Original Research Article

J. Funct. Mater. Biomol. 10 (1) (2026) pp 1336-1348

SACRED HEART RESEARCH PUBLICATIONS

Journal of Functional Materials and Biomolecules

Journal homepage: www.shcpub.edu.in

ISSN: 2456-9429

The Hidden Microbial World: Diversity, Ecology, and Stability of the Human Gut Ecosystem

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Received on 28 April 2026, accepted on 08 June 2026,

Published online on June 2026

Abstract

The intricate ecosystem that makes up the human gut microbiota is crucial to preserving health. The theory that the human host is a "holobiont" made up of the host and the microbiota is now supported by DNA sequencing technology, which enables us to study the microbiota in previously unheard-of depth. The makeup and evolution of the gut microbiota are thoroughly covered in this review article, including less studied topics like the "mycobiome" and "virome." Additionally, it talks about how the immune system, host genetics, and food all have an impact on the microbiota. Other microbiota, like "prophages," are crucial in addition to bacteria. "Prophages" have the potential to enhance bacterial pathogenicity, transfer antibiotic resistance, impact host adaption, and modify the immune system. Anorexia nervosa, bulimia nervosa, and binge eating disorder have all been linked to changes in the gut microbiota's makeup. Even in the absence of antibiotic use, the gut microbiota serves as a significant reservoir for the spread of antibiotic resistance. The significant impact of this microbial system on the host's physiology is demonstrated and new therapeutic and preventive approaches can be developed by combining the bacterial, viral, and fungal components of the gut microbiota.

Keywords: Virome, Mycobiome, Holobiont, Microbial Cross-Feeding, Human Gut Microbiota

1. Introduction

The human gut microbiota is a complex ecology that is essential for controlling immunity, digestion, and disease resistance [1]. The human body functions as a holobiont, or a complete system made up of the host and symbionts, according to recent advances in DNA sequencing techniques that have enabled researchers to delve deeply into this intricate ecosystem [2]. With a focus on the lesser-known mycobiome and virome as well as the key variables influencing this intricate ecosystem, this review seeks to provide a thorough overview of the composition and evolution of the gut microbiota [3]. The immune system, environment, host genetics, and diet are the main contributing factors. Along with bacteria, other microbes such as prophages are known to be playing a crucial role [4]. Prophages are known to be involved in the virulence of bacteria, antibiotic resistance, and the immune system and adaptability of the host [5]. The gut microbiota has come to be regarded as a critical factor for health and disease [6]. Another ecological process in the human microbiota is

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cross-feeding, mediated by the exometabolome, the complex mix of secreted metabolites [7]. Cross-feeding is beneficial in that it increases nutrient levels, phylogenetic diversity, and biomass, thus stabilizing the community [8]. Human health is significantly impacted by these natural processes. For example, eating disorders such bulimia nervosa, anorexia nervosa, and binge eating disorders have been linked to changes in the composition of the gut microbiota [9]. Even in the absence of exposure to such antibiotics, the gut is a reservoir of drug-resistant bacteria, including those resistant to colistin [10]. In order to highlight the complexity of this intricate ecosystem and its significant implications on human physiology, this study attempts to give an overview of the present level of knowledge regarding the bacterial, viral, and fungal components of the human gut microbiota [11]. With an emphasis on the direction of the field's future research, the review also seeks to offer insights into the preventive and therapeutic approaches now in development [12]. (Table 1).

Table 1: Summary of Key Components and Interactions in the Human Gut Ecosystem

Microbial Component	Key Genera/Examples	Primary Functions/Roles	Associated Health Effects	Key Interactions
Bacteria (Beneficial)	*Lactobacillus, Bifidobacterium, Akkermansia muciniphila, Faecalibacterium prausnitzii*	Vitamin production, fiber fermentation, SCFA production, gut barrier maintenance, immune modulation	Enhanced digestion, reduced inflammation, protection against obesity and diabetes, defense against IBD	Cross-feeding, metabolic reciprocity
Bacteria (Pathogenic)	Pathogenic *E. coli, Clostridium difficile, Salmonella, Fusobacterium nucleatum, Helicoccter pylori, Bacteroides fragilis*	Toxin production, inflammation induction, cell damage	Diarrheal disease, colitis, colorectal cancer, gastric cancer	Competition with beneficial bacteria, host immune evasion
Phages/Prophages		Bacterial population control, gene transfer, virulence modulation	Cognitive performance (some phage groups), community stabity	Lytic/lysogenic cycles, horizontal gene transfer prophage induction
Virome	Tailed phages, *Caudovirales*	Bacterial population control, gene transfer, virulence	Homeostasis in healthy individuals; dysbiosis in disease	Phage-bacteria interactions, host immunity modulation
Mycobiome	Diverse viral communities	Regulation of bacterial populations, immune system training	Homeostasis in healthy individuals; dysbiosis in disease	Phage-bacterial interactions, mycotoxin production
Mycobiome	*Candida, Saccharomyces, Malassezia, Cladosporium*	Nutrient cycling, immune modulation	Probiotic effects (*S. boulardii*); opportunistic infections (*Candida*): association with colon cancer (Malassezia))	
Exometabolome	Secreted metabolites, SCFAs, organic acids	Community stability, increased biodiversity		
Antibiotics	Secreted metabolites, SCFAs, organic acids	Community stability, increased biodiversity		

2. GUT BACTERIAL DIVERSITY

The human gut contains a variety of beneficial bacteria that are essential for digestion, metabolism, and immunity [13]. Bacteria that ferment carbohydrates, create vitamins, and strengthen immunity are examples of beneficial bacteria. Among the beneficial bacteria are *Lactobacillus* and Bifidobacterium [14]. The finest example of the advantages of these bacteria is their ability to ferment dietary fiber and create short-chain fatty acids, such acetate, which are essential for the energy requirements of the cells in the gut and maintain a healthy gut environment [15]. The finest example of *Lactobacillus* bacteria's beneficial impacts is their ability to ferment lactose and produce lactic acid, which enhances lactose digestion and maintains the pH of the gut acidic, so reducing harmful bacteria. *Lactobacillus* produces antibiotic compounds called bacteriocins, which alter the composition of the gut microbiome by stopping the growth of dangerous bacteria [16]. *Akkermansia muciniphila* contributes to maintaining the integrity of the gut barrier by dissolving mucin, the main component of mucus that fortifies the barrier and prevents bacteria from entering the gut wall [17]. It has also been demonstrated to play a part in reducing inflammation, enhancing glucose metabolism, and preventing obesity and diabetes [18]. *Faecalibacterium prausnitzii* secretes anti-inflammatory butyrate, a short-chain fatty acid that strengthens, nourishes, and reduces inflammation in colon lining cells. It has a major role in preventing inflammatory bowel diseases like Crohn's disease and ulcerative colitis [19].

On the other hand, harmful bacteria include pathogenic strains of Escherichia coli, whose toxins harm the digestive tract and result in serious, often fatal conditions like diarrhea [20]. Certain pathogenic strains of E. coli can create shiga toxins,[21] which can cause potentially lethal diseases such hemolytic uremic syndrome and bloody diarrhea [22]. Antibiotic use can also result in an infection with Clostridium difficile, which can induce colitis and possibly severe diarrheal diseases due to the toxins' destruction of the lining of the digestive tract [23]. Foodborne bacteria like Salmonella enterica cause diarrheal diseases, fever, and abdominal pain by adhering to intestinal epithelial cells and generating inflammation [24]. Colorectal cancer may result from inflammation caused by *Fusobacterium nucleatum* [25]. Similarly, *Helicobacter pylori* increases the risk of stomach lining ulcers, inflammation, and tumor development of stomach cancer. Adhesion-damaging Bacteroides fragilis toxins may cause tumor development [26].

3. PHAGE AND PROPHAGE LIFECYCLE AND DIVERSITY IN THE HUMAN GUT

Phages are the most common biological entities on Earth; they infect bacterial populations in all environments, including the human gut microbiome [27]. As part of their replication cycles, they might be essential to the preservation of a balanced human gut microbiota in healthy individuals. During the lytic cycle, the phage infects the target cell, copies its genetic information using the target cell's machinery, produces new phage particles, and then lyses the target cell to release the newly formed phage particles [28]. During the lysogenic cycle, the phage genome can integrate as prophages in the target bacterial cells' genomes as part of phage-driven regulatory switches that modify bacterial gene expression, leading to notable changes in the bacterial physiology and genetics [29]. A vital component of the human gut microbiota are prophages [30]. In bacterial genomes, tens of thousands of putative prophage sections have been found [31]; some of these regions contain genes involved in the manufacture of toxins [32], antibiotic resistance, and other crucial functions [33] to bacterial interactions with the host [34]. Prophage induction can be impacted by environmental factors including nutrition [35]. In conclusion, there is a complicated and important relationship between phages and prophages in the human stomach.

4.ADVANCES IN METAGENOMICS FOR FOOD MICROBIOME CHARACTERIZATION

Recent developments in metagenomic research have greatly aided the food microbiome field by enabling in-depth analysis of food samples [36]. Because of its precision and affordability, short-read sequencing technique is still widely used even if it may not be effective in handling low-abundance species and complicated microbial community structures [37]. Because it can construct entire microbial genomes, third-generation sequencing technology is also becoming more and more

popular as an alternate method for handling microbial food samples [38].

Experimental design is usually the first step in this process, followed by DNA extraction, which can occasionally be challenging for specific food systems [39]. Functional analysis and taxonomic resolution are both attainable with shotgun metagenomics [40]. Because 16S rRNA gene sequencing is less expensive, it can also be used [41]. By directly assembling the metagenome-assembled genomes (MAGs) from the sequencing data, assembly-based methods can be used to identify new species [42]. These are essential for creating reference databases that enable sensitive species-level taxonomic and functional evaluation. Biostatistical analysis, which can be carried out with the aid of a multidisciplinary approach, is then used to interpret the results [43].

5. HORIZONTAL GENE TRANSFER OF COLISTIN RESISTANCE GENES IN THE GUT

Antibiotic resistance genes (ARGs) can spread in a dynamic environment within the complicated human gastrointestinal tract [44]. Among the most concerning antibiotic resistance genes are the mobile colistin resistance (mcr) genes, which spread by horizontal gene transfer (HGT) processes such conjugation, transposition, and recombination [45]. Conjugative plasmids, insertion sequences, or transposons that facilitate HGT between bacterial genomes frequently carry colistin resistance genes, especially mcr-1 [46]. Even among phylogenetically distinct species, mcr genes can quickly proliferate in the human gut microbiome due to this genetic flexibility. The possibility that commensal, non-pathogenic bacteria in the human gut could pick up and discreetly store mcr genes during co-colonization before transferring them to more pathogenic pathogens is one of the primary worries [47]. These resistant plasmids are highly transferable, as demonstrated by experiments [48]. The human intestinal environment increases the likelihood of resistant plasmid transmission [49]. Conjugative plasmid transfer is facilitated by biofilm formation, intimate physical contact between microorganisms, and the presence of antibiotics [50]. In order to address this, surveillance techniques that encompass not only pathogens but also the entire microbial population in the human gut must be developed [51].

6. MICROBIAL DIVERSITY: CONCEPTS AND MEASUREMENTS

Microbial diversity is a tool used by ecologists to assess the makeup and functionality of microbial communities [52]. Alpha diversity, which refers to the diversity of a single habitat; beta diversity, which refers to the richness of different habitats; and gamma diversity, which refers to the diversity of different regions, are the three types of diversity measurements that Whittaker described [53]. The identification of the species unit remains a challenge in diversity measures, but it is frequently overcome by classifying genomic sequences as operational taxonomic units. High species variety is crucial for enhancing ecological processes like resource efficiency, robustness, and decreased vulnerability to invasion [54]. For ecological inference, including ecological patterns in

nature, diversity measures are therefore essential. It's still unclear if people, including the microbial community in the gastrointestinal system, benefit from high or low variety [55].

7. FUNCTIONAL ECOLOGY AND FOOD FOR THOUGHT

Scientific evidence also supports the notion that humans are an ecosystem in evolution, or a holobiont, as there is a clear link between more microbial variety and favorable health outcomes including improved mental health and a lower incidence of allergies [56]. Nevertheless, a correlation between decreased microbial diversity and inflammatory disorders has also been observed. Similar to evolutionary psychology, this hypothesis could be intriguing since it could address the organism's phenotypic level and the extent to which its microorganism, behaviors, or dietary choices could influence it [57].

The communication between the enteric neural system, the gut microbiota, and the central nervous system is referred to as the "gut-brain axis" [58]. This idea of the gut-brain axis has already been well investigated and continues to be an intriguing field of study because it may extend to the organism's phenotypic level and the extent to which its microorganism, behaviors, or dietary choices may affect it [59].

8. THE EXOMETABOLOME AS AN ECOLOGICAL RESOURCE FOR MICROORGANISMS

The metabolites that microorganisms discharge into the environment are referred to as the exometabolome [60]. Because they may serve as nutrients for other microorganisms, affecting their interaction and community formation, they have a major ecological significance [61].

8.1. Facilitation

When an organism secretes compounds that benefit other species but not itself, this is known as facilitation. By promoting the growth of specific microbes, including those that are heterotrophic and need resources from outside the cell, facilitation can improve an ecosystem's biomass and taxonomic diversity [62]. It has been discovered that certain bacteria that are unable to break down chitin can flourish in organic acids that other bacteria can break down chitin secrete [63]. Evolutionary theories like the BQH suggest that when a nutrient is continuously supplied by a "leaky" producer, selection may promote loss of biosynthetic capacities, potentially resulting in interdependent populations of auxotrophs and prototrophs [64].

8.2. Syntropy

When two or more microorganisms work together to break down a single substrate that cannot be broken down by any one of them alone, this process is known as syntrophy. The cooperation between fermentative bacteria and methanogenic archaea in an anaerobic environment is the best example; the bacteria break down the substrates and release hydrogen gas, which the methanogens then use to keep the concentration low and allow the bacteria to break down the substrates [65].
In syntrophy, the activity of several microbes can

accelerate growth, in contrast to when a single microorganism operates on the substrates.

8.3. Metabolic Reciprocity

The exchange of distinct but necessary metabolites between the two organisms in the connection is known as metabolic reciprocity [66]. Strains that would not be able to develop separately in a separate culture may be able to co-grow through reciprocal cross-feeding. It has been demonstrated that auxotrophic mutant colonies engage in reciprocal cross-feeding in vitro [67]. In complex natural ecosystems, these relationships involving the flow of vitamins, amino acids, or cofactors may contribute to the interdependence of taxonomically distinct populations [68]. Because cooperators may be physically close, spatial organization, such as that found in biofilms, may enhance such connections. However, the connection could hypothetically be disrupted by "cheater" strains that take advantage of nutrients without participating in the interaction [69].

9. THE ROLE OF THE MICROBIOTA IN REGULATING THE GUT–BRAIN AXIS

The brain-gut axis, which leads to cellular homeostasis in the organism, is regulated by the intestinal microbiota [70]. An increase in intestinal permeability could lead to a systemic inflammatory problem. Stress and mental disease have been linked to this. The gut microbiome is involved in the synthesis of several neurotransmitters [71]. For instance, Bifidobacterium and *Lactobacillus* are involved in the synthesis of gamma-aminobutyric acid (GABA) [72]. The body uses other microbes to produce serotonin [73]. One important nerve for communication along this axis is the vagus nerve, which has significant innervation to the intestinal system. Early in life, it is clear that the gut microbiota plays a role in immune system development [74]. It is unclear whether immune system dysfunction regulates or initiates autoimmune disorders that appear to be associated with mental health disorders through the process of molecular mimicry or the production of metabolites of the kynurenine pathway [75].

(Table 2).

Table 2: Clinical and Disease Associations of Gut Microbiota

Disease/ Condition	Microbial Involved	Mechanism/Association	Section Reference
Inflammatory Bowel Disease	Reduced *F. prausnitzii*, altered mycobiome	Loss of anti-inflammatory butyrate production, fungal dysbiosis	2, 11
Colorectal Cancer	*F. nucleatum*, *B. fragilis*, *Malassezia*	Chronic inflammation, toxin production, tumor promotion	2, 11
Obesity and Diabetes	Reduced *A. muciniphila*	Impaired gut barrier, metabolic dysfunction	2
Eating Disorders	Altered overall microbiota composition	Gut-brain axis disruption, neurotransmitter modulation	1, 9
Antibiotic Resistance	mcr-carrying bacteria, commensal ARG reservoirs	Horizontal gene transfer in gut environment	5
Depression/Anxiety	Altered GABA and serotonin-producing bacteria	Neurotransmitter dysregulation, leaky gut, inflammation	9
Autoimmune Conditions	Early life dysbiosis, viral triggers	Immune system misprogramming, molecular mimicry	9, 10.2
HIV/AIDS	Expanded opportunistic viruses	Immune dysfunction permitting viral overgrowth	10.2

10. MAJOR FACTORS INFLUENCING THE COMPOSITION OF THE GUT VIROME

10.1. Dietary Structure and Living Environment

Dietary practices have a major impact on gut virome. A diet high in fiber promotes bacterial fermentation, which supports the growth of lysogenic phages [76]. Diets heavy in fat and sugar may help the virus survive. Because urban inhabitants may not be exposed to ambient microbial

reservoirs, their gut microbiome diversity may be lower than that of rural communities with typical high-fiber diets [77].

10.2. Host Genetics and Immunity

The gut virome is significantly affected by host immune systems and genetics [78]. The identification and removal of enteric viruses can be influenced by genetic variables that impact antiviral immunity [79]. Maintaining homeostasis in the virome depends on innate immunity and mucosal immunity, including IgA synthesis and interferon responses. However, weakened immunity, as shown in HIV-positive people, might cause opportunistic viruses to proliferate unchecked in the gut, impacting the virome and gut diseases [80].

11. GUT MYCOBIOME: IMPORTANT FUNGI RESIDING IN THE HUMAN GUT

The predominant microorganisms in the human gut mycobiome are yeasts, with the most prevalent yeasts being Candida, Saccharomyces, and Malassezia. Age, nutrition, location, and health state all affect the composition of the mycobiome. Human mycobiome makeup is formed early in life and is impacted by nursing, delivery method, and surroundings [81]. In healthy humans, Saccharomyces, Cladosporium, and Candida make up the mycobiome. Despite being an opportunistic infection, Candida can cause illness in immunocompromised individuals, increasing inflammation and illness [82]. It has been discovered that the yeast *Saccharomyces boulardii* is useful for maintaining gut barrier integrity and preventing diarrhea. Although the exact causes are still unknown, *Malassezia*, which has historically been identified as a skin pathogen, is also present in the human gut and is linked to colon cancer and potential intestinal inflammation [83]. Food-borne fungus Aspergillus and Penicillium are known to briefly colonize the human gut and are linked to the development of mycotoxins, which can be hazardous to the liver and kidneys.It has been reported that a vast, very sophisticated microbial population made up of bacteria, fungi, viruses, and archaea inhabits the human digestive tract [84]. These microbial organisms have a new constellation of interactions that are influenced by host genetic, dietary, and environmental factors. These relationships include competition, predation, and cross-feeding [85]. Numerous illnesses, such as cancer, mental illnesses, metabolic abnormalities, and inflammation, have been linked to these connections. Furthermore, it has been reported that the human intestine system serves as a reservoir for the emergence of antibiotic resistance, which subsequently spreads across the environment [86]. Recent developments in sequencing techniques are making it possible to carry out extensive research to identify the microbial entities that exist in this invisible universe as well as how they interact biochemically with one another in comprehensively coordinated systems to control host-microbial relationships. Future research will focus heavily on developing novel techniques to rebalance this microbial connection [87].

12. CONCLUSION

The human gut microbiota represents a highly complex and dynamic ecosystem composed of bacteria, viruses, fungi, archaea, and their associated genetic elements. This microbial community plays a fundamental role in maintaining host physiology through regulation of metabolism, immune responses, nutrient processing, gut barrier integrity, and the gut–brain axis. Emerging evidence highlights those microbial interactions, including cross-feeding, syntropy, and metabolic reciprocity, contribute significantly to ecosystem stability and functional diversity. Alterations in gut microbial composition have been associated with numerous disorders, including inflammatory diseases, metabolic abnormalities, mental health conditions, eating disorders, and cancer. Recent advances in metagenomics and sequencing technologies have greatly expanded understanding of the gut microbiome, virome, and mycobiome, enabling deeper exploration of microbial diversity and ecological interactions. The gut also acts as an important reservoir for antibiotic resistance genes, emphasising the need for continuous surveillance and strategies to limit resistance dissemination. Furthermore, environmental factors, diet, host genetics, and immune function strongly influence microbial composition and stability throughout life. Understanding the hidden microbial world of the human gut offers promising opportunities for developing microbiome-based diagnostics, personalised nutrition, probiotics, and targeted therapeutic interventions. Future research integrating bacterial, viral, fungal, and host interactions will be essential to uncover mechanisms underlying health and disease, ultimately advancing precision medicine approaches aimed at restoring and maintaining microbial balance for improved human health.

References

[1] E. Rinninella, P. Raoul, M. Cintoni, F. Franceschi, G.A.D. Miggiano, A. Gasbarrini and M.C. Mele, Microorganisms 7(1), (2019) 14.

[2] J.C. Simon, J.R. Marchesi, C. Mougel and M.A. Selosse, Microbiome 7, (2019) 5.

[3] R.K. Singh, H.W. Chang, D. Yan, K.M. Lee, D. Ucmak, K. Wong, M. Abrouk, B. Farahnik, M. Nakamura, T.H. Zhu and T. Bhutani, Journal of Translational Medicine 15(1), (2017) 73.

[4] J.K. Goodrich, J.L. Waters, A.C. Poole, J.L. Sutter, O. Koren, R. Blekhman, M. Beaumont, W. Van Treuren, R. Knight, J.T. Bell and T.D. Spector, Cell 159(4), (2014) 789–799.

[5] R. Feiner, T. Argov, L. Rabinovich, N. Sigal, I. Borovok and A.A. Herskovits, Nature Reviews Microbiology 13(10), (2015) 641–650.

[6] A.K. Nash, T.A. Auchtung, M.C. Wong, D.P. Smith, J.R. Gesell, M.C. Ross, C.J. Stewart, G.A. Metcalf, D.M. Muzny, R.A. Gibbs and N.J. Ajami, Microbiome 5(1), (2017) 153.

[7] L.S. Zaramela, C. Martino, F. Alisson-Silva, S.D. Rees, S.L. Diaz, L. Chuzel, L.V. Blanton, C.H. Taron, P. Secrest, C. Zuñiga and K.C. Huang, Nature Microbiology 6(2), (2021) 197–209.

[8] K.Z. Coyte, J. Schluter and K.R. Foster, Science 350(6261), (2015) 663–666.

[9] J. Seitz, S. Trinh and B. Herpertz-Dahlmann, Psychiatric Clinics 42(1), (2019) 93–103.

[10] Y. Wang, Y. Hu, J. Cao, Y. Bi, Y. Zhang, Y. Wang, L. Huang, J. Cheng and J. Lu, Journal of Infection 83(5), (2021) 607–635.

[11] E. Thursby and N. Juge, Biochemical Journal 474(11), (2017) 1823–1836.

[12] C. Hill, F. Guarner, G. Reid, G.R. Gibson, D.J. Merenstein, B. Pot, L. Morelli, R.B. Canani, H.J. Flint, S. Salminen and P.C. Calder, Nature Reviews Gastroenterology & Hepatology 11(8), (2014) 506–514.

[13] A. Rivière, M. Selak, D. Lantin, F. Leroy and L. De Vuyst, Frontiers in Microbiology 7, (2016) 979.

[14] K. Selle and T.R. Klaenhammer, FEMS Microbiology Reviews 37(6), (2013) 915–935.

[15] P.D. Cotter, R.P. Ross and C. Hill, Nature Reviews Microbiology 11(2), (2013) 95–105.

[16] M. Hayes, C. Stanton, H. Slattery, O. O'Sullivan, C. Hill, G.F. Fitzgerald and R.P. Ross, Applied and Environmental Microbiology 73(14), (2007) 4658–4667.

[17] M. Derrien, E.E. Vaughan, C.M. Plugge and W.M. de Vos, International Journal of Systematic and Evolutionary Microbiology 54(5), (2004) 1469–1476.

[18] A. Everard, C. Belzer, L. Geurts, J.P. Ouwerkerk, C. Druart, L.B. Bindels, Y. Guiot, M. Derrien, G.G. Muccioli, N.M. Delzenne and W.M. de Vos, Proceedings of the National Academy of Sciences 110(22), (2013) 9066–9071.

[19] S. Miquel, R. Martin, O. Rossi, L.G. Bermúdez-Humarán, J.M. Chatel, H. Sokol, M. Thomas, J.M. Wells and P. Langella, Current Opinion in Microbiology 16(3), (2013) 255–261.

[20] N. Kamada, S.U. Seo, G.Y. Chen and G. Núñez, Nature Reviews Immunology 13(5), (2013) 321–335.

[21] J.B. Kaper, J.P. Nataro and H.L. Mobley, Nature Reviews Microbiology 2(2), (2004) 123–140.

[22] M. Rupnik, M.H. Wilcox and D.N. Gerding, Nature Reviews Microbiology 7(7), (2009) 526–536.

[23] A. Fabrega and J. Vila, Clinical Microbiology Reviews 26(2), (2013) 308–341.

[24] A.D. Kostic, E. Chun, L. Robertson, J.N. Glickman, C.A. Gallini, M. Michaud, T.E. Clancy, D.C. Chung, P. Lochhead, G.L. Hold and E.M. El-Omar, Cell Host & Microbe 14(2), (2013) 207–215.

[25] T.L. Cover and M.J. Blaser, Gastroenterology 136(6), (2009) 1863–1873.

[26] C.L. Sears, Clinical Microbiology Reviews 22(2), (2009) 349–369.

[27] M.R. Clokie, A.D. Millard, A.V. Letarov and S. Heaphy, Bacteriophage 1(1), (2011) 31–45.

[28] C. Howard-Varona, K.R. Hargreaves, S.T. Abedon and M.B. Sullivan, The ISME Journal 11(7), (2017) 1511–1520.

[29] J. Bondy-Denomy, J. Qian, E.R. Westra, A. Buckling, D.S. Guttman, A.R. Davidson and K.L. Maxwell, The ISME Journal 10(12), (2016) 2854–2866.

[30] A.N. Shkoporov and C. Hill, Cell Host & Microbe 25(2), (2019) 195–209.

[31] J. Mayneris-Perxachs, A. Castells-Nobau, M. Arnoriaga-Rodríguez, J. Garre-Olmo, J. Puig, R. Ramos, F. Martínez-Hernández, A. Burokas, C. Coll, J.M. Moreno-Navarrete and C. Zapata-Tona, Cell Host & Microbe 30(3), (2022) 340–356.

[32] T.D. Sutton and C. Hill, Frontiers in Endocrinology 10, (2019) 784.

[33] S. Roux, M. Krupovic, R.A. Daly, A.L. Borges, S. Nayfach, F. Schulz, A. Sharrar, P.B. Matheus Carnevali, J.F. Cheng, N.N. Ivanova and J. Bondy-Denomy, Nature Microbiology 4(11), (2019) 1895–1906.

[34] M.T. Jahn, K. Arkhipova, S.M. Markert, C. Stigloher, T. Lachnit, L. Pita, A. Kupczok, M. Ribes, S.T. Stengel, P. Rosenstiel and B.E. Dutilh, Cell Host & Microbe 26(4), (2019) 542–550.

[35] J.M. Łoś, M. Łoś, A. Węgrzyn and G. Węgrzyn, Microbial Pathogenesis 57, (2013) 82–89.

[36] A.M. Walsh, F. Crispie, M.J. Claesson and P.D. Cotter, Annual Review of Food Science and Technology 8, (2017) 113–134.

[37] C. Quince, A.W. Walker, J.T. Simpson, N.J. Loman and N. Segata, Nature Biotechnology 35(9), (2017) 833–844.

[38] V. Marx, Nature Methods 20(1), (2023) 18–22.

[39] [39] F. De Filippis, E. Parente and D. Ercolini, Microbial Biotechnology 10(1), (2017) 91–102.

[40] R. Knight, A. Vrbanac, B.C. Taylor, A. Aksenov, C. Callewaert, J. Debelius, A. Gonzalez, T. Kosciolek, L.I. McCall, D. McDonald and A.V. Melnik, Nature Reviews Microbiology 16(7), (2018) 410–422.

[41] J. Alneberg, B.S. Bjarnason, I. de Bruijn, M. Schirmer, J. Quick, U.Z. Ijaz, L. Lahti, N.J. Loman, A.F. Andersson and C. Quince, Nature Methods 11(11), (2014) 1144–1146.

[42] E. Pasolli, F. Asnicar, S. Manara, M. Zolfo, N. Karcher, F. Armanini, F. Beghini, P. Manghi, A. Tett, P. Ghensi and M.C. Collado, Cell 176(3), (2019) 649–662.

[43] M.L. Marco, D. Heeney, S. Binda, C.J. Cifelli, P.D. Cotter, B. Foligné, M. Gänzle, R. Kort, G. Pasin, A. Pihlanto and E.J. Smid, Current Opinion in Biotechnology 44, (2017) 94–102.

[44] M.O. Sommer, G. Dantas and G.M. Church, Science 325(5944), (2009) 1128–1131.

[45] Y.Y. Liu, Y. Wang, T.R. Walsh, L.X. Yi, R. Zhang, J. Spencer, Y. Doi, G. Tian, B. Dong, X. Huang

and L.F. Yu, The Lancet Infectious Diseases 16(2), (2016) 161–168.

[46] L. Poirel, N. Kieffer, A. Brink, J. Coetze, A. Jayol and P. Nordmann, Antimicrobial Agents and Chemotherapy 60(7), (2016) 4394–4397.

[47] K. Zurfluh, M. Nüesch-Inderbinen, J. Klumpp, L. Poirel, P. Nordmann and R. Stephan, Antimicrobial Resistance & Infection Control 6, (2017) 91.

[48] R. Wang, L. van Dorp, L.P. Shaw, P. Bradley, Q. Wang, X. Wang, L. Jin, Q. Zhang, Y. Liu, A. Rieux and T. Dorai-Schneiders, Nature Communications 9(1), (2018) 1179.

[49] N.A. Lerminiaux and A.D. Cameron, Canadian Journal of Microbiology 65(1), (2019) 34–44.

[50] J. Bengtsson-Palme, E. Kristiansson and D.J. Larsson, FEMS Microbiology Reviews 42(1), (2018) fux053.

[51] R.H. Whittaker, Taxon 21(2–3), (1972) 213–251.

[52] P.D. Schloss and S.L. Westcott, Applied and Environmental Microbiology 77(10), (2011) 3219–3226.

[53] D. Tilman, P.B. Reich and J.M. Knops, Nature 441(7093), (2006) 629–632.

[54] [54] C.A. Lozupone, J.I. Stombaugh, J.I. Gordon, J.K. Jansson and R. Knight, Nature 489(7415), (2012) 220–230.

[55] J. Lehtimäki, J. Thorsen, M.A. Rasmussen, M. Hjelmsø, S. Shah, M.S. Mortensen, U. Trivedi, G. Vestergaard, K. Bonnelykke, B.L. Chawes and K. Bønnelykke, Journal of Allergy and Clinical Immunology 148(1), (2021) 234–243.

[56] M. Levy, A.A. Kolodziejczyk, C.A. Thaiss and E. Elinav, Nature Reviews Immunology 17(4), (2017) 219–232.

[57] C.G. Buffie and E.G. Pamer, Nature Reviews Immunology 13(11), (2013) 790–801.

[58] J.F. Cryan, K.J. O'Riordan, C.S. Cowan, K.V. Sandhu, T.F. Bastiaanssen, M. Boehme, M.G. Codagnone, S. Cussotto, C. Fulling, A.V. Golubeva and K.E. Guzzetta, Physiological Reviews 99(4), (2019) 1877–2013.

[59] E.A. Mayer, K. Nance and S. Chen, Annual Review of Medicine 73, (2022) 439–453.

[60] R. Dawkins, The Extended Phenotype, Oxford University Press, (1982).

[61] O. Ponomarova and K.R. Patil, Current Opinion in Microbiology 27, (2015) 37–44.

[62] J.E. Goldford, N. Lu, D. Bajić, S. Estrela, M. Tikhonov, A. Sanchez-Gorostiaga, D. Segrè, P. Mehta and A. Sanchez, Science 361(6401), (2018) 469–474.

[63] M.S. Datta, E. Sliwerska, J. Gore, M.F. Polz and O.X. Cordero, Nature Communications 7, (2016) 11965.

[64] J.J. Morris, R.E. Lenski and E.R. Zinser, mBio 3(2), (2012) e00036-12.

[65] A.J. Stams and C.M. Plugge, Nature Reviews Microbiology 7(8), (2009) 568–577.

[66] A.R. Pacheco, M. Moel and D. Segrè, Nature Communications 10(1), (2019) 103.

[67] M.T. Mee, J.J. Collins, G.M. Church and H.H. Wang, Proceedings of the National Academy of Sciences 111(20), (2014) E2149–E2156.

[68] K. Zengler and L.S. Zaramela, Nature Reviews Microbiology 16(6), (2018) 383–390.

[69] C.D. Nadell, K. Drescher and K.R. Foster, Nature Reviews Microbiology 14(9), (2016) 589–600.

[70] M. Carabotti, A. Scirocco, M.A. Maselli and C. Severi, Annals of Gastroenterology 28(2), (2015) 203.

[71] S.P. Wiertsema, J. van Bergenhenegouwen, J. Garssen and L.M. Knippels, Nutrients 13(3), (2021) 886.

[72] M. Maes, M. Kubera and J.C. Leunis, Neuroendocrinology Letters 29(1), (2008) 117–124.

[73] P. Strandwitz, K.H. Kim, D. Terekhova, J.K. Liu, A. Sharma, J. Levering, D. McDonald, D. Dietrich, T.R. Ramadhar, A. Lekbua and N. Mroue, Nature Microbiology 4(3), (2019) 396–403.

[74] B. Bonaz, T. Bazin and S. Pellissier, Frontiers in Neuroscience 12, (2018) 49.

[75] D. Erny, A.L. Hrabě de Angelis, D. Jaitin, P. Wieghofer, O. Staszewski, E. David, H. Keren-Shaul, T. Mahlakoiv, K. Jakobshagen, T. Buch and V. Schwierzeck, Nature Neuroscience 18(7), (2015) 965–977.

[76] M.K. Mirzaei and C.F. Maurice, Nature Reviews Microbiology 15(7), (2017) 397–408.

[77] G. Zhao, T. Vatanen, L. Droit, A. Park, A.D. Kostic, T.W. Poon, H. Vlamakis, H. Siljander, T. Härkönen, A.M. Hämäläinen and A. Peet, Proceedings of the National Academy of Sciences 114(30), (2017) E6166–E6175.

[78] C.K. Yinda, E. Vanhulle, N. Conceição-Neto, L. Beller, W. Deboutte, C. Shi, S.M. Ghogomu, P. Maes, M. Van Ranst, J. Matthijnssens and E. Heylen, mSphere 4(1), (2019) e00585-18.

[79] E. Kernbauer, Y. Ding and K. Cadwell, Nature 516(7529), (2014) 94–98.

[80] C.L. Monaco, D.B. Gootenberg, G. Zhao, S.A. Handley, M.S. Ghebremichael, E.S. Lim, A. Lankowski, M.T. Baldridge, C.B. Wilen, M. Flagg and J.M. Norman, Cell Host & Microbe 19(3), (2016) 311–322.

[81] H.E. Hallen-Adams and M.J. Suhr, Virulence 8(3), (2017) 352–358.

[82] T.A. Auchtung, T.Y. Fofanova, C.J. Stewart, A.K. Nash, M.C. Wong, J.R. Gesell, J.M. Auchtung, N.J. Ajami and J.F. Petrosino, mSphere 3(2), (2018) e00092-18.

[83] M.L. Richard and H. Sokol, Nature Reviews Gastroenterology & Hepatology 16(6), (2019) 331–345.

[84] C.A. Kumamoto, Current Opinion in Microbiology 14(4), (2011) 386–391.

[85] D. Czerucka, T. Piche and P. Rampal, Alimentary Pharmacology & Therapeutics 26(6), (2007) 767–778.

[86] J.J. Limon, J. Tang, D. Li, A.J. Wolf, K.S. Michelsen, V. Funari, M. Gargus, C. Nguyen, P. Sharma, V.I. Maymi and I.D. Iliev, Cell Host & Microbe 25(3), (2019) 377–388.

[87] S. Marín, A.J. Ramos, G. Cano-Sancho and V. Sanchis, Food and Chemical Toxicology 60, (2013) 218–237.