Could the Gut Microbiome Revolutionize Medical Care?

Current Status and Initial Considerations for Successful Development and Commercialization of Microbiome Therapies

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Contents

Synopsis

Research in the area of live biotherapeutics has exploded in the last seven years. Even so, there is still much to learn about whether a dysregulated gut microbiome causes disease, or whether disease leads to dysbiosis. Dysbiosis has been implicated in multiple therapy areas including gastrointestinal disorders, immunology, neurology and oncology, among others. In addition, the therapeutic effects of several pharmaceuticals have been shown to be mediated by the gut microbiome.

Despite the scientific questions that remain to be investigated, several biotechnology companies have emerged with a focus on testing various approaches to developing therapies targeting the gut microbiome. Large, established pharmaceutical companies have also recognized the potential of live biotherapeutics and are investing in partnerships with these companies—or, as in the case of at least one company, are establishing an entire institute dedicated to the development of live biotherapeutics.

Although three therapies have reached Phase III development so far, they face numerous challenges in reaching the market—e.g., achieving regulatory approval, determining an appropriate price and obtaining reimbursement, and overcoming barriers to adoption of live biotherapeutics. Our paper provides a summary of the current gut microbiome therapy development landscape and an overview of the commercialization challenges faced.

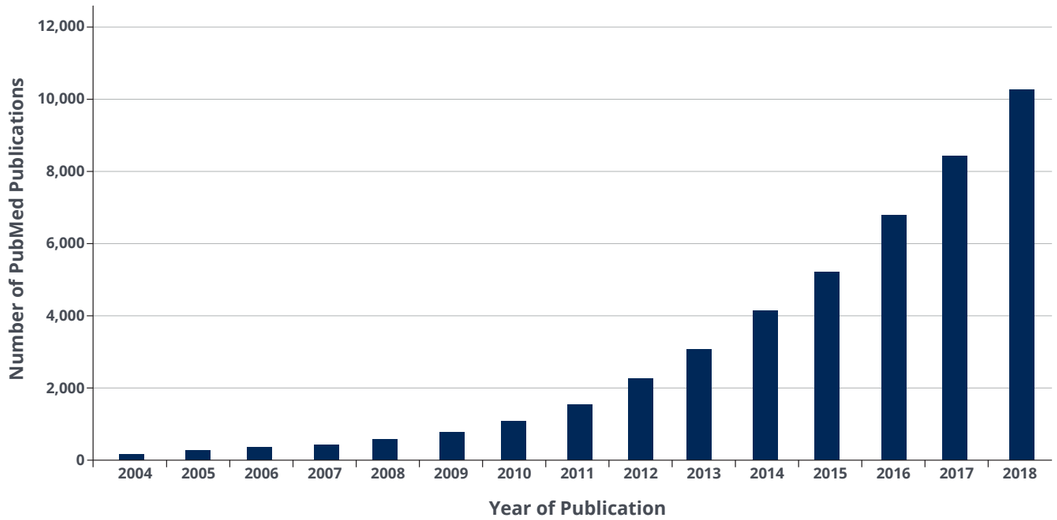
The Microbiome: A Closer Look

The microbiome is an ecosystem of bacteria. Bacteria exist in the environment as well as in or on many parts of our bodies, including on our skin and in our eyes and gut. The gut microbiome, specifically, is also known as the “second brain” or “second genome”—the names alluding to the importance of the gut microbiome to our health. There are approximately 10 trillion bacterial cells on the human body, 80 percent of which are beneficial. The microbiome is assembled at birth, develops with the host and is influenced by environmental factors such as diet and antibiotics.[1] Recently, a role for human genetic variation has emerged as also being influential in accounting for interpersonal differences in microbiomes.

An explosion in basic and applied biomedical research

Understanding of the microbiome and its relationship to health and disease has grown exponentially over the past decade. The Human Microbiome Project, a five-year project initiated by the National Institutes of Health (NIH), was conducted to characterize the microbial communities at five major body sites and to create a baseline database for future health and disease research connected to microbiomes. Federal investments in microbiome research tripled from 2012 to 2014, totaling more than $922 million during that period, according to a report from the National Science and Technology Council.[2] In 2016, the National Microbiome Initiative was launched with $121 million of funding to support research on the microorganisms that live in or on the human body, plants and other ecosystems and to provide a better understanding of their role in human and environmental health.[3] In 2018, a group of 23 U.S. government agencies, including the National Science Foundation (NSF), announced they have joined to produce a five-year Interagency Strategic Plan for Microbiome Research, which outlines the objectives, structure and principles for coordinated microbiome research.[4]

Figure 1. Increased Academic and Biomedical Research into the Microbiome (2004-2018)

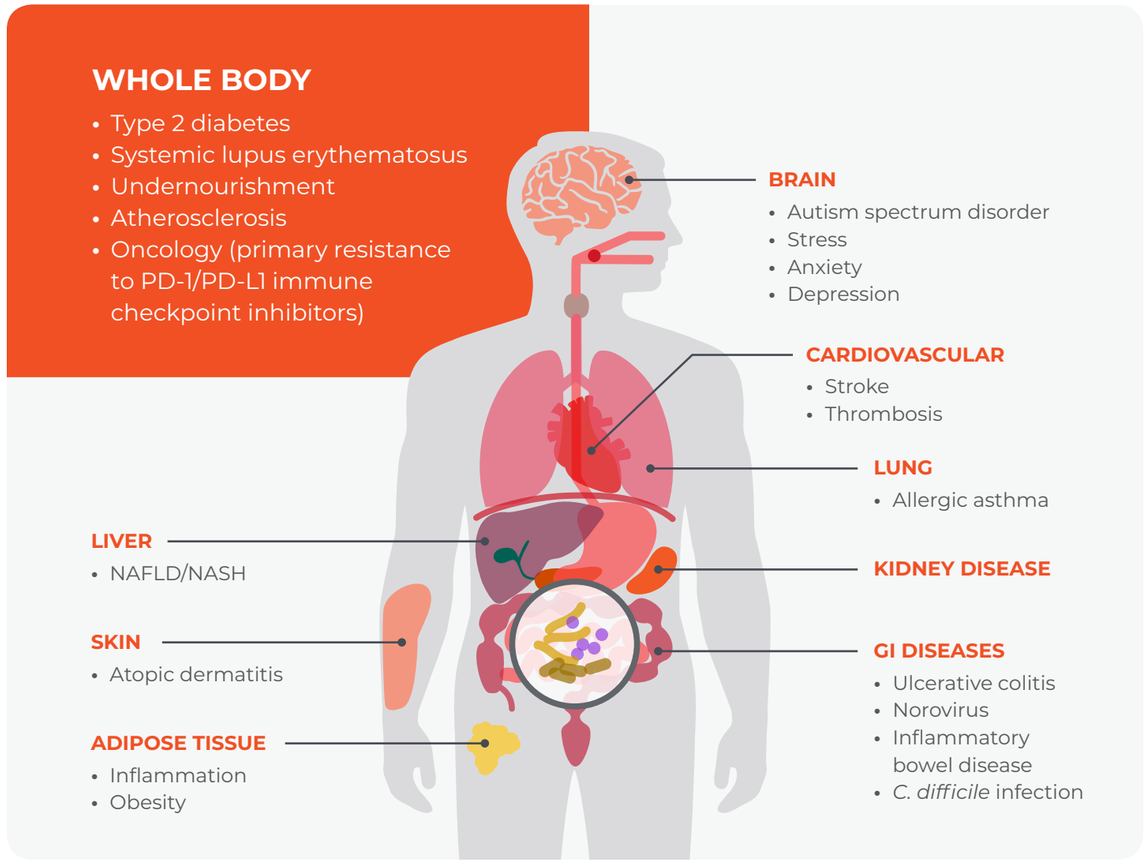


The European Union has already funded 216 projects under the Seventh Framework Programme (2007-2013) and Horizon 2020 (2014-2020) to promote metagenomics (the study of genetic material recovered directly from environmental samples) and advance knowledge of microbes.[5] This support started with the MetaHIT project, which has produced a catalogue of gut microbes, and now includes the advanced multidisciplinary SYSCID research project, which is looking at the role of the microbiome in chronic inflammatory diseases (inflammatory bowel disease, systemic lupus erythematosus and rheumatoid arthritis) as well as mechanisms of microbiome resilience and disruption. Together, these projects involve an investment of more than €498 million. While lower than U.S. funding, all of this is specifically targeted at the human microbiome.

Progress in this area is also demonstrated by the exponential growth in research publications over the past decade (Fig. 1). Momentum in microbiome research has been enabled by advances in technology, such as gene sequencing and profiling, to the point that the Cleveland Clinic listed the microbiome as the top medical innovation of 2017.[6]

Research to date shows that the gut microbiota, via alterations in composition, diversity and microbial metabolites, is associated with various diseases in humans affecting the brain, lung, liver, skin, gastrointestinal tract and adipose tissue, as well as "whole body" diseases including type 2 diabetes, systemic lupus erythematosus, undernourishment and atherosclerosis (Fig. 2). The relationship between the microbiome and health or disease is associative, with causality so far not clearly demonstrated. However, evidence for a causative role of the gut bacteria is strongest in metabolic disease (e.g., obesity, insulin resistance, and type 1 and type 2 diabetes).[7]

Figure 2. Association of the Gut Microbiome with Disease in the Human Body



NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

There are multiple mechanisms by which drugs and therapies have been shown to exert their therapeutic effect via the gut microbiome (Table 1). In the area of metabolic disease, for example, metformin has been shown to alter composition of the gut microbiome, inducing functional changes associated with improved glucose tolerance.[8] In oncology, antibiotic treatment (which affects the composition of resident gut bacteria) has been shown to affect the response of cancer patients to treatment with immune checkpoint inhibitors targeting the PD-1/PD-L1 axis.[9] It has also been shown that patients with a favorable gut microbiome have enhanced response to anti–PD-1 immunotherapy.[10]

Table 1: Association of the Gut Microbiome with Therapeutic Effects of Drugs

Disease	Drug/therapy	Mechanism of therapeutic effect
Type 2 diabetes	Metformin[a]	Metformin alters the gut microbiome composition and induces functional changes, which lead to improved glucose tolerance.[8]
Obesity, and cardiovascular and neurodegenerative diseases	Photobiomodulation (PBM)[a]	PBM can alter microbiome diversity in healthy mice and increase numbers of Allobaculum, a bacterium associated with a healthy microbiome. If this is confirmed in humans, the possibility exists for PBMt to be used as an adjunct therapy in treatment.[16]
Ulcerative colitis	Moxibustion treatment[a]	Moxibustion treatment restored the colonic mucosa and decreased submucosal inflammatory cell infiltration in colitis rats. Findings suggest that moxibustion exerts its therapeutic effect by repairing mucosal tissue damage and modulating the gut microbiome and intestinal mucosal immunity.[17]
Kidney disease	Magnesium lithospermate B (MLB)[a]	The therapeutic effect of MLB on kidney injury might be attributed (at least partially) to its ability to modulate the disordered gut microbiome and bile acid metabolism. In streptozotocin-treated mice, 24-h urinary albumin levels and total fecal BAs, especially cholic acids and deoxycholic acids, were greatly increased compared with control mice.[18]
Obesity-induced insulin resistance and type 2 diabetes	Cucumis melo L. (Cucumis)[a]	Administration of Cucumis improved insulin-resistance by reducing inflammation, thereby changing the gut microbiota composition. Cucumis is thus a promising treatment for obesity-induced insulin resistance and the inflammatory state.[19]
Norovirus infection	Vitamin A	Vitamin A supplementation significantly increased the abundance of Lactobacillus sp. during norovirus infection, which played a crucial role in antiviral efficacy, inhibiting murine norovirus. The antiviral effect of vitamin A occurred via modulation of gut microbiota.[20]
Resistance to immune checkpoint inhibitors targeting PD-1/PD-L1	Oral supplementation of Akkermansia muciniphila	Primary resistance to immune checkpoint inhibitors targeting the PD-1/PD-L1 axis can be attributed to abnormal gut microbiome composition. Oral supplementation with A. muciniphila restored the efficacy of PD-1 blockade.[9]

[a] Drugs/therapies tested on animals.
BA, bile acid; PD-1, programmed death receptor-1; PD-L1, programmed death ligand 1.

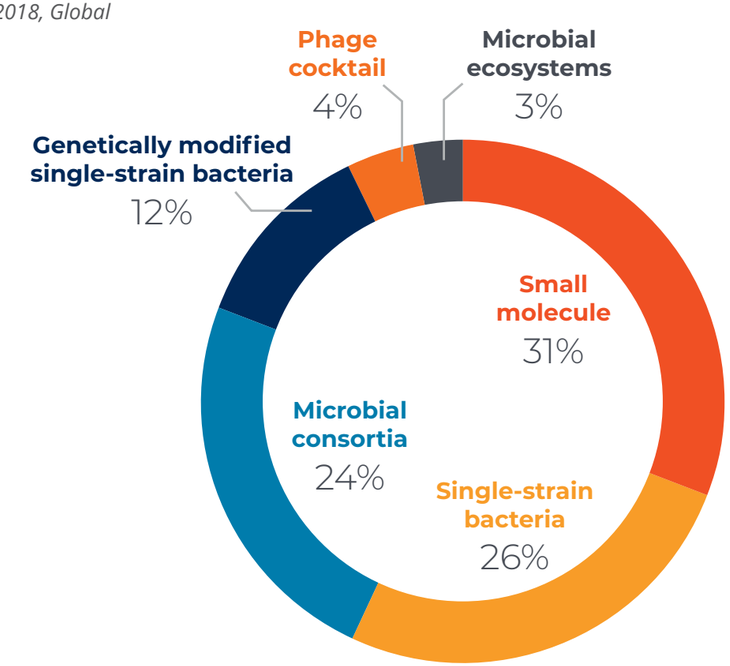
The New Microbiome Industry

Given the link between the gut microbiome and therapeutic effects in a wide array of diseases and conditions, numerous start-up companies focused on microbiome research and therapeutics have emerged in recent years. A number of these are focused specifically on services and data for the research industry, including gene testing and sequencing companies. Fewer companies are focused on therapeutics. In this latter group, some are focused on the skin microbiome but most are developing therapeutics targeting the gut microbiome (the focus of this paper), which have a more rigorous development pathway and stringent regulatory pathway than products for the consumer market (i.e., nutritional supplements/probiotics).

There are several approaches to developing microbiome therapies. Companies such as BiomX and Seres Therapeutics are testing multiple approaches, while most other well-known players in the field, such as Assembly Biosciences, Enterome, Rebiotix and Vedanta Biosciences, are focused on testing a single approach. Small-molecule therapies are the most common in development (Fig. 3), followed by single-strain whole bacteria. Approaches using microbial ecosystems are less common because they are more challenging, due to the involvement of multiple bacterial populations, which therefore greatly increases the number of variables in play, making it difficult to determine cause and effect.

Figure 3. Microbiome Approaches Adopted for Pipeline Assets[a,b,c]

2018, Global



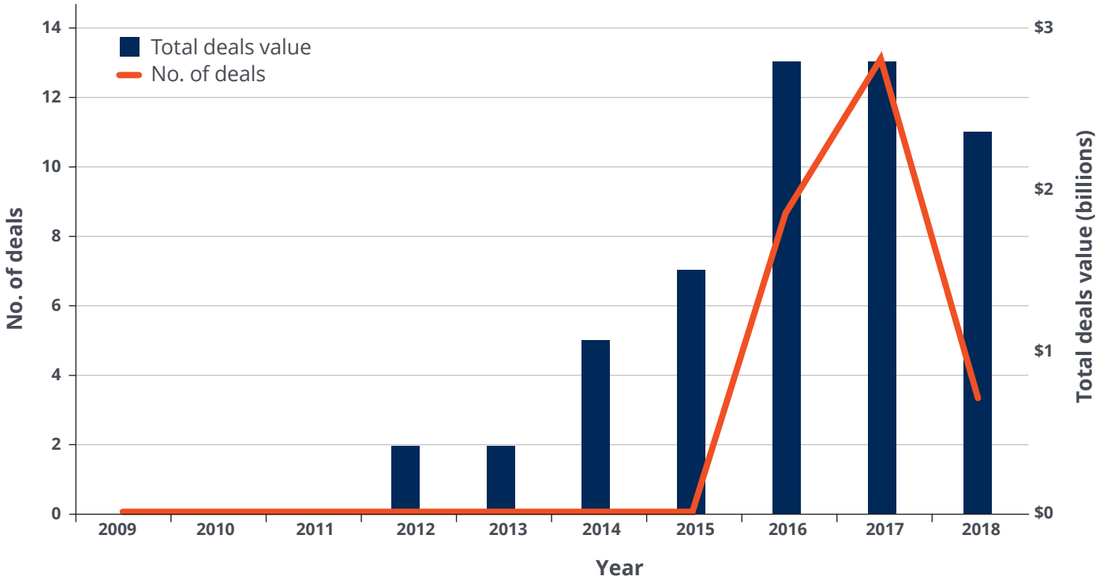
The most common approaches used are small-molecule therapies, single-strain bacteria, and microbial consortia.

[a] Excludes products that do not have a development stage published.
[b] Analysis excludes companies not listed in Table 2.
[c] Excludes 27 assets lacking clarity on technology adopted.

Microbiome investments and dealmaking on the rise

The increasing interest in microbiome therapies can be seen in the rising levels of both dealmaking and investment over the last decade (Fig. 4). Since 2015 alone, more that $5.4 billion has been spent on partnerships and acquisitions in the therapeutic microbiome space.

Figure 4. Microbiome Deals over the Past Decade



Large pharmaceutical seeing the potential

The global human microbiome market, encompassing therapeutics, the consumer market (probiotics) and research products (instruments and technology), is expected to reach $899 million by 2025;[11] the microbiome therapeutics market will contribute just under 50 percent of this value—$433 million—by 2025.[12] Large pharmaceutical companies are seeing this potential and have begun partnering with select biotech companies at an increasing rate (Table 2). While these deal values are typically undisclosed, when they are disclosed we are seeing that payments are largely back-loaded—for example, with Nestlé Health Science and Allergan making upfront payments of 2 to 6 percent of the total deal value, and then sharing development costs or making clinical development, regulatory and commercial milestones payments. A few large pharmaceutical companies are at the forefront of microbiome dealmaking, with Janssen creating the Human Microbiome Institute and Takeda's prolific partnering with biotechs (including Enterome, Finch Therapeutics and NuBiyota).

Table 2. Microbiome Licensing Deals Between Big Pharma and Biotech (2014-Q1 2019)

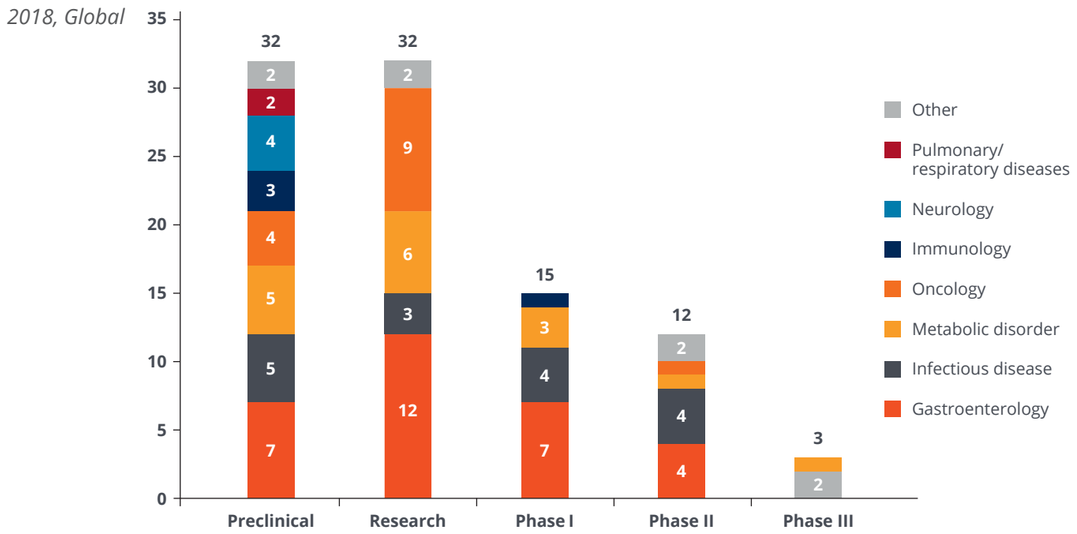
Licensing partner	Company	Deal details			
		Potential overall deal value	Development milestones	Commercial milestones	Comments
abbvie[a]	Holobiome	Undisclosed			Noninvasive biomarker for Crohn's disease
	synlogic	Undisclosed			AbbVie's expertise in metabolic and inflammatory diseases combined with Synlogic's platform
Allergan	assembly biosciences	$2.78B, $50M upfront	$630M	$2.15B	Development costs will be shared up to $75M through proof-of-concept (POC) studies for 4 candidates; Allergan to cover post-POC costs
AstraZeneca	SERES THERAPEUTICS		AstraZeneca will pay $20M in three equal installments over two years to Seres		Three-year research collaboration to explore the use of microbiome therapy in boosting the efficacy of cancer immunotherapy; AstraZeneca will also reimburse Seres for research activity carried out as part of the collaboration
Bristol-Myers Squibb	enterome	Undisclosed; $15M upfront			Immuno-oncology focused; CDx and tx for cancer
FERRING PHARMACEUTICALS	Rebiotix				Full acquisition of Rebiotix, who will maintain autonomy due to the highly specialized nature of the microbiome drug development space
Johnson & Johnson	Holobiome	Undisclosed			Research collaboration to develop proprietary bacterial consortia to treat digestive disorders; upfront payment plus additional payments contingent upon completing development milestones
	VEDANTA BIOSCIENCES	$241M			Develop and commercialize
Nestlé HealthScience	Holobiome	Undisclosed			Joint venture; for all non-oncology biomarkers/Dx
	SERES THERAPEUTICS	$1.9B; $120M upfront			$660M in milestone payments
Takeda[a]	enterome	Undisclosed			Use of its proprietary metagenomic platform to support the discovery of potential novel agents (small molecules or biologics) derived from gut bacteria and directed to the GI targets selected by Enterome and Takeda
	FINCH THERAPEUTICS	$10M upfront; total value undisclosed			Exclusive, global rights to develop and commercialize FIN-524
	NUBIYOTA	Undisclosed			Research to advance oral microbial consortia products developed by using NuBiyota's microbiome platform for GI indications

[a] Status of Enterome's collaboration with these companies unknown since Nestlé Health Science joint venture was initiated.
Source: Company websites, press releases

The microbiome therapeutic pipeline is growing, with *Clostridium difficile* therapies leading the way

While the vast majority of microbiome R&D is in the preclinical and basic research phase, several "to watch for" therapies are currently in Phase II and III clinical trials (Fig. 5).[13] Two of these, SER-109 (Seres Therapeutics) and RBX-2660 (Rebiotix), are in Phase III and specifically indicated for the treatment of *C. difficile* infection, considered to be one of the leading threats to public health. Synthetic Biologics has completed Phase II testing of SYN-004, a first-in-class oral enzyme prophylactic therapy designed to degrade certain IV beta-lactam antibiotics within the GI tract and maintain the natural balance of the gut microbiome for the prevention of *C. difficile* infection, overgrowth of pathogenic organisms and the emergence of antimicrobial resistance. In metabolic disease, RP-G28 (Ritter Pharmaceuticals) is in Phase III trials for the treatment of lactose intolerance.

Figure 5. Start-up Microbiome Pipeline Assets



Source: EvaluatePharma, company websites

Development and Commercialization Challenges… and Some Open Questions

Assuming SER-109, RBX-2660, and RP-G28 demonstrate positive results in their respective trials, it is likely that in the next one to two years the first-ever commercially developed microbiome-based therapies will be approved by the FDA. Even though these molecules have reached Phase III clinical trials, development and commercialization challenges in this new therapeutic field abound.

The intellectual property conundrum

Microbiome research presents some unique intellectual property and patent protection complexities, with implications for attracting investment. For example, patent law prohibits patenting naturally occurring materials, live organisms and "natural phenomena." There are also issues relating to definiteness—the requirement that patent claims be specific with regard to the microorganism(s) encompassed by the claims. For any one beneficial function, however, it is likely there are others—perhaps many—organisms with the same beneficial effects. With patent law still evolving in this area, it remains to be determined to what degree patents for a collection of microbes patented by one company would exclude another company from developing a therapeutic with the same combination and ratio of microbes.

Clinical development and trial design considerations

Additional challenges in microbiome therapeutics R&D stem from the fact that a person's microbiome is changeable when perturbed and the precise mix of bacteria being administered therapeutically (e.g., via fecal microbiota transplantation, or FMT) cannot be known. The many variables in these studies are difficult to control.

Choosing the right patient population and accurately diagnosing patients for clinical testing can also create development challenges. For example, after the first Phase II study of SER-109 failed to meet its primary endpoint, an in-depth analysis of the data suggested that misdiagnosis of recurrent *C. difficile* infection may have contributed to the "unexpected" results, along with suboptimal dosing. Working with the FDA to redesign the trial, Seres Therapeutics initiated a new study using a different diagnostic method for both study entrance and endpoint evaluation—a direct test for the presence of *C. difficile* cytotoxins in stools—rather than testing for the presence of the cytotoxin genes.[14]

Regulatory wayfinding

Regulatory frameworks have not caught up to microbiome-based therapies, and it is not yet clear through which route these therapies will be evaluated, although the FDA has issued draft guidance and signaled a willingness to discuss with industry.[15] Whether this results in the creation of a new regulatory pathway for microbiome-based therapies within the regulatory agencies remains to be seen. Regulatory agencies require a lot more certainty as to what they are putting into patients, and a microbe that is poorly defined is a cause of great anxiety at the FDA and EMA. The undefined probability of success makes it hard for many companies to raise the investments needed to make inroads. As with other therapies, amidst this uncertainty companies should engage regulatory bodies early and throughout development in discussions about endpoint determination and trial design.

The experience biosimilars faced with the regulatory bodies may be relevant. Initially the regulatory challenges were considerable, resulting in a number of large pharmaceutical companies leaving the space. Over time, however, the cost-savings potential of biosimilars pushed regulatory bodies to outline a developmental path that would expedite market entry while maintaining quality standards. With regard to microbiome-based therapies, the FDA has acknowledged the potential benefit offered by these products and has stated a commitment to advancing the clinical science necessary to understand their safety and efficacy.

While the FDA has been working on addressing the new category of live biotherapeutics, the EMA seems to be lagging behind. This could affect numerous new drug products coming to market in the future, potentially resulting in this revolution in medicine reaching European patients much later. This is difficult to grasp, as Europe has been a leader in microbiome research. Biotechnology companies are being created in staggering numbers in the U.S., however, while in Europe, the lack of regulatory framework is impeding these companies' financing and growth.

Manufacturing and technology considerations

Manufacturing standards for microbiome-based therapies are sure to be highly scrutinized, especially considering the batch-to-batch variations with living organisms. Live culture compositions will need to be standardized (to some as yet-to-be–defined degree) to give regulatory bodies confidence in reproducibility. Key concerns may include potency (the amount of product necessary to achieve the desired efficacy); purity (no detectable pathogens); and identity (the presence of certain organisms, especially when those responsible for therapeutic effect are currently unknown). Further requirements may also be introduced, such as additional containment areas to ensure "clean" areas remain sterile. Formulations will need to be prepared in such a way that the beneficial effects persist throughout the supply chain to the consumer and through to the expiration date of the product.

Expectations and hype versus reality: commercial considerations

Because microbiome-based therapies constitute an entirely new therapeutic category, there is much uncertainty about the best paths to commercialization. Media attention and hype may create unrealistic expectations among physicians, patients and payers. Unrealistic expectations coupled with a fear of inadequate efficacy or uptake for the first few products entering the market could be devastating to the field. Venture capitalists might stop funding, and physicians might doubt the therapeutic strategy and/or be unwilling to collect clinical samples for databases. Careful and early consideration and planning is required to ensure continued investment to generate all the data needed to advance these therapeutics and to enhance adoption.

From the physician perspective, topics of concern that will need to be addressed include the setting of care, diagnostic methods, product positioning, where the therapy fits in the overall treatment paradigm (acute, chronic or preventive) and antimicrobial stewardship. Microbiome-based therapies are relatively unknown to the general population, and awareness and education efforts will be needed to explain and differentiate them. Patient perceptions will need to be managed with regard to donor (e.g., fecally-derived) versus manufactured product as well as the dosing method (oral, IV, colonoscopy, enema). Once approved, education and support for patients and caregivers will be needed to enhance understanding of the science behind microbiome-based therapies, increase acceptance and facilitate compliance.

From the payer perspective, if the FDA's current stance on the use of FMTs does not change, the eligible population to receive these agents will be limited (both agents in Phase III trials have received orphan drug designation for recurrent *C. difficile* infection by the FDA). In order to justify their development, it is likely that manufacturers will price these agents at a premium. While this pricing strategy is common in other drug categories, this approach may curb uptake in this market, where most of the available antibiotics are generic and cheap, and "homemade" FMTs or those obtained from stool banks have a relatively low cost. Consideration will need to be given early in the development cycle to evidence generation beyond safety and efficacy, including real-world data necessary to demonstrate value to payers and to support reimbursement.

Concluding Thoughts

While currently there are plenty of unanswered questions and challenges and very few certainties, it is clear that microbiome-based therapies, such as those targeting *C. difficile* infection, have potential in areas of high unmet need and significant public health importance. It is also clear that the FDA is willing to work with industry on the development of FMTs as commercially available agents. Regardless of the outcome, microbiome-based therapies for *C. difficile* infection will undoubtedly pave the way for targeting other indications, ushering into the clinic a new class of therapies and treatment approaches. Companies investigating this new frontier will benefit from careful attention to maintaining collaborative interactions with the regulatory bodies regarding trial design and regulatory pathways, and consideration of commercialization challenges early on—including thorough market landscape assessment, education and evidence needs of multiple stakeholders—to help prepare physicians, patients and payers for this new category of therapy.

Stay tuned for additional microbiome perspectives through 2019, where we will track progress in the gut microbiome field and elaborate on the challenges, additional considerations, and the potential for addressing them.

References

1. Goodrich JK, Davenport ER, Clark AG, Ley RE. The relationship between the human genome and microbiome comes into view. *Annu Rev Genet.* 2017;27(51):413-433.
2. National Science and Technology Council. Report of the fast-track action committee on mapping the microbiome. November 2015. Available at: https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/NSTC/ftac-mm_report_final_112015_0.pdf
3. White House Office of Science and Technology Policy. Announcing the National Microbiome Initiative. Available at: https://obamawhitehouse.archives.gov/blog/2016/05/13/announcing-national-microbiome-initiative
4. National Science Foundation. Available at: https://www.nsf.gov/news/news_summ.jsp?cntn_id=245289
5. Hadrich D. Microbiome research is becoming the key to better understanding health and nutrition. Front Genet. 9:212. doi: 10.3389/fgene.2018.00212
6. Cleveland Clinic. Available at: https://innovations.clevelandclinic.org/Summit/Top-10-Medical-Innovations/Top-10-for-2017/1-The-Microbiome-to-Prevent,-Diagnose,-and-Treat
7. Schroeder BO, Backhed F. Signals from the gut microbiota to distant organs in physiology and disease. *Nature Medicine.* 2016;22(10):1079-1089.
8. Wu H, Esteve E, Tremaroli V, et al. Metformin alters the gut microbiome of individuals with treatment-naïve type 2 diabetes, contributing to the therapeutic effects of the drug. *Nat Med.* May 2017; doi:10.1038/nm.4345.
9. Routy B, Le Chatelier E, Derosa L, et al. Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors. *Science.* 2018;359:91-97.
10. Gopalakrishnan V, Spencer CN, Nezi L, et al. Gut microbiome modulates response to anti-PD-1 immunotherapy in melanoma patients. *Science.* 2018;359:97-103.
11. Markets and Markets. Human microbiome market worth 899.1 million USD by 2025. Available at: https://www.marketsandmarkets.com/PressReleases/human-microbiome.asp
12. Grand View Research. Microbiome therapeutics market size to reach USD 433.5 million by 2025. Available at: https://www.grandviewresearch.com/press-release/global-microbiome-therapeutics-market
13. Pharma Intelligence. Microbiome modulator drugs – the new generation of therapeutic. Available at: https://pharmaintelligence.informa.com/~/media/informa-shop-window/pharma/whitepapers/pharmaprojects-microbiome-whitepaper.pdf
14. Seres Therapeutics. Press release, October 3, 2018. Available at: https://www.businesswire.com/news/home/20181003005055/en/Seres-Therapeutics-Present-New-Data-Supporting-SER-109
15. Food and Drug Administration. Statement from FDA Commissioner Scott Gottlieb, M.D., on advancing the science and regulation of live microbiome-based products used to prevent, treat, or cure diseases in humans. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm617168.htm
16. Bicknell B, Liebert A, Johnstone D, Kiat A. Photomodulation of the microbiome: implications for metabolic and inflammatory diseases. *Lasers Med Sci.* 2019;34(2):317-327.
17. Qi Q, Liu YN, Jin XM, et al. Moxibustion treatment modulates the gut microbiota and immune function in a dextran sulphate socium-induced colitis rat model. *World J. Gastroenterol.* 2018;24(28):3130-3144.
18. Zhao J, Zhang QL, Shen JH, Wang K, Liu J. Magnesium lithospermate B improves the gut microbiome and bile acid metabolic profiles in a mouse model of diabetic nethropathy. *Acta Pharmacol Sin.* 2019:40(4):507-513.
19. Lee D, Yoo JH, Lee BC. Therapeutic effeci of *cucumis melo* L. Extract on insultin resistance the the gut microbiome in Lepob/Lepob mice. *Evidence-Based Complementary and Alternative Medicine.* Available at https://doi.org/10.1155/2018/8159261
20. Lee H, Ko GP. New perspectives regarding the antiviral effect of vitamin A on norovirus using modulation of gut microbiota. *Gut Microbes.* 2017;8(6):616-620.

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