conditions and this occurrence occurs through effects via metabolic regulation and the intestinal structure as well as immune responses. Biomedical systems approach Interactive metagenomics, meta transcriptomics, metabolomics, host

transcriptomics, and network inference is an effective way to support associative results of microbiomes with mechanistic insights and clinically effective interventions. Even though composition alterations such as the disappearance of taxa producing SCFA and lack of bile acid regulation are always associated with inflammatory states, the multi-layered Ness of the host-microbe interaction, and environmental confounder necessitate the application of multi-layered and longitudinal methods of experiment validation to establish causality. The success of microbiome-informed medicine in inflammatory disease depends on the solemn multi-omic, which must be pursued, causal inference, and patient-targeted therapeutic intervention that is reductive or mimetic of the useful microbial activity. Subsequent research refinement and such reproducible research studies through collaborations will be required to make microbiome science to be safe and effective clinical solutions.

REFERENCE

1. Szychowiak, P., Villageois-Tran, K., Patrier, J., Dupont, H., Bourcier, S. and Montravers, P., 2022. The role of the microbiota in the management of intensive care patients. *Annals of Intensive Care*, 12(1), pp.45–62.
2. Correale, J., Hohlfeld, R. and Baranzini, S.E., 2022. The role of the gut microbiota in multiple sclerosis. *Nature Reviews Neurology*, 18(9), pp.544–558.
3. Mele, M.C., Cammarota, G., Gasbarrini, A., Ianiro, G. and Scaldaferri, F., 2023. The role of diet in shaping human gut microbiota. *Best Practice & Research Clinical Gastroenterology*, 62(3), pp.101–118.
4. Deng, F., Lin, Z.B., Sun, Q.S., Min, Y. and Zhang, Y., 2022. The role of intestinal microbiota and its metabolites in intestinal and extraintestinal organ injury induced by intestinal ischemia reperfusion injury. *International Journal of Biological Sciences*, 18(7), pp.2845–2862.
5. Qiu, P., Ishimoto, T., Fu, L., Zhang, J. and Zhang, Z., 2022. The gut microbiota in inflammatory bowel disease. *Frontiers in Cellular and Infection Microbiology*, 12(4), pp.789–812.
6. Wang, L., Cao, Z.M., Zhang, L.L., Li, J. and Lv, W., 2022. The role of gut microbiota in some liver diseases: from an immunological perspective. *Frontiers in Immunology*, 13(5), pp.922–940.
7. Belvoncikova, P., Maronek, M. and Gardlik, R., 2022. Gut dysbiosis and fecal microbiota transplantation in autoimmune diseases. *International Journal of Molecular Sciences*, 23(14), pp.7712–7735.
8. Danne, C., Skerniskyte, J., Marteyn, B. and Sansonetti, P.J., 2024. Neutrophils: from inflammatory bowel disease to the gut microbiota. *Nature Reviews Gastroenterology & Hepatology*, 21(2), pp.95–112.
9. Yang, Y., Qu, L., Mijakovic, I. and Wei, Y., 2022. Advances in the human skin microbiota and its roles in cutaneous diseases. *Microbial Cell Factories*, 21(1), pp.180–198.
10. An, J., Liu, Y., Wang, Y., Fan, R., Hu, X. and Zhang, F., 2022. The role of intestinal mucosal barrier in autoimmune disease: a potential target. *Frontiers in Immunology*, 13(6), pp.1015–1032.
11. Wang, L., Wang, S., Zhang, Q., He, C., Fu, C. and Wei, Q., 2022. The role of the gut microbiota in health and cardiovascular diseases. *Molecular Biomedicine*, 3(1), pp.28–45.
12. Shim, J.A., Ryu, J.H., Jo, Y. and Hong, C., 2023. The role of gut microbiota in T cell immunity and immune mediated disorders. *International Journal of Molecular Sciences*, 24(9), pp.4521–4540.
13. Bielka, W., Przezak, A. and Pawlik, A., 2022. The role of the gut microbiota in the pathogenesis of diabetes. *International Journal of Molecular Sciences*, 23(18), pp.10450–10470.
14. Shaheen, W.A. and Quraishi, M.N., 2022. Gut microbiome and autoimmune disorders. *Clinical and Experimental Immunology*, 209(3), pp.233–248.
15. Shahini, A. and Shahini, A., 2023. Role of interleukin-6-mediated inflammation in the pathogenesis of inflammatory bowel disease: focus on the available therapeutic approaches and gut microbiome. *Journal of Cell Communication and Signaling*, 17(2), pp.345–362.
16. Miyauchi, E., Shimokawa, C., Steimle, A. and Hornef, M.W., 2023. The impact of the gut microbiome on extra-intestinal autoimmune diseases. *Nature Reviews Immunology*, 23(7), pp.447–462.
17. Christovich, A. and Luo, X.M., 2022. Gut microbiota, leaky gut, and autoimmune diseases. *Frontiers in Immunology*, 13(8), pp.998–1016.
18. Salliss, M.E., Farland, L.V., Mahnert, N.D. and Missmer, S.A., 2022. The role of gut and genital microbiota and the estrobolome in endometriosis, infertility and chronic pelvic pain. *Human Reproduction Update*, 28(4), pp.592–611.
19. Sittipo, P., Choi, J., Lee, S. and Lee, Y.K., 2022. The function of gut microbiota in immune-related neurological disorders: a review. *Journal of Neuroinflammation*, 19(1), pp.154–172.
20. Ding, G., Yang, X., Li, Y., Wang, Y., Du, Y. and Wang, M., 2025. Gut microbiota regulates gut homeostasis, mucosal immunity and influences immune-related diseases. *Molecular and Cellular Immunology*, 22(3), pp.301–320.
21. Maciel-Fiuza, M.F., Muller, G.C., Campos, D.M.S. and Santos, C.F., 2023. Role of gut microbiota in infectious and inflammatory diseases. *Frontiers in Immunology*, 14(2), pp.1185–1203.
22. Gill, P.A., Inniss, S., Kumagai, T. and Rahman, F.Z., 2022. The role of diet and gut microbiota in regulating gastrointestinal and inflammatory disease. *Frontiers in Gastroenterology*, 13(9), pp.880–898.
23. Shan, Y., Lee, M. and Chang, E.B., 2022. The gut microbiome and inflammatory bowel diseases. *Annual Review of Medicine*, 73(1), pp.455–470.

24. Haneishi, Y., Furuya, Y., Hasegawa, M. and Picarelli, A., 2023. Inflammatory bowel diseases and gut microbiota. *International Journal of Molecular Sciences*, 24(11), pp.9234–9255.
25. Andoh, A. and Nishida, A., 2023. Alteration of the gut microbiome in inflammatory bowel disease. *Digestion*, 104(4), pp.345–356.
26. Madhogaria, B., Bhowmik, P. and Kundu, A., 2022. Correlation between human gut microbiome and diseases. *Infectious Medicine*, 1(3), pp.145–158.
27. Zheng, J., Sun, Q., Zhang, J. and Ng, S.C., 2022. The role of gut microbiome in inflammatory bowel disease diagnosis and prognosis. *United European Gastroenterology Journal*, 10(6), pp.575–586.
28. Zhao, M., Chu, J., Feng, S., Guo, C., Xue, B. and He, K., 2023. Immunological mechanisms of inflammatory diseases caused by gut microbiota dysbiosis: a review. *Biomedicine & Pharmacotherapy*, 163(1), pp.114–132.
29. Zhang, F., Fan, D., Huang, J. and Zuo, T., 2022. The gut microbiome: linking dietary fiber to inflammatory diseases. *Medicine in Microecology*, 11(1), pp.100–112.
30. Perler, B.K., Friedman, E.S. and Wu, G.D., 2023. The role of the gut microbiota in the relationship between diet and human health. *Annual Review of Physiology*, 85(1), pp.449–472.
31. Maciel-Fiuza, M.F., Muller, G.C., Campos, D.M.S., do Socorro Silva Costa, P., Peruzzo, J., Bonamigo, R.R., Veit, T. and Vianna, F.S.L., 2023. Role of gut microbiota in infectious and inflammatory diseases. *Frontiers in microbiology*, *14*, p.1098386.