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GCV Special Report:

The human microbiome

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Feature

AI and genome sequencing open up new treatments

By Robert Lavine

Technology is starting to make it possible to understand the complex interactions of the microbiome in more detail.

"In nature, when a plant or animal is taken out of the forest it can cause a ripple effect through the rest of the area – that's what goes on in your gut," says Greg McParland, an investment director at the venture arm of nutritional product provider DSM and board member at probiotic supplement producer Sun Genomics.

Advances in gene sequencing technology and computational power are giving researchers and healthcare professionals an increasingly detailed view of how the human microbiome – the trillions of microorganisms that exist on or in the human body – affect our health.

Whole-genome sequencing allows scientists to see rarer types of bacteria in the gut in greater detail, says McParland, and it is opening up new treatment methods for a variety of conditions.

"They're finding all these less prevalent types of bacteria people thought were insignificant, these low-abundance species we weren't seeing before," he says. It's now possible to study the interactions between different species as well as metabolites, the substances created when the body breaks down food or tissue.

"That's been a huge change over the last 10 years or so, but it's shown how complex it is," McParland adds.

San Diego-based Sun Genomics is one of a crop of startups taking advantage of the growing precision of microbiome research. It raised money from DSM Venturing in January this year and combines whole-genome sequencing with gut composition analysis to personalise each customer's supplements.

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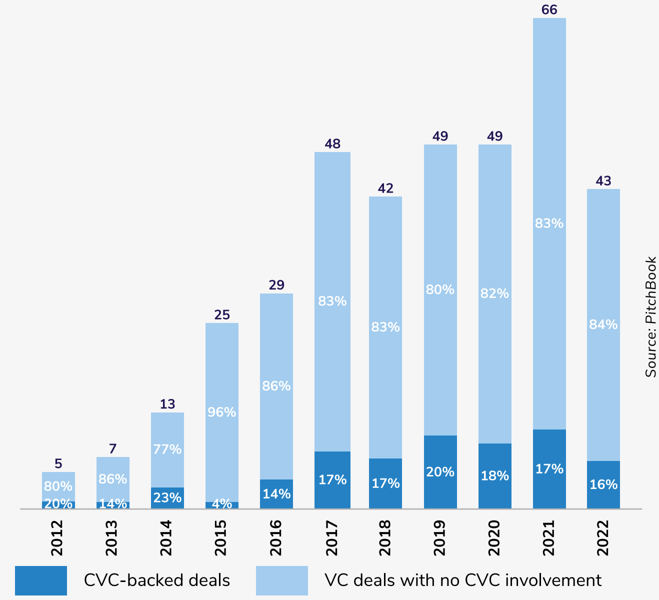
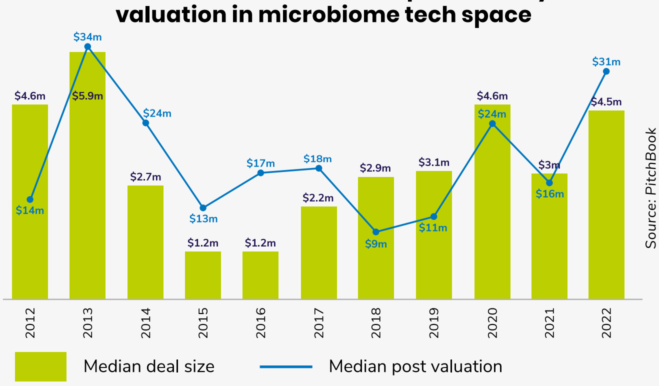
Dashboard

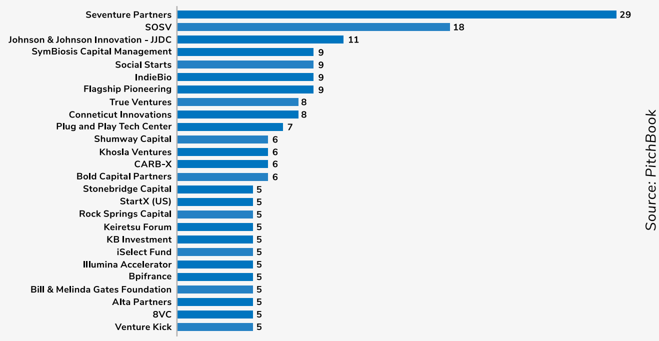
Microbiome tech deals 2012-2022



Median deal size & median post-money valuation in microbiome tech space



Top investors in microbiome tech 2012-22



DSM is one of several corporates backing microbiome startups, a group mostly coming from the pharmaceutical industry (Johnson & Johnson, Lundbeck) or fast-moving consumer goods and nutrition (Unilever, Roquette).

Studies estimate there are three times as many microbial cells than human cells in the body, yet relatively little was known about their effect before 2007 when the US National Institutes of Health launched the Human Microbiome Project to research how they influence health.

A significant challenge has been the complexity of different microbiomes, and a game changer for research has been the sharp drop in the cost of genome sequencing, which has fallen from over $100m per genome in 2001 to below $1,000 in 2021.

Taking things a step further to study not just the microbes themselves but how they interact with each other and with the body requires substantial computational power. But this is now coming, says Owen Lozman, managing director of M Ventures, the corporate venture capital subsidiary of pharmaceutical company Merck.

"In the last five or six years, computation has developed significantly and we have things like quantum computing on the horizon which are going to be able to address these complex multidimensional problems, with generative AI models also helping," Lozman says.

A year ago, M Ventures invested in Concerto Biosciences, creator of a platform that experimentally measures millions of microbial interactions to gauge how they will actually work as treatments in the overall human body.

"The combination of [advanced computing] with advanced manufacturing technologies, the movement of some chip manufacturing technologies into the biotech industry so that we can enable technologies like Concerto's have to really produce the science that underpins all of this – I think it all starts to build the knowledge we need to make this a really interesting field."

Beyond the gut

Although the gut has traditionally been the focus of microbiome research, several parts of the body have their own microbiome and startups have begun springing up with products targeting them to improve health in new areas.

The skin is home to more than 1,000 species of bacteria and its microbiome is increasingly being used as the basis for cosmetics. DSM-backed Cybele has released a range of serums for eczema and ageing while Straand, a natural hair care startup focusing on the scalp microbiome, recently secured $2m in pre-seed financing from Unilever Ventures.

Another of those areas is oral health. GSK's Re/Wire Health Studio has backed a startup called Bristle, which offers a microbiome test to inform personalised care by assessing links to conditions like gum inflammation or oral thrush. Evvy has developed a similar test for vaginal care, and both companies are roughly three years old, signifying how the sector is expanding.

The most promising area within the body could potentially be the gut-brain axis, a form of biochemical signaling in which chemicals in the gut can affect the central nervous system. Companies such as Kallyope and Axial Therapeutics are harnessing research and bringing treatments for conditions that include gastrointestinal disease, diabetes and autism spectrum disorder into clinical trials.

"I think there will be some progress in cosmetics, some in pharma and a little bit back and forth," says Sarah Luppino, an M Ventures investor who sits on Concerto's board of directors.

"It doesn't have to be 'take this microbe and that's your medicine', it can also be 'pair this medicine you always take with this microbe or a metabolite product from a (microbial) consortia you realise is super powerful'. It can roll out in different waves and different flavours over time."

So far, however, few companies have had microbiome drug candidates get through the clinic, and the ones that have listed on the public markets have met mixed fortunes.

Next steps

Getting detailed data is important but the next stage will require it to be analysed in greater detail, says Artem Khlebnikov, director of bioeconomy, food and nutrition for Eagle Genomics, a company that structures and contextualises microbiome data. The current state of play is like knowing the alphabet and being able to put syllables together without knowing how to read, he says.

And while the gut-brain axis and gut-skin axis are hot research areas right now, understanding the human microbiome could have an impact on the planet, Klebnikov adds.

If we can get our gut microbiome to break down food so we get the right balance of fats, sugars and proteins in our diet, it could lead to more nutritious plants which need less land, in turn leading to less deforestation. In the future, microbiome projects could even be in line for carbon credits.

"My kids are millennials, and they ask me about the microbiome all the time," McParland says. "I tell them: 'Your generation and your kids are really going to benefit from this research'.

"That doesn't mean it isn't helping people today, but it's a journey of many, many years we're on."

Investor and startup views

Greg McParland, investment director at DSM Venturing

There will be more targeted prescription medicines and more targeted nutraceuticals heading our way, for more specific conditions, as we understand more about how our it's really working in our gut. Same thing for the skin.

I think there will be more prescription medicines coming to market in the next five years, and you're also going to see much more effective nutraceutical applications and clinically-backed treatments for specific health conditions.

Owen Lozman, managing director at M Ventures

We're now seeing more complex approaches that really require understanding of how system-level approaches and how those bacteria interact with their environment.

Given our visibility on what's happening and the waves of approvals that have gone through or not and the challenges people have had with clinical trials, this is starting to become more of a clinical topic, and we've seen more complex studies emerge recently.

Sarah Luppino, investor at M Ventures

It is much more data driven, trying to understand what's there, knowing there's some bacteria you can't culture and there are blind spots we know we have, but as more data and solutions and technology become more available, people are trying to leverage them.

It's going to be more and more data driven, in a good way, moving away from what was originally mostly based on inference.

I think there will be some progress in cosmetics, some in pharma and a little bit back and forth…it can roll out in different waves and different flavours over time.

Startups to watch

Altis Biosystems

Based in: US
Founded: 2015
Funding to date: $4.46m

Altis Biosystems is a US-based developer of RepliGut in vitro platform, a form of stem cell technology that recreates the human small intestine and colonic epithelium for microbiome research and disease modelling.

Christopher Sims, the startup's president, co-founded the company with Nancy Allbritton and Michael Biron in 2015. Sims also founded life science companies Cell Microsystems Inc and Intellego Inc, which have a combined net worth of $359.13m.

In August 2020, the UNC-Chapel Hill Biomedical Engineering Department spinout raised $3.2m from RTP Capital and Hatteras Ventures. In total it has raised $4.5m.

It received the National Institutes of Health research award for the commercialisation of RepliGut and the creation of its microfluidic organ-on-chip human colon mimicker.

BioCorteX

Based in: UK
Founded: 2021
Funding to date: undisclosed

BioCorteX plans to change the relationship between bacteria and medication by developing a clinically validated and knowledge-driven human microbiome platform. Its product, CarbonMirror uses AI to simulate how microbiota interact with therapeutics, helping de-risk pre-clinical trials,

The UK startup, launched in 2021, hopes to usher in a new era of tackling resistant cancers by altering the patient microbiome before chemotherapy. Cofounder Nik Sharma worked for 10 years as a neuroscientst at UCL, while cofounder Mo Alomari was the European AI hub lead at carmaker Rolls Royce.

BioCorteX has yet to disclose its total funding. It has developed four AI engines that have successfully produced 100,000 of previously unknown drug microbiome interactions and delivered several potential therapeutic options.

BiomeSense

Based in: US
Founded: 2018
Funding to date: $3.4m

Biomesense is a US-based spinout of the University of Chicago developing microbiome precision medicine. The company is developing a "smart bathroom unit" that can collect stool samples for ongoing analysis, creating a more complete picture of the gut microbiome.

It was founded in 2018 by Kevin Honaker and Jack Gilbert. Honaker is skilled in STEM commercialisation and served as a consultant at Healthscape Advisors for three years. Gilbert is a global leader in microbiome research. He co-founded the Earth Microbiome Project and the American Gut Project.

Biomesense has raised $3.4m in funding, with its latest round in 2019 when the spinout raised $2m in seed money from venture capital firms including BioX Clan and SOSV's biotech accelerator IndieBio. The funding has been used to complete Biomesense's prototype biosensor and data modelling platform.

Bitbiome

Based in: Japan
Founded: 2018
Funding to date: $8.06m

Bitbiome, a spinout of Waseda University, has developed a single-whole genome analysis platform that targets microbes and analyses microbiomes to understand disease-linked microorganisms. This technology removes the need to cultivate cells, which are commonly used in traditional microbiome assays.

Masahito Hosokawa, the spinout's chief scientific officer, founded the company in 2018. He has more than eight years of research experience in the application of novel microfluidic tools for single cell genomics. He was awarded The Young Scientists' Prize in 2019 by the Minister of Education.

The spinout has raised a total $8.06m. Its last funding round was in 2020 when it raised $6.6m in a series B round. The University of Tokyo's Edge Capital Partners, Universal Materials Incubator and the Japan Science and Technology Agency participated in the round.

CC Bio

Based in: UK
Founded: 2012
Funding to date: $1.22m

UK-based CC Bio develops microbiome editing technologies that harness enzymes derived from bacterial viruses to locate and kill disease-causing bacteria. Its drug discovery platform Zeus allows for the engineering and editing of the microbiome with surgical precision.

David Corcoran and Matthew Cummings co-founded the startup in 2012 to enhance the potential of the therapeutic microbiome. Both founders acquired doctorates in the scientific field: Cummings majored in synthetic biology and microbiology, and Corcoran has a PhD in medical chemistry.

CC Bio has raised a total of $1.22m. In 2021 it raised $1.05m in a seed funding round. Investors in that round included CMS Ventures, the corporate venture arm of medical company China Medical Systems, the UK government agency Innovate UK and venture capital firm Sana Capital.

Holobiome

Based in: US
Founded: 2015
Funding to date: $1.3m

Holobiome, a US-based company, has begun uncovering the link between gut microbiome and mental health. The startup has capitalised on epidemiology and animal studies research to create one of the world's largest collections of human gut microbiome. This will be used to produce new treatments and next-generation prebiotics for brain and nervous system disorders such as autism.

Philip Standwitz, Mike La Fleur and Kim Lewis launched Holobiome in 2015. Standwitz did research on bacterial cultivation and gut-brain axis at Northeastern University.

Since its launch, the startup has raised a total $1.3m. Japanese venture capital firm Corundum System Biology contributed $1m to support Holobiome's two year research. Johnson & Johnson recently announced a partnership with the startup to help develop prebiotics for infant and maternal immune health.

BiomeSense
Based in: US
Founded: 2018
Funding to date: $3.4m

Could a "smart toilet" solve the microbiome industry's data problem?

By Roshini Bains

BiomeSense, a University of Chicago spin out, wants to create a 10m record dataset for the microbiome sector.

The microbiome has become the latest healthcare craze, but there's one elephant in the room: there's just not enough reliable data to make it a useful treatment tool.

"Everyone in the field is aware of this crisis because the measurement tools we use for microbiome, such as stool collection kits, were never intended for microbiome itself. This process is outdated and has high error rates, whilst being time consuming," says Kevin Honaker, the chief executive officer and co-founder of BiomeSense, a startup developing an at-home microbiome testing kit.

Honaker says stool samples can be highly inaccurate. They might fail to detect colon cancer, for example, if a patient doesn't happen to have bleeding polyps and blood in the faecal matter.

"The measurement technology is just very ineffective, and we are forced to use this because there are no alternatives to date," he says.

It is also hard to know what is "normal" as there is a lack of data to compare a sample to.

"Even after all these years, there is no large existing curated microbiome database, which when compared to the genomics sector, has multiple companies that have data sets," says Honaker.

Measurement and datasets are the two problems BiomeSense, wants to solve with its "GutLab" product, an automated laboratory system small enough to sit by the side of a domestic toilet and do daily analysis of a user's gut microbiome.

"We have basically created a consumer-facing form of laboratory equipment," says Honaker, "Our goal is to unlock the next stage of microbiome from a clinical research and scientific perspective by increasing data and getting time series maps with the hope that the average consumer could have access to this technology and build microbiome monitorisation into their daily life, something that is not possible with today's lab-based solutions."

BiomeSense plans to use the data it collects from these daily testing kits to create a gut microbiome dataset.

"We want leverage that to help solve this data crisis by creating a time series million plus dataset, and scale that up to five-ten million records over the next few years in a faster manner at the fraction of the cost," Honaker says.

The plummeting investment climate

Microbiome startups have been receiving an increased amount of funding in recent years from venture capital firms and corporations such as Johnson & Johnson, but Honaker says backing is still difficult to get.

"In my personal opinion, investment in the microbiome sector seems to be plummeting," he says, "From my experience and what I have heard from other microbiome startups, the field is big on hype but short on results."

He continues: "If you look at the average consumer, how do they use microbiomes for the betterment of their health? Well, they don't and there is no way to do it. A company may make the claim that your microbiome score might be good, but you may get differing results from another, and this is because none of them have any a clear idea of what they are talking about because the data to back these claims just does not exist.

"The companies who are the worst offenders in making these claims are also no longer among us. This has meant that venture capital firms will not wish to persist in investing in microbiome startups when they can't tell the difference in microbiome data, and even now many venture firms are unresponsive to microbiome startups," says Honaker.

Microbiome startups that have received significant levels of funding have taken decades to do so. Micreos, the Netherlands-based startup, for example, was launched in 2005 but only last year passed the $100m mark in funding after raising $26.5m from Altria's corporate arm, Altria Ventures. Compare this to other healthcare startups such as Headspace, the mental health app, which has raised a total of $215m in funding since 2010.

"Hopefully there will be a turnaround soon, and there is still a lot of hope in the consumer side of the microbiome, but within the biotechnology sector the response has been more stagnant," says Honaker.

Investment from venture firms and corporations
BiomeSense is a spin out from the University of Chicago, founded in 2018. It has raised a total of $3.4m in funding, including a $2m seed round in 2021, led by BioX Clan and SOSV's biotechnology accelerator IndieBio.

"We are using our funding to build a prototype of our technology, and a few weeks ago, we in fact closed another $3m round. So, our goal is to launch our product by the end of the year," he says.

"We are working with leading researchers across the US and have many clinical scientists who have signed up for us to replace how they typically do their clinical studies. This means they can use our technology to support their studies with a drastic increase in the quality and quantity of data generated to push the field further forward."

Honaker became involved with the company through his work as an innovation consultant at UChicagoTech where he advises early-stage startups on how to refine business plan. He also has more than 11 years of experience in the investment healthcare field, serving as a consultant for the US-based healthcare focused management consulting firm, HealthScape Advisors. He was also previously the director of finance and operations at Prescript IQ, the developer of genomic prescribing systems.

In addition to Honaker, the company's leadership is comprised of six people: co-founder Jack Gilbert, Dylan Nichols, the chief technology officer, Yoshiki Vázquez Baeza, bioinformatics lead, Nikhil Boddu, mechatronics engineer, and Madison Tuffield, research associate.

BiomeSense has been approached by an undisclosed corporate investor says Honaker, "I think it is important to have the support of venture firms and corporations, especially if you have a unique idea, having that strategic input from an outside perspective truly helps. It further shapes the startup, and provides the team with the confidence and direction for some of the development efforts occurring."

"Microbiome is super exciting," concludes Honaker, "It's had its struggles in the sector and will continue to, but once we take a rational look at it and acknowledge the gaps in the industry, its potential could be unstoppable. We have only scratched the surface with microbiome and it leads to an exciting question of what it could become in the future."

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Startups to watch

Juno Bio

Based in: UK
Founded: 2018
Funding to date: $251k

UK-based Juno Biome provides at-home test kits to help women understand their vaginal microbiome. The data is being is being used to form a better understanding of recurrent health conditions such as bacterial vaginosis.

Co-founder Hana Janebdar discovered the much-needed opportunity to close the gender health gap while working as a biologist in the microbiome industry. Janebdar and fellow co-founder Leighton Turner organised a management team of vaginal microbiome experts including Gregory Buck, the principal investigator on the NIH-funded Human Vaginal Microbiome Project.

Juno Bio has raised a total of $251,000 in funding. Its main investor is venture capital firm Acequia. The company also raised an undisclosed seed funding in 2019. Illumina Accelerator, a part of US biotech company Illumina, participated in that round.

Metagen Therapeutics

Based in: Japan
Founded: 2020
Funding to date: $1.68m

Japan-based Metagen Therapeutics is developing A treatment known as intestinal flora transplantation. It uses faecal microbiota to predict the safety and efficacy of a drug. It will help develop Japan's first gut microbiota bank.

The startup was formed by Japan-based venture capital firm Fast Track Initiative and the venture arm of Keio University.

Co-founders, Taku Nakahara, Dai Ishikawa, Shinji Fukuda and Takuji Yamada, established the company in 2020. They worked in the biosciences and gastroenterology departments at their respective universities.

Since its launch, Metagen Therapeutics has raised $1.68m (¥90M). Its last funding round was in 2022 when it raised $1.02m in a pre-series A round, with participation from Japanese investment company Jafco.

Micreos

Based in: Netherlands
Founded: 2005
Funding to date: $102m

Micreos is a Dutch biotech company developing a sustainable alternative to antibiotics. It develops an endolysin called Stapefekt, which selectively kills only harmful bacteria. It is incorporated into its skincare brand Gladskin,

Gladskin is used to treat inflammatory skin conditions such as acne and rosacea.

The startup was founded in 2005 by Mark Offerhaus and Hans-Poul Veldhuyzen van Zanten. Matt Regan, chief executive, has 30 years of experience in drug discovery and development.

The startup has raised a total $102m. Its most recent funding round was in 2022 when it raised $26.5m. Altria Ventures, the corporate venture arm of tobacco products group Altria, backed the company. Investors include the European Innovation Council and Dutch accelerator ScaleUpNation.

MRM Health

Based in: Belgium
Founded: 2020
Funding to date: $14.8m

The Belgium-based biotechnology company MRM Health focuses on treatments based on human microbiomes. The company's main target is inflammatory bowel disease. It recently developed a platform that provides differentiated microbiome consortia therapeutics for a variety of diseases.

The startup was established in 2020 by Sam Possemiers, who was a managing director at Ghent University spinout ProDigest, which specialises in customised solutions in the food and pharmaceutical markets.

MRM Health has raised a total of $14.8m, with its last funding round occurring in 2020. Du Pont's corporate venture arm, Du Pont Nutrition & Biosciences, and Belgian investor Ackermans & van Haaren participated in the last undisclosed round. The company partners with Du Pont Nutrition and Biosciences to jointly develop therapies for metabolic diseases.

ResBiotic

Based in: US
Founded: 2020
Funding to date: $3m

ResBiotic is a US-based startup developing prebiotics to treat lung cancer. The company has developed a drug dubbed resB Lung Support, which is a blend of anti-inflammatory herbs and prebiotic strains that target the gut-lung axis. It has been shown to reduce neutrophilic inflammation in sufferers of chronic respiratory illnesses.

The company was founded by C. Vivek Lal, a scientist at the University of Alabama, in 2020. Lal, who serves as the startup's chief executive, developed ResBiotic's formula at the university's Microbiome Lab.

ResBiotic has used the $3m it raised in a seed funding round in 2021 to create evidence-based treatments that can be made accessible to the general population. The lead investor in the round was Timberline Holdings, a US private equity firm that invests in sectors ranging from real estate to healthcare.

Seqbiome

Based in: Ireland
Founded: 2019
Funding to date: $20k

Seqbiome, a spinout of University College Cork, uses microbiome research to provide technical and scientific services through sample processing and sequencing data analysis. The data aims to provide insights into gut microbes linked to health conditions. It can also be used in sectors such as agriculture and sports.

Seqbiome was launched in 2019 by microbiome experts Marcus Claesson, Paul Cotter and Brad Wrigley, who together have published more than 350 papers on the topic. Claesson also serves as the company's chief executive and is a principal investigator at the APC Microbiome Institute at the university.

The startup has raised $20,000. Its last funding round was in 2021. The investors were not disclosed. The company was also selected in 2021 to take part in PepsiCo's Greenhouse Accelerator programme.

Market overview

By Kaloyan Andonov

While we have been aware of microorganisms since the discovery of the microscope in the 17th century, it is only more recently that science has become aware of the complex interactions of different microbes hosted by humans and the effect they have on our bodies.

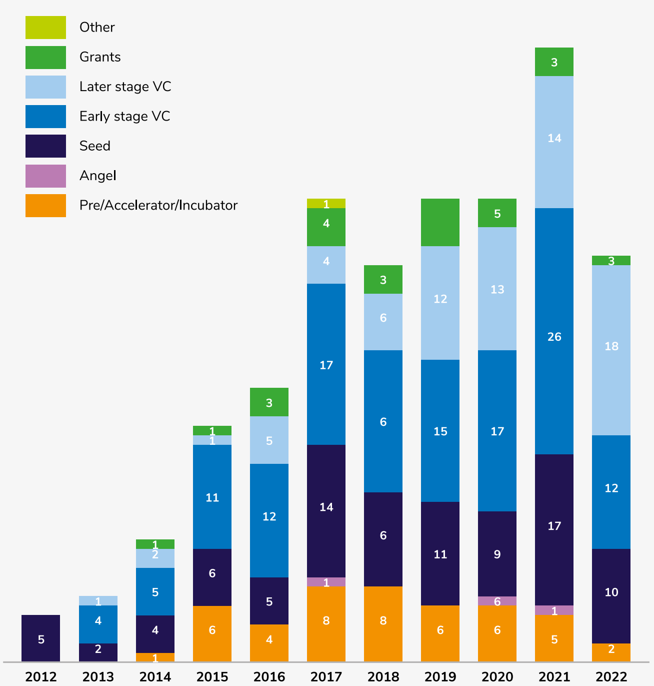
The idea that the collection of microorganisms living on the human body have an influence on our health and immune function has become popular in the healthcare sector. Sometimes called the "last organ under active research", the human microbiome and therapeutics relating to it are attracting dollars and interest in the innovation community – albeit still from a low base.

According to ***Strategic Market Research***, the human microbiome market worldwide is expected to witness a robust CAGR of 31%. The market itself was, according to the report, valued at merely \$115m in 2021 but is expected to reach \$1.3bn by 2030.

Another report from ResearchandMarkets, put the 2022 microbiome market higher — at \$390m — and forecast it would grow to \$570m by the end of 2023.

That is miniscule compared with, say, the global oncology market estimated at \$286bn in 2021, according to a report by Precedence Research. The market for microbiome-based treatments is still nascent.

VC-backed deals in microbiome tech 2012-2022 by deal stage

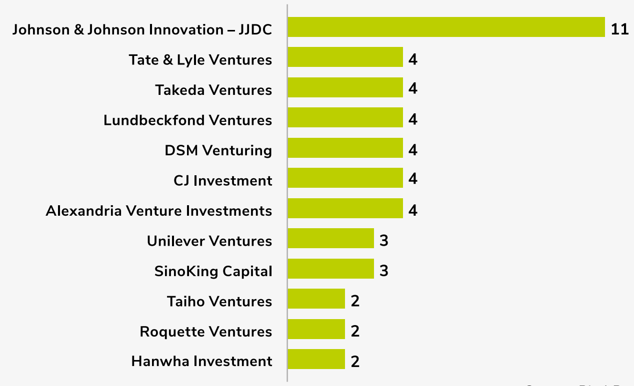


Source: PitchBook

The number of VC-backed deals in the human microbiome space is still relatively modest even on a global scale as the above chart illustrates. Moreover, it is not an area with a great deal of corporate investment — the share of corporate-backed deals in this field is less than 20%.

Johnson and Johnson Innovation – JJDC has been one of the most active corporate investors into microbiome startups with 11 deals in this space in the last decade. Last year, for example, the venturing arm backed the \$35m series B round raised by Locus Biosciences. The company develops precision medicines for bacterial infections and microbiome diseases, designed to tackle growing antimicrobial resistance.

Top corporate investors in microbiome tech 2012-22



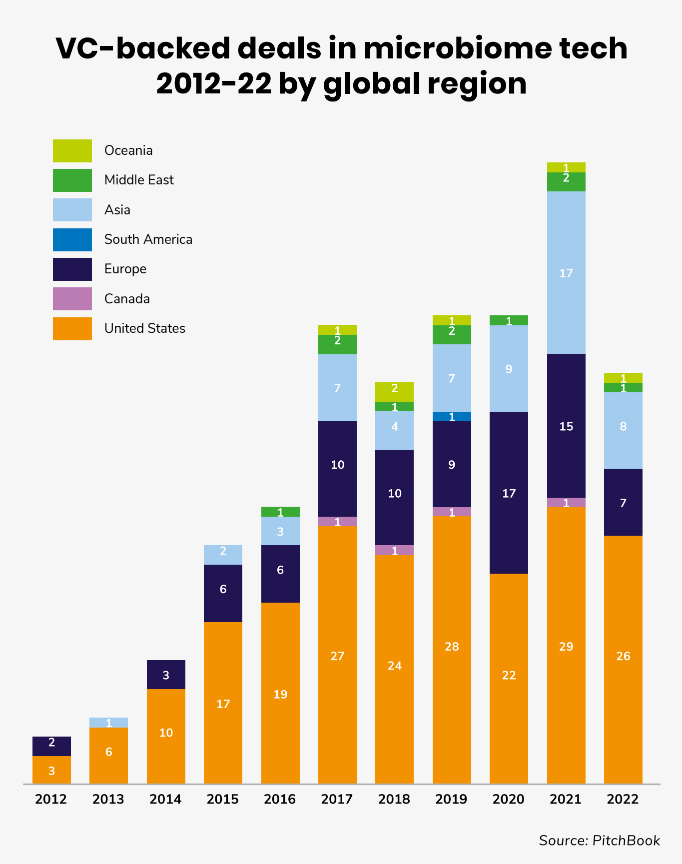
Source: PitchBook

Most of the funding rounds that have gone ahead are at the seed or early stage.

Median deal sizes are relatively modest — just \$4.5m last year and the median post-money valuations of the startups raising the funding tends to be low.

North America and Europe have been the biggest regions for microbiome funding rounds, although there is an increasing number also in Asia Pacific.

Market overview (cont.)



Gut feeling

Microbiota, depending on where they are located, can be subsumed broadly into respiratory, oral, gut and skin microbiota. Gut bacteria is the most studied of these with a clear connection already established between the gut microbiome and specific medical conditions.

One of the best known is inflammatory bowel disease (IBD), which is a chronic immune-mediated gastrointestinal disease consisting of two subtypes - ulcerative colitis (UC) and Crohn's disease.

According to a 2019 paper by scientists from the American Academy of Allergy, Asthma & Immunology, studies with human subjects demonstrate the gut microbiome differs significantly in patients with IBD versus healthy control subjects.

There is a huge potential addressable market for this, with the US Center for Diseases Control and Prevention estimating that in 2015, 1.3% of US adults (roughly 3 million people) reported having been diagnosed with IBD.

There is a growing interest in developing microbiome-modulating interventions for IBD, from probiotics and prebiotics through antibiotics to faecal microbiota transplantation (FMT) and gene manipulation.

FMT, for example, is often employed to treat IBD as well as Clostridioides difficile, a bacterium that causing diarrhoea and inflammation of the colon. In fact, there are some historical records that suggest it was first used in traditional Chinese medicine as early as the III century AD.

The potential stumbling block for growth of the space, however, is the still relative high cost of microbial therapies. For example, according to estimates from a study conducted in Denmark, the weighted average cost of FMT stood at between €2,864 and €3,326 per patient, depending on the method used. That cost can put FMT out of reach for many, although there are some studies suggesting it is relatively cost-effect when compared with other treatment options for recurrent infection from Clostridioides difficile.

Metabolite treatments and metabolite sensing

Metabolites are an emerging area of human microbiome treatment. A metabolite is a substance made or used when the body breaks down food, drugs or chemicals. Studying the metabolites produced by intestinal microbes can be an early-warning sign of disease, and in some case the metabolites themselves may cause illness — so therapies that target them can be useful.

However, according to research by the Perelman School of Medicine at the University of Pennsylvania, "numerous challenges need to be overcome on the path toward using microbial metabolites for therapies."

Microbial ecosystems are very complex and can change in different circumstances, so they are difficult to map. One emerging technology which could help overcome some of those challenges is metabolite sensing. Metabolite sensors combine biotechnology with electronics to detect metabolite levels. Today they are often used to analyse bodily fluids in vitro, but there are an increasing number of non-invasive, wearable metabolite sensors emerging, such as an ear-clip that is able to measure the glucose levels of diabetic patients from their earlobe tissue.

A 2022 paper by the American Chemical Society examining the variety of bioelectronic devices currently available concluded that: "Overall, we anticipate seeing breakthroughs in organic electronic metabolite sensors thanks to their unique set of features, especially in wearable and implantable forms and at the interface with in vitro tissues. The exploration of multifunctional semiconductors, unconventional device architectures and systematic study of intrinsic mechanisms will further develop this exciting field."

Skin deep

Microbiome treatments extends beyond the gut flora. Terms like "skin microbiome" and "lung microbiome" are increasingly circulating in the public space.

Researchers from the Hong Kong University of Science and Technology have found a positive correlation between gut microbiota at birth and development of asthma and skin eczema later in life. Changes in the microbiome are believed to be involved in the "atopic march" where patients have a progressive series of ailments – atopic dermatitis, food allergy, allergic rhinitis and finally asthma.

There is some recent evidence of the effectiveness of topical probiotics on skin health, although most recent studies, like this Keio University study, acknowledge that much further exploration is needed.

There is no shortage of examples of products marketed as "skin probiotic cosmetics" today across most of the developed world. Cosmetic and personal care products are subject to more lax oversight by regulators, compared to medicinal drugs.

A recent paper published by MPDI examined the marketing practices of businesses selling such products and concluded:

Market overview (cont.)

"Terms such as probiotics, prebiotics and microbiome were unheard of in cosmetic products a mere twenty years ago. Their use would be encouraging if it coincided with strong scientific research supporting claims and uncovering the mechanisms of action of the strains and material being promoted. Unfortunately, this is rarely the case."

About half of the companies marked as microbiome-related in the PitchBook dataset we examined seemed to be related to treatments or cosmetics for skin conditions.

Deep breaths
When it comes to the lung microbiome, scientific studies are similarly still in their infancy.

One study by the Shanghai Veterinary Research Institute suggested that a connection between gut and lung is due to potential microbial exchange via the lymph circulation of the Shanghai Veterinary Research Institute.

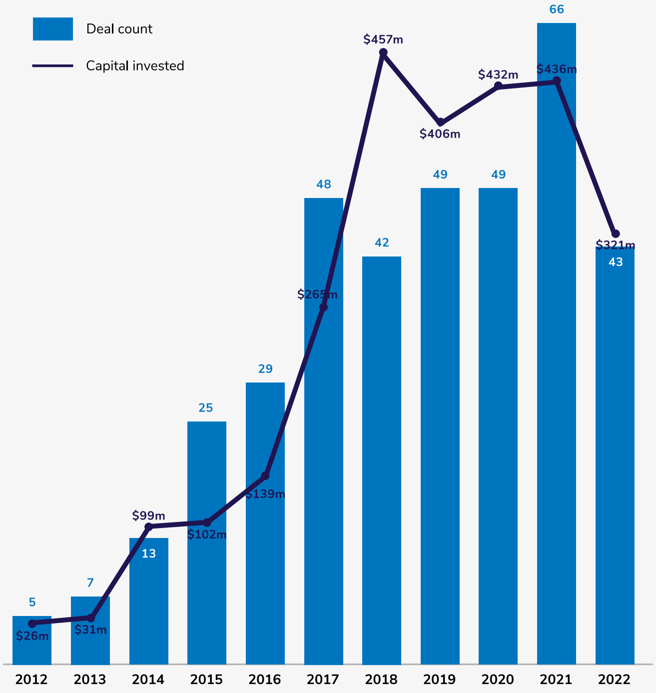
A 2022 paper on the emerging role of the lung microbiome in lung cancer diagnostics and treatment stated that the microbiome might impact tumour progression and response to therapy, particularly immunotherapy, and might also contribute to the early development of lung cancer.

The authors of the study warned, however, that "studies to date have been small, single centre with significant methodological variation." And further: "Large, multicentre longitudinal studies are needed to establish the clinical potential of this exciting field."

uBiome – the Theranos of microbiome?
Although microbiome tech offers tantalising possibilities, investors would do well to be cautious. Some "bad apples" have already appeared in this field.

The highly publicised case of uBiome was, for example, uncannily reminiscent of the Theranos fiasco. The Silicon Valley-based startup was developing an at-home test kit for human faeces, aiming to enable patients to know about the makeup of their microbiome. It raised $83m in 2019, but in 2021, uBiome's founders and co-CEOs Zachary Schulz Apte and Jessica Sunshine Richman faced US federal charges for an alleged scheme to defraud health insurance providers and investors. As of 2021, the founders of the company were reported to be FBI fugitives.

VC-backed deals in microbiome tech 2012-22



Source: PitchBook

There are also recent disappointments for listed microbiome companies. Among the ones that have gone public, US-based Kaleido wound down its business after clinical trials of a microbiome-based treatment for C. difficile infections failed. Finch Therapeutics, also called off its C. difficile treatment trials earlier this year.