

Insights from the Analytics of the Microbiome

December 2021

What is Arogyam

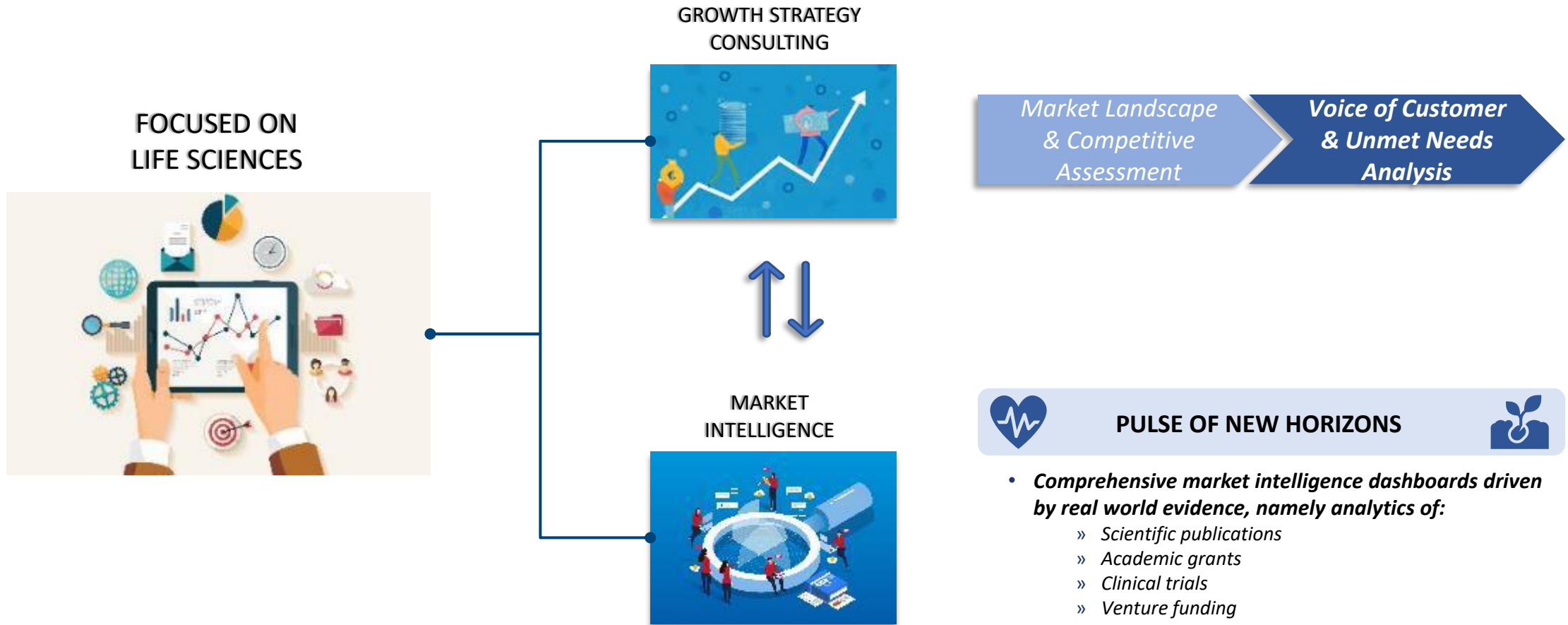


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Microbiome Market Snapshot

Ready to be transformational?



A community of microorganisms (such as bacteria, fungi, & viruses) that inhabit a particular environment

2020



~75K+
PUBLICATIONS



\$1+B
GRANTS



~150*
TRIALS

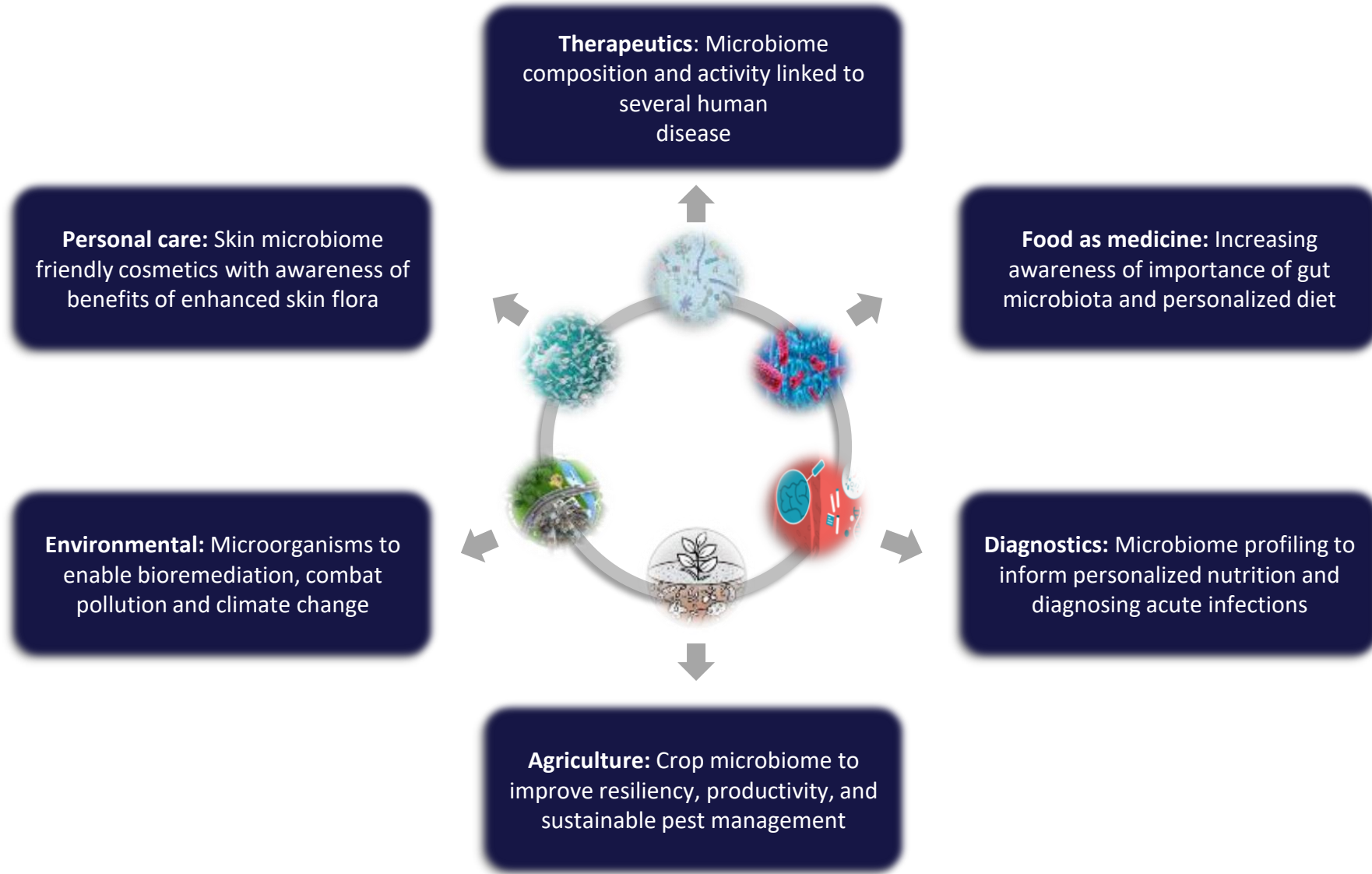
* Ongoing trials



\$1.5+B
VENTURE
FUNDING

For the first time, venture funding has substantially exceeded grant funding. This could indicate market is moving from nascent to emerging/developing

Microbiome is Advancing Several Market Segments

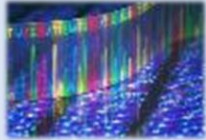


Market Evolution

Advances in enabling technologies have allowed numerous studies to be performed which in turn have provided key insights into the various market segments

ENABLING TECHNOLOGIES

Next Generation Sequencing



Bioinformatics



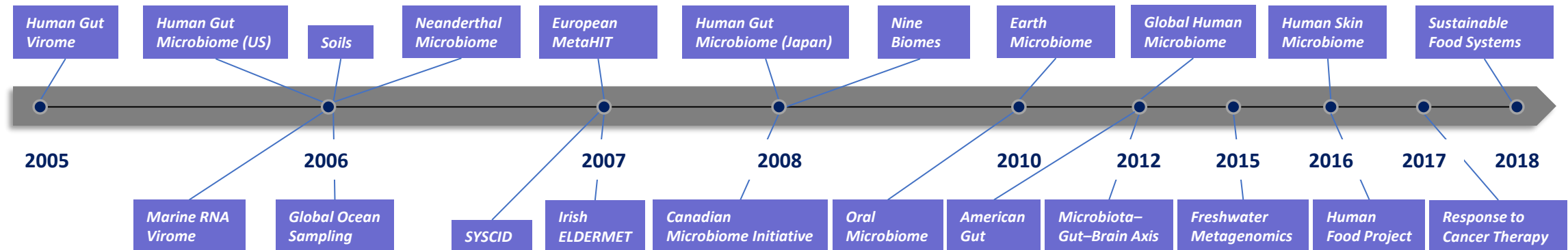
Gene Editing



Synthetic Biology



Metabolomics



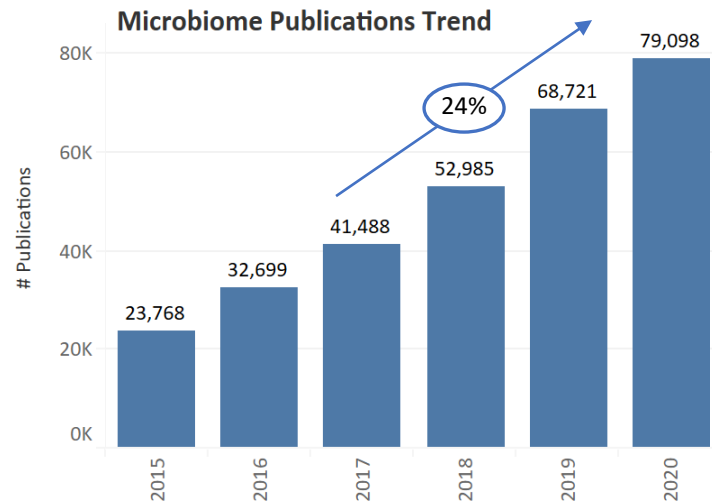
Source: Arogyam research, Malla MA, Dubey A, Kumar A, Yadav S, Hashem A, Abd Allah EF. Exploring the Human Microbiome: The Potential Future Role of Next-Generation Sequencing in Disease Diagnosis and Treatment. *Front Immunol.* 2019 Jan 7;9:2868, "Milestones in human microbiota research", *Nature*, 6.18.2019, *Dimensions Digital Science*

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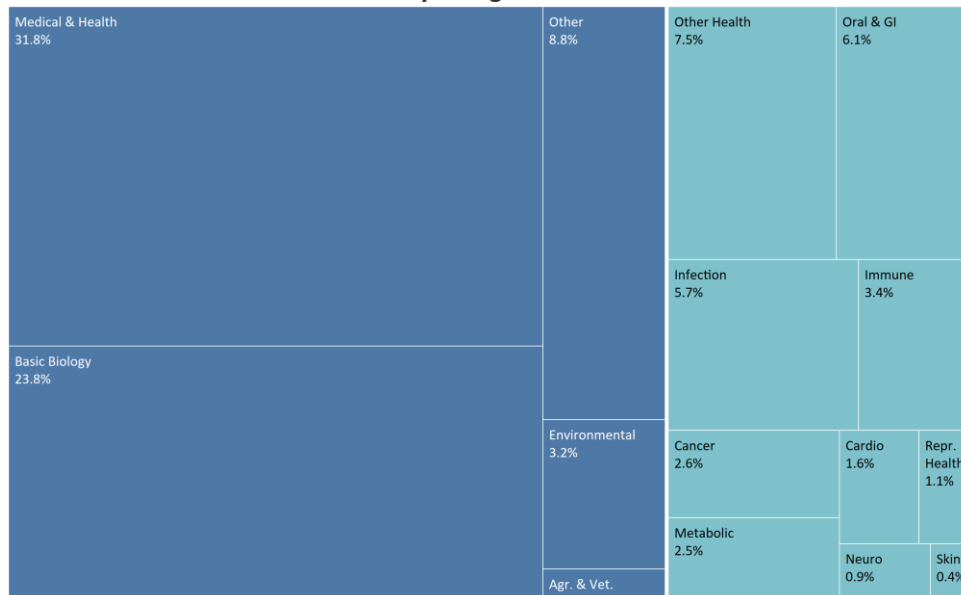
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Publication Analytics Overview

Healthy output continued in 2020 despite COVID with utility in a variety of markets



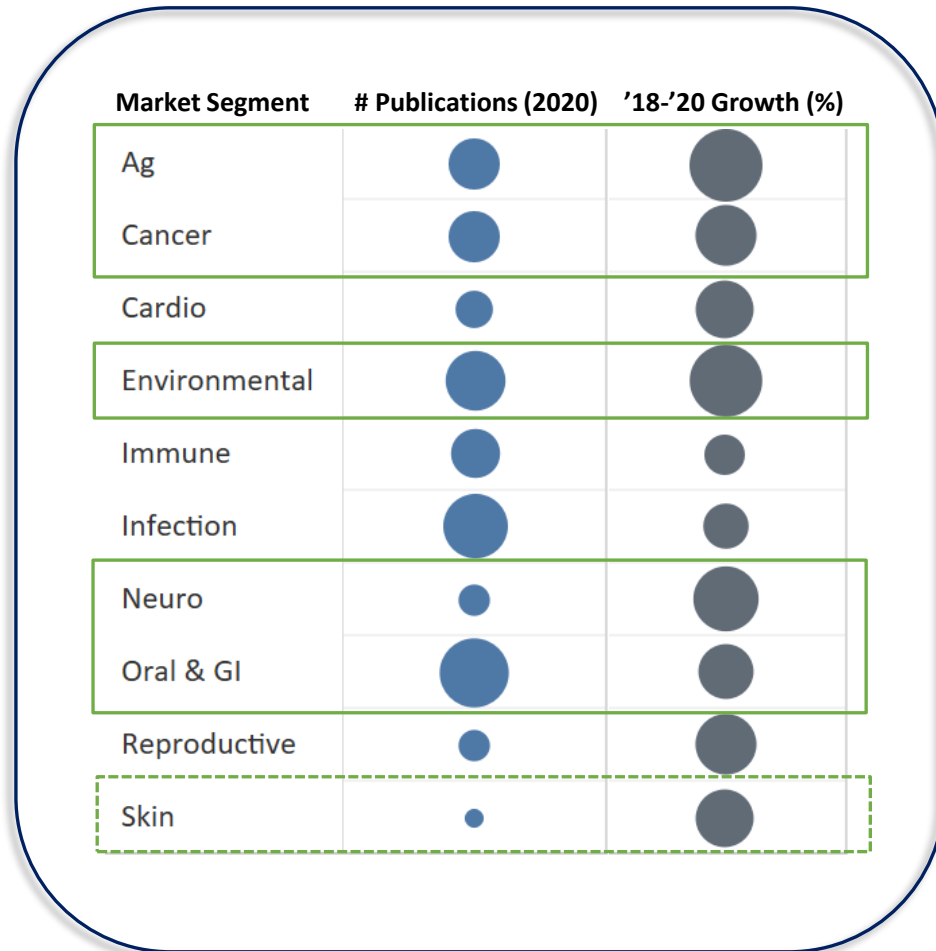
Publications By Categories



- Publication of scientific papers focused on microbiome research has been surging with over 70K publications. Microbiome research has increased dramatically in recent years, driven by advances in technology and significant reductions in the cost of analysis. Stable growth of 24% in the past three years
- This wealth of research has enabled utility in a diverse spectrum of fields spanning environmental, agriculture, medical to consumer markets such as food and personal care
- Catalyzed by landmark projects such as the Human microbiome project, the EU MetaHit projects, understanding of how the microbiome affects health and disease has exploded.
 - Majority is targeting GI diseases (gut dysbiosis, Inflammatory bowel disease), interactions between nutrition & gut microbiome and infectious diseases (C. difficile and antibiotic resistance)
 - Followed by research to understand the implication of the microbiome in immune diseases such as allergies, type 1 diabetes, thyroid, rheumatoid arthritis, and lupus
 - Numerous studies are investigating associations of microbiome and cancer, from oncogenesis and cancer progression to resistance or response to therapy
- Basic biology of the microbiome, fundamental host/microbiota interactions is still a large bolus
- Environmental research is focused on harnessing the microbiome to predict ecosystem response such as engineering of microbiomes to modify structures of the microbiota and restoring ecological balance
- Microbiome engineering and plant microbiome interactions are being researched to improve agricultural productivity

Peeling Back the Layers

Surge in Environmental, Ag, Cancer, Neuro while Oral & GI, Infection show continued progress



- Microbiome research on the environment is gaining steam and attention from a historically human health focused field. Research is focused on understanding the ecology microbiome, its dynamics, and how engineering strategies can help control harmful effects such as plastic pollution
- Crop yields need to continue to increase to meet global demand. Research is uncovering the complex, plant-soil microbiome to enhance growth, productivity and sustainability
- Increasing research is showing that gut microbiome plays a significant role in cancer immune responses and that microbiome therapies could potentially be utilized to overcome resistance to checkpoint inhibitors
- Microbiota-gut-brain (MGB) research is a fast-growing field. Microbiota is manipulated to reveal connections between intestinal microbiota and normal, pathological brain states. This could potentially lead to new avenues of treatment
- High awareness of healthy nutrition’s influence on maintaining gut microflora (Potential for probiotics ability to positively modulate the microbiome) and antibiotic resistance have led to infectious disease and gastrointestinal areas being highly characterized.
- Skin research has smaller number of publications, but high growth indicates that it is on the cusp of gaining traction. Influence of skin topography on microbial colonization and host specific factors such as age are being studied

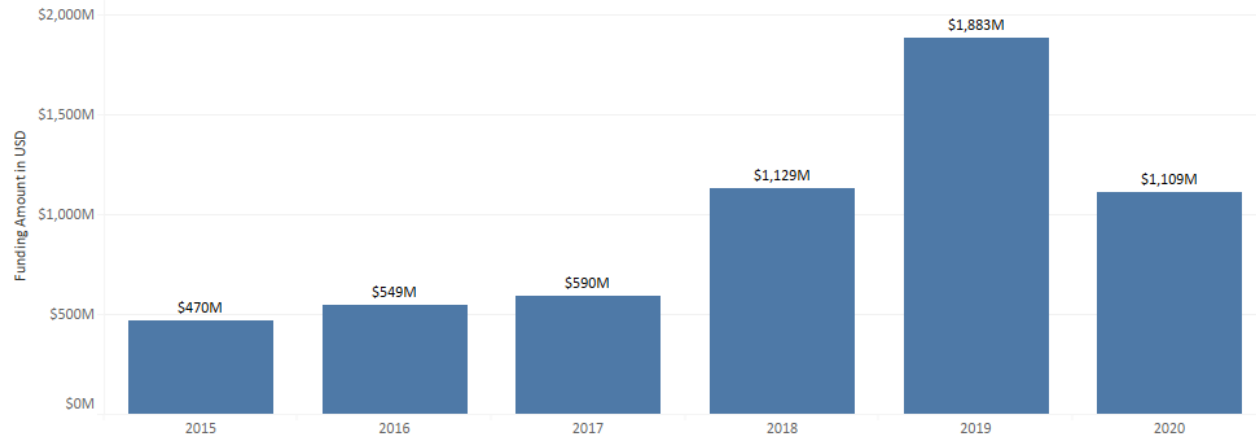
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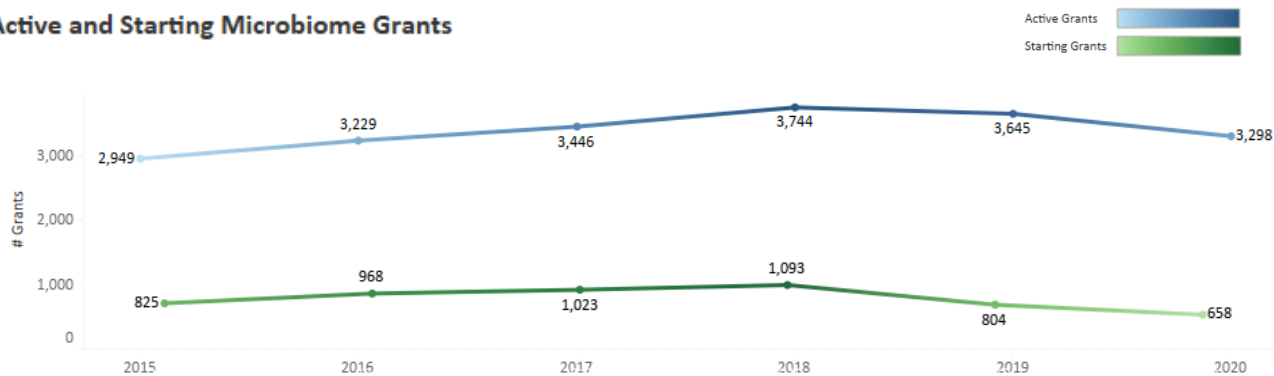
Grant Analytics Overview

Dented by COVID, significant dip in funding amount from 2019

Microbiome Grants Trend



Active and Starting Microbiome Grants



- COVID has significantly impacted grant funding, marked dip in funding amount in 2020
- Several pioneering studies from 2006, laid the foundation for this field, showing an upward trend to 2019
- One could potentially disregard 2020 as an exception and expect 2021 to catch up and reflect this upward trend
 - This sentiment is consistent with announcements from publicly traded life science companies such as Illumina, that experienced headwinds in their core business from COVID and is expecting a rebound in 2021
 - Although there was a slight dip in the number of active and starting grants in 2019

Zooming In

Basic biology and increasing focus on Environment by funding agencies is noteworthy

Microbiome Grants by Categories



Market Segment Grant \$ (2019) '18-'19 Growth (%)



- On an overall basis, Basic biology, Environmental, and Ag make up the bulk of grants. On the health front, majority is Oral & GI, Infectious diseases, and Immunology
- Analysis on grant dollars and growth will focus on 2019 as 2020 was affected by COVID
- Considerable grants are focused on basic biology studies characterizing microbial signaling in communities and functional studies within communities likely to catalyze our understanding of concepts such as quorum sensing and drive the field of microbiome engineering forward
- Environmental is garnering more attention with grants that are on tackling environmental pollution, climate change, and habitats
- Infection, Immune studies have steadily been on the rise, focused on antibiotic resistance, impact of altered gut microbiome in areas such as type 1 diabetes, asthma, and lupus
- Cancer and skin are smaller in terms of funds but have shown big jump in funding compared to prior years. Studies are on tackling cancer progression to resistance and Atopic Dermatitis. Skin tends to be more challenging than the gut as the skin microbiome varies by skin site, hygiene level, and environmental conditions

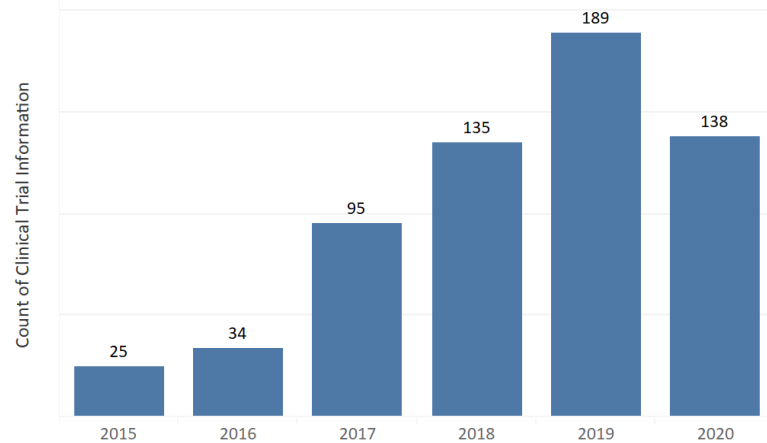
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Clinical Trial Analytics

Impacted by COVID but spurred by a trio of clinical trial successes

Number of Ongoing Clinical Trials Examining the Microbiome



On 10 August 2020, Seres Therapeutics reported that its flagship product, SER-109, had met its primary end point in a phase 3 trial



Rebiotix and Ferring announced positive preliminary phase 3 data from FMT product, RBX2660 in May



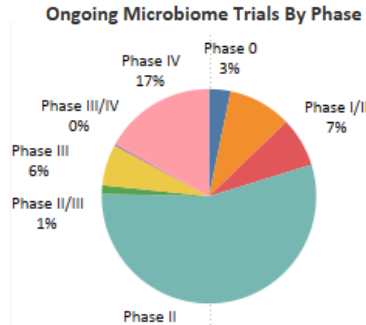
Finch Therapeutics released phase 2 data in June revealing a statistically significant benefit



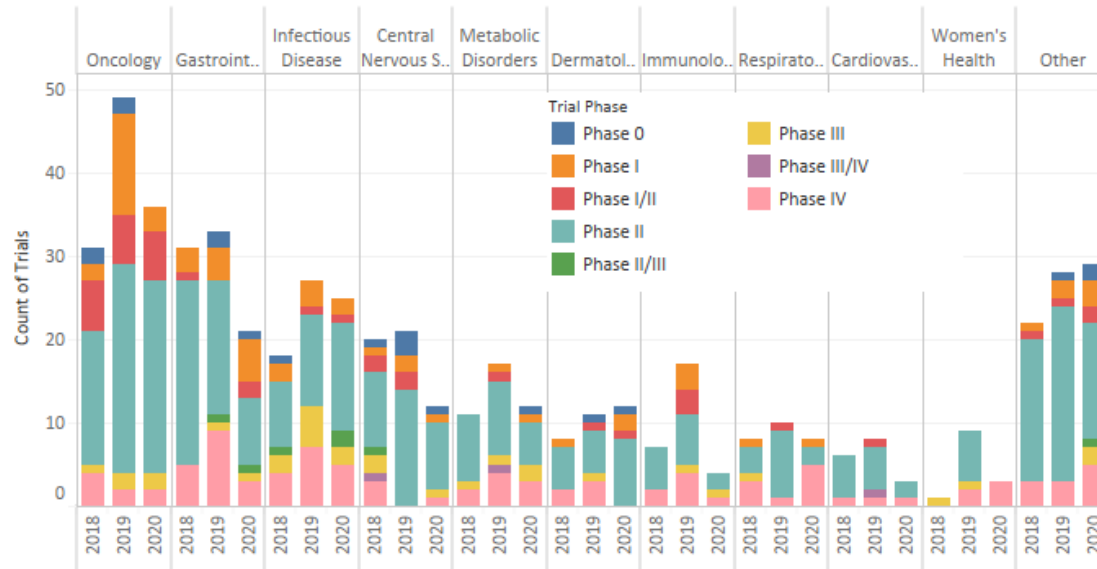
- The number of ongoing clinical trials with focus on the microbiome have risen substantially from 2015–2019, with almost seven times the number of trials recorded in 2019 relative to 2015
- Like in clinical trials in other spaces, COVID-19 has impacted the number of ongoing clinical trials in 2020. These can be expected to re-initiate in 2021
- Success of Seres, Rebiotix, and Finch has spurred the industry. All three companies target recurrent *C. diff* infections. These breakthroughs pave the way for other indications
- The possibilities targeting the spectrum of mechanisms through which microbiota is influencing our body and modulating key processes and systems, the immune system being one example is electrifying the market
- However, regulatory uncertainties regarding classification and frameworks remains a barrier

Therapy Area and Phase

Marching towards mainstream; Oncology is the top therapy area



Ongoing Microbiome Trials By Phase and Therapy Area



- 50+% have moved to phase II, given recent positive success stories, there is relative optimism around pipelines
- Oncology is leading the trials spurred by studies from three years ago, that had shown that gut microbiome composition differences influences response to therapy in cancer patients. Bacterial strains that can boost immune responses are being studied to amplify the effects of checkpoint inhibitors. Others are investigating mitigating the side effects of chemotherapy
- This followed by GI disorders, largely inflammatory bowel disease (loss of commensal bacteria that would keep the immune system at bay causes/increases inflammation) and infectious disease such as C. diff using fecal transplant (FMT) and other interventions such as modulators. Note: The FDA ruled that FMT may not be regulated as a drug except for recurrent C.diff infections
- CNS based trials on Gut-Brain Axis connections to treat conditions such as Autism, Parkinson's disease are next

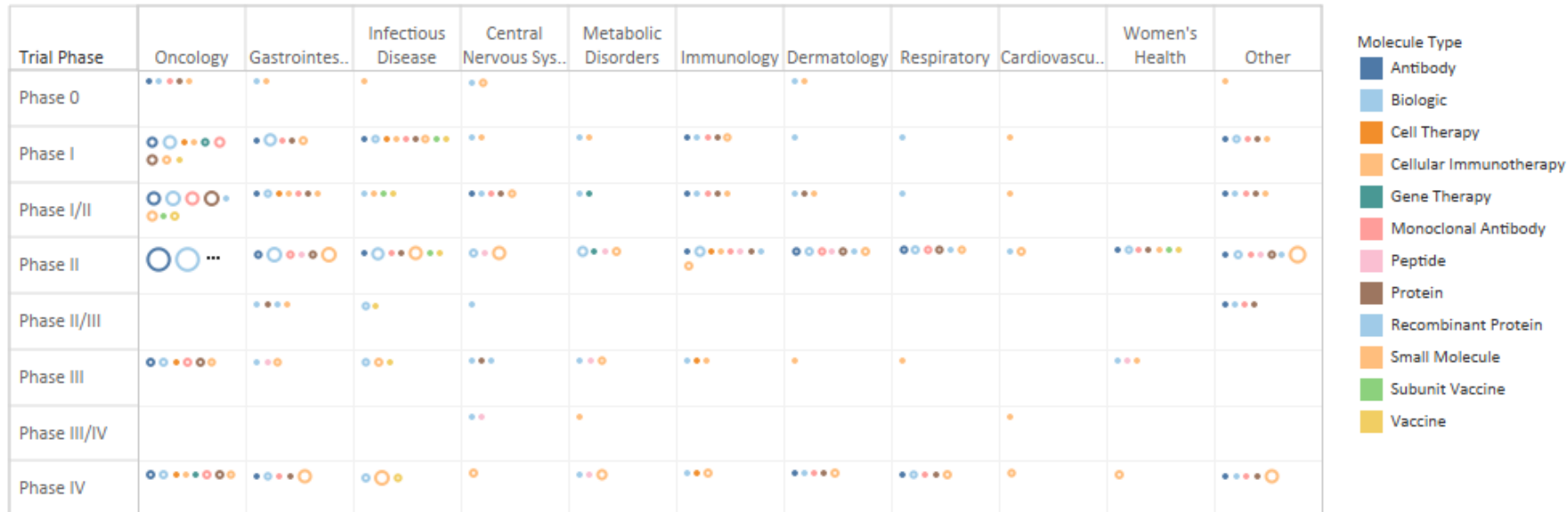
Therapeutic Approaches

Many roads to success

<p>Fecal Microbiota Transplantation</p>	<p>Introduces microbiota from a healthy donor by administering a preparation of fecal matter into a patient</p>	<p>Biologic</p>	<p>Inf. Diseases., GI</p>		<p>Limited by the need for donor stool, sample quality and safety concerns</p>
<p>Live Biotherapeutic Product (LBP)</p>	<p>Introduction of hand-picked single strain or consortia of cultured microbes based on comparison of microbiome signature libraries of healthy and unhealthy individuals</p>	<p>Biologic Small Molecule Antibody, Vaccine</p>	<p>Onco, Inf. Dis., GI, Metabolic, CNS, Immunology</p>		<p>Consistency, difficult to culture microbes, and complex formulation process</p>
<p>Bacteriophage & Viruses</p>	<p>Introduction of bacteriophages to eliminate pathogenic bacteria or as a delivery vehicle for gene editing systems</p>	<p>Vaccine Cell Therapy Gene Therapy</p>	<p>Onco, Inf. Dis., GI, Immunology</p>		<p>Generation of resistance, stability and gene transfer to other bacteria are concerns</p>
<p>Small Molecules or Biologics</p>	<p>Introduces biologically active molecules produced by the microbiome, rather than the microorganisms themselves</p>	<p>Small Molecule Peptide/Protein Biologic</p>	<p>Onco, Inf. Dis., Derm, Metabolic, CNS</p>		<p>Questions remain on whether same level of coverage, durability of effect of LBPs can be seen</p>

← NOT EXHAUSTIVE →

Ongoing Microbiome Trials By Therapy Area, Molecule Type and Phase

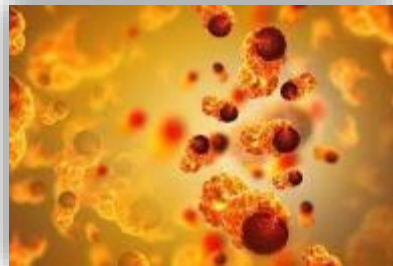


Big Pharma is Starting to Take Notice

Inflammatory Bowel Disease



Cancer



Pharmacomicrobiomics



- The year 2020 marks a decade since the term Pharmacomicrobiomics was coined
- The Pharmacomicrobiomics database collects, classifies and cross-references known drug-microbiome interactions, over 60 drugs have been identified as having microbiome interactions
- Many more are likely to be uncovered in the coming years

Source: Genetic Engineering News: Translating Pharmacomicrobiomics: Three Actionable Challenges/Prospects in 2020

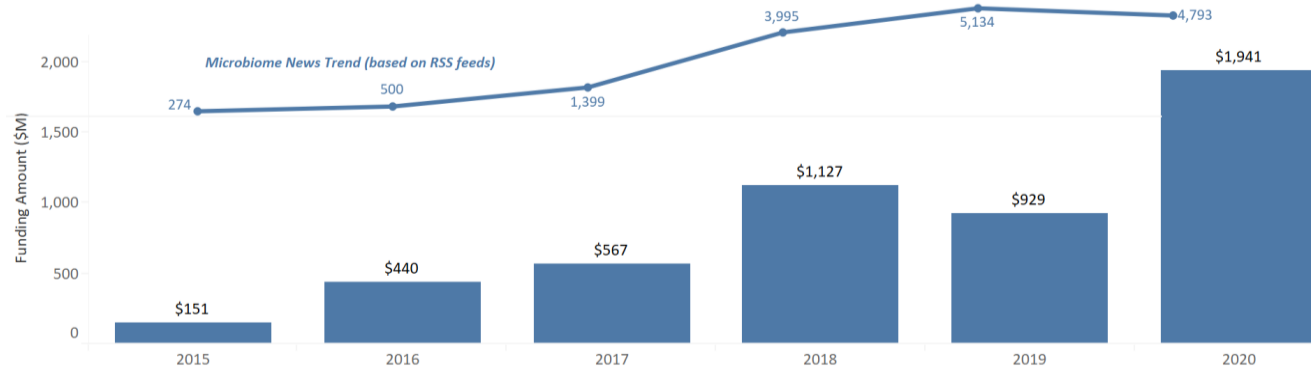
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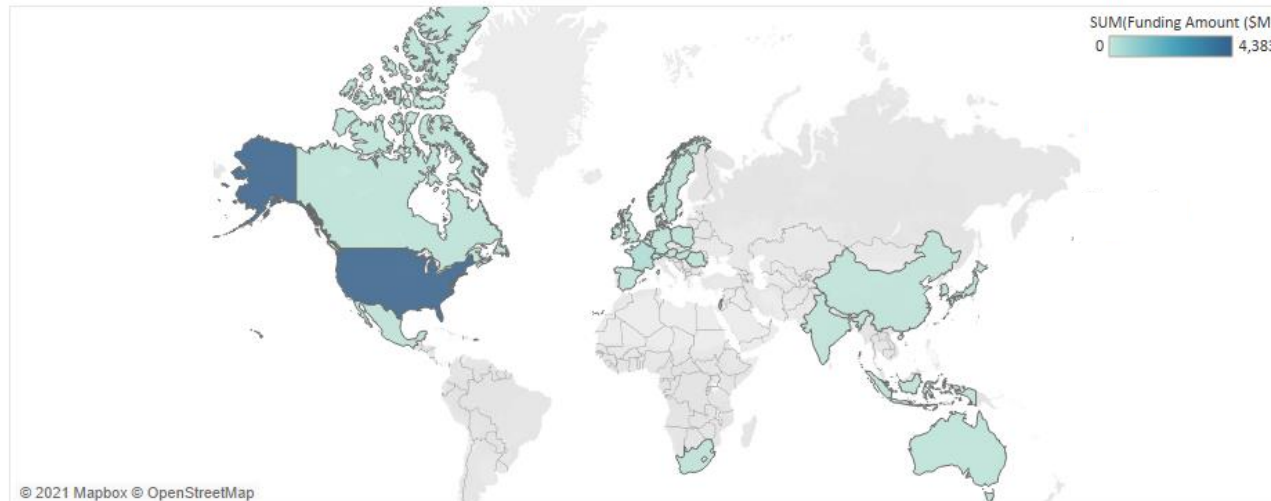
Venture Funding Analytics

Investor enthusiasm has been the bright spot that has powered the market through the pandemic

Investments in Microbiome Companies Over Time (\$M)



Microbiome Funding By Geography

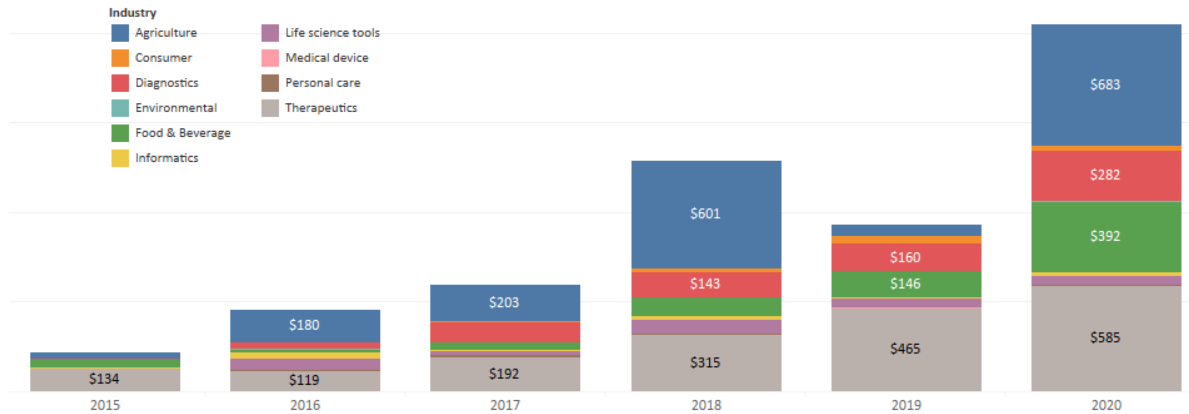


- Funding reached historic levels of ~\$2B in 2020; the line chart is the news trend based on RSS feeds
 - Early on, funding seemed to correlate to the news trend pattern, but as scientific understanding has grown, that correlation does not seem to tie
- Funding from US investors dominates, followed by EU, in France, UK, and Ireland

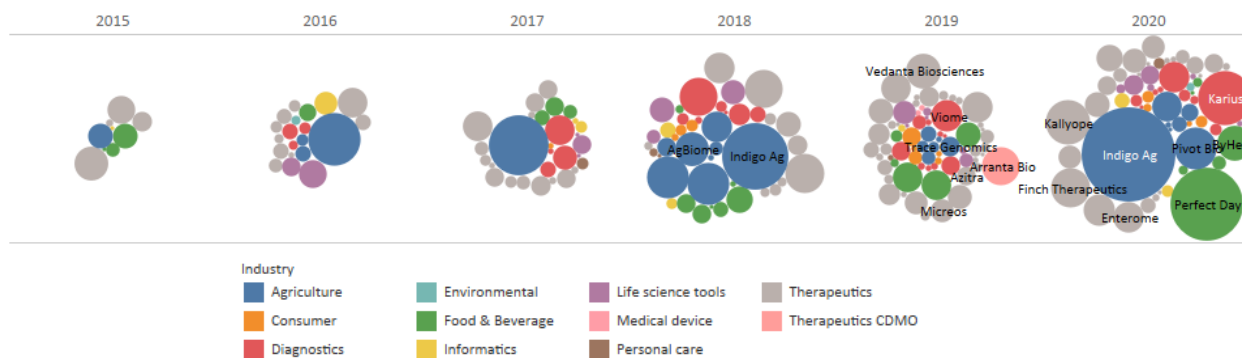
Proliferation of Startups Thriving in a Lucrative Market

Diverse markets with Agriculture, Therapeutics, and Food leading the way

Microbiome Funding by Industry (\$M)



Microbiome Startups Landscape



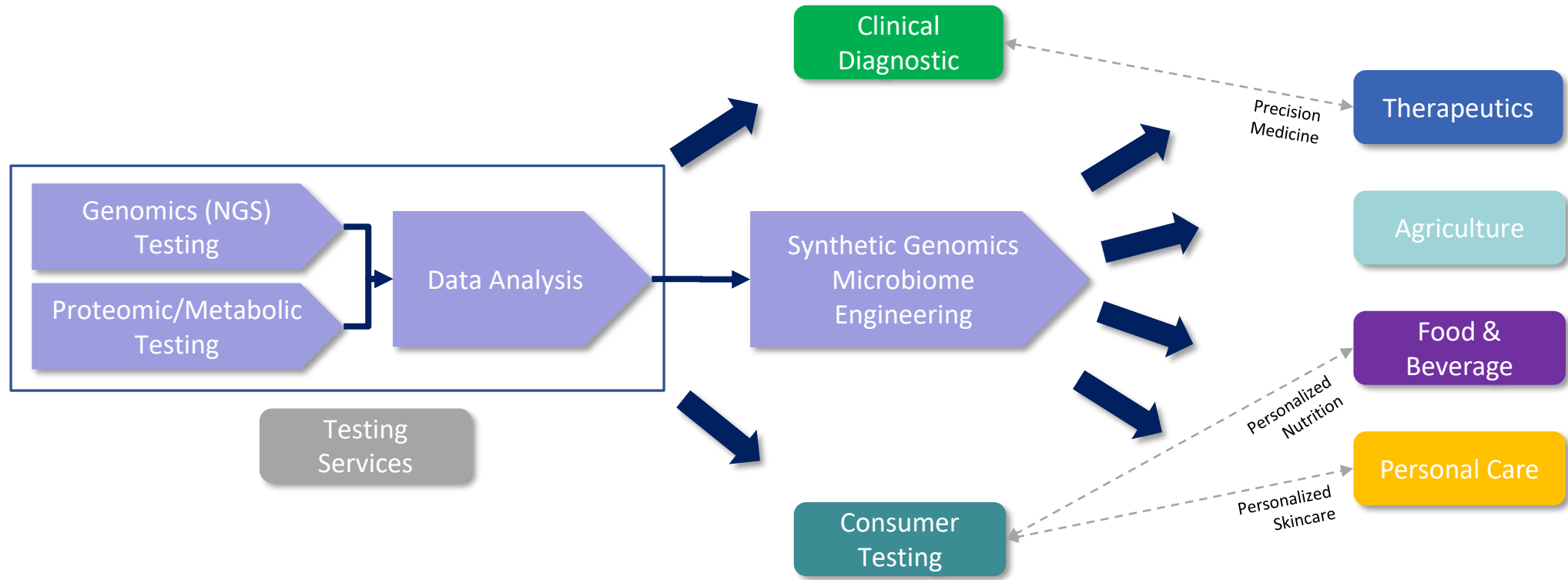
- Agriculture companies, though not a media attention grabber, led the fund-raising race with huge potential for smarter soil management and improving plant health



 - ✓ Record breaking, nearly \$700M raised in 2020 by several breakout companies with transformational microbiome based soil management solutions such as IndigoAg, PivotBio, AgBiome
- Therapeutics companies have consistently received funding buoyed by clinical trial successes in 2020. Besides GI, infectious disease, companies focused on areas such as oncology, CNS, metabolic and skin are receiving funding (Vedanta, Kallyope, Enterome, & Azitra). Companies like Enterome are employing omics platforms to generate precision drugs

 - Building a consistent drug product from the various therapeutic approaches requires time and investments. CDMO's like Arranta Bio are garnering attention
- The food & beverage segment with nutrition and wellness solutions based on functional ingredients such as probiotics, prebiotics, and others to establish a healthy microbiome have received ample funding, e.g. Perfect Day, ByHeart
- Last but not the least, diagnostics companies utilizing NGS, advanced machine learning such as Karius for clinical infectious testing and Vivante Health for consumer testing to guide personalized nutrition are leading the pack

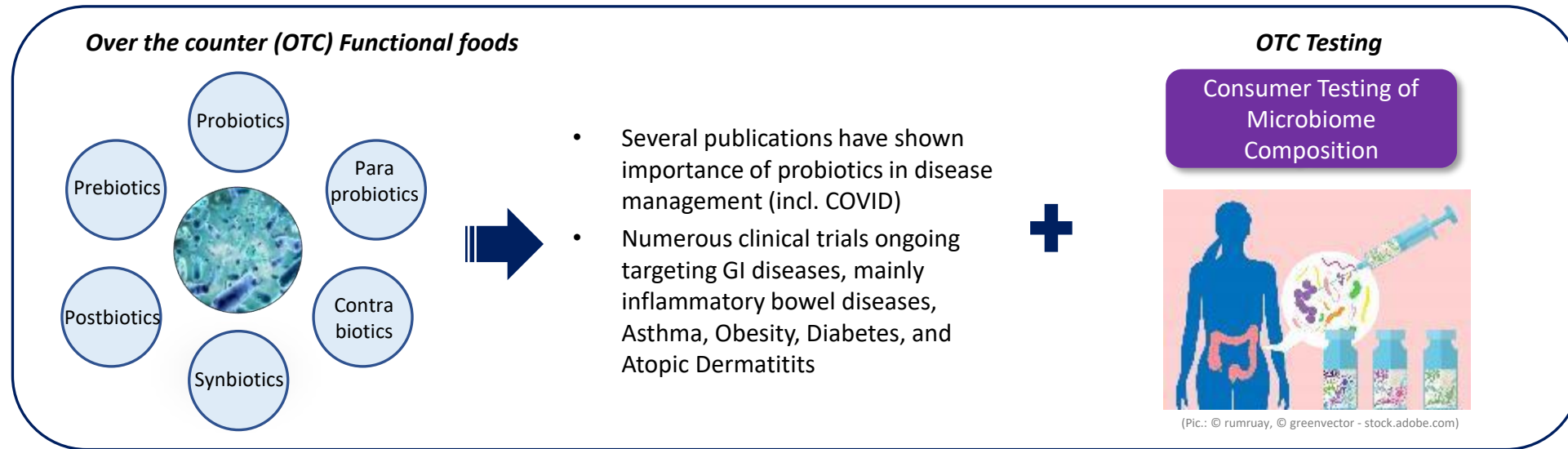
Microbiome Market Ecosystem

Interconnected and driven by microbiome mining tools and data analysis



 = Tools
 = Markets

Are Medicinal Foods Likely to Impact Therapeutics?



DEFINITIONS

Probiotics	<i>Live microorganisms that, when administered in adequate amounts, confer a health benefit</i>
Prebiotics	<i>Non-viable food components that improve host gut health via altering the microbiota</i>
Paraprobiotics	<i>Inactivated microbial cells or cell fractions that confer health benefit to the host</i>
Postbiotics	<i>substance released by or produced through the metabolic activity of the microorganism, which exerts a beneficial effect on the host</i>
Contrabiotics	<i>Certain dietary fibers can block bacterial-epithelial adherence</i>
Synbiotics	<i>Combination of probiotics and prebiotics in food ingredients or supplements in a form of synergism</i>

- Driven by increased consumer awareness of benefits of good gut health
- Probiotics along with prebiotics and other food options are likely to become increasingly important in treating patients, when combined with personalized recommendations based on consumer testing, these medical/functional foods can become a powerful over the counter option for the consumer
- However, lack of data that takes multifaceted measures such as dietary diversity and food interactions into account is likely to remain a challenge to formulate medical foods as a meaningful therapeutic. Future studies and clinical trials are taking some of these measures into account and making progress in this key dimension

Some Success Stories

Microbial feed additives

Clean Cow Project

How to reduce methane emission by a minimum of 25%.

The 'Dairy hoof print'
 2.5 billion gallons of milk produced per year in the US.
 100 million gallons of feed used per year.

Environmental impact of milk produced per year:
 148,000 million kg of CO₂ equivalent.
 22.25 billion cubic meters of methane gas.

Food-of-concept shows that there are ways to reduce methane.
 Safety program, Nutritional development, Feed efficiency program.

DSM

1. Methanogenesis inhibitors
 Reduce methane production by inhibiting the methanogenic pathway.

2. Cell wall permeability modifiers
 Increase the permeability of the cell wall, allowing for better nutrient absorption.

3. Cell wall synthesis inhibitors
 Inhibit the synthesis of the cell wall, leading to cell death.

4. Cell wall damage
 Damage the cell wall, leading to cell death.

5. Cell wall repair
 Repair the cell wall, leading to cell death.

6. Cell wall turnover
 Turnover the cell wall, leading to cell death.

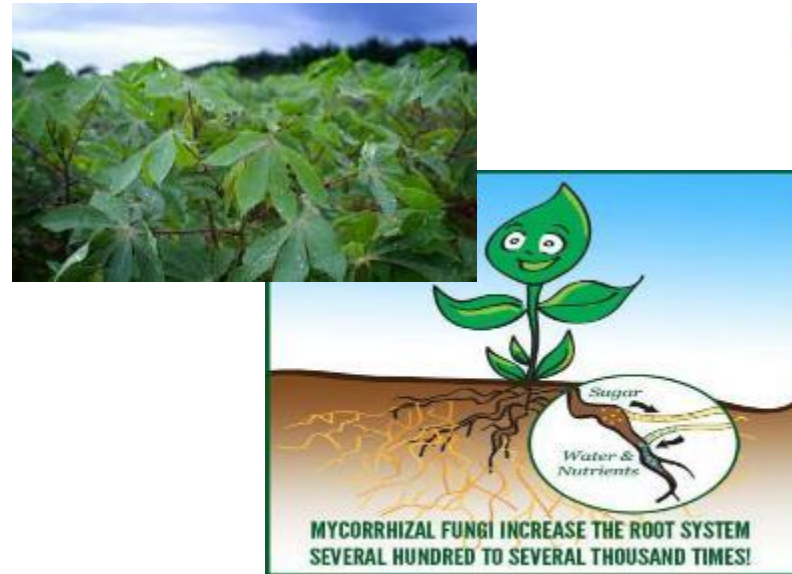
7. Cell wall turnover inhibitors
 Inhibit the turnover of the cell wall, leading to cell death.

8. Cell wall turnover enhancers
 Enhance the turnover of the cell wall, leading to cell death.

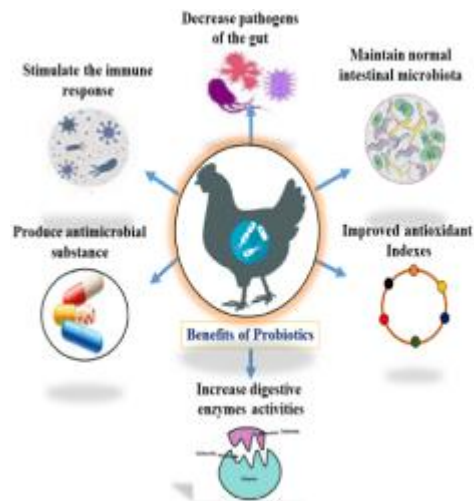
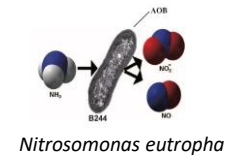
9. Cell wall turnover inhibitors/enhancers
 Inhibit/enhance the turnover of the cell wall, leading to cell death.

10. Cell wall turnover inhibitors/enhancers
 Inhibit/enhance the turnover of the cell wall, leading to cell death.

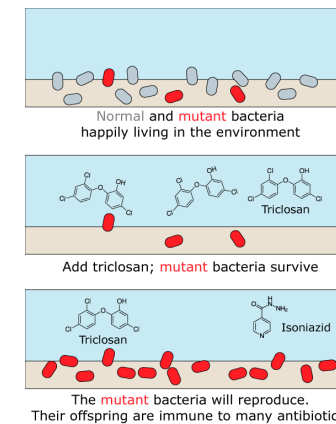
Increased Cassava yield



Skin microbiome promoting personal care



FDA bans antibacterial soaps



Triclosan

Where

- Antibacterial soaps
- Toothpaste
- Cosmetics
- Teats
- Band-aids
- Matresses

Linked To

- Chlorine disinfection
- Heart cancer
- Resistant bacteria
- Microorganisms
- Antibiotic resistance

Safer Options

- Wash hands with plain soap and water for at least 20 seconds
- Avoid products labeled or marketed as "antimicrobial," "odor fighting," "germ-killing," or "antibacterial"
- Read labels to avoid triclosan

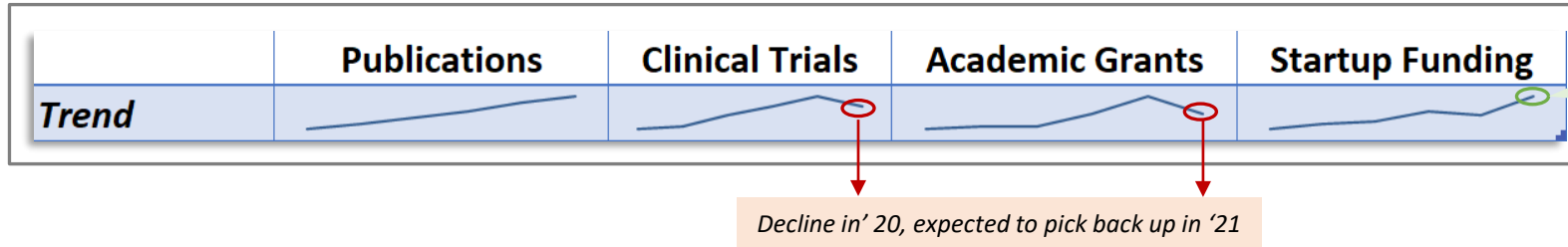
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Key Takeaway

Robust trends, ascent in venture finding implies transformational potential across multitude of industries

TREND SUMMARY












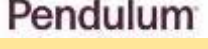














AROGYAM SCORE BY CATEGORY







Category	Publications Score	Grants Score	Clinical Trials Score	Startup Funding Score
Environmental	Green	Yellow	Grey	Red
Ag & Food	Green	Yellow	Grey	Green
Immune	Red	Yellow	Yellow	Yellow
Infection	Yellow	Yellow	Yellow	Yellow
Oral & GI	Green	Yellow	Green	Yellow
Cancer	Yellow	Red	Green	Yellow
Metabolic	Yellow	Red	Yellow	Yellow
Neuro	Yellow	Yellow	Yellow	Yellow
Skin	Red	Yellow	Red	Yellow
Cardio	Yellow	Red	Red	Red
Reproductive	Yellow	Red	Yellow	Yellow
Basic Biology (tools + Informatics + Dx+ CDMO)	Green	Green	Grey	Yellow









- The most exciting areas that has upward scores across the board is Ag and food. The potential in Ag to improve crop yields, while protecting soil health and sequestering carbon and better animal feed is disruptive. While the role of microbiome in nutrition is well known with the rise of prebiotics and probiotics, personalized, tailor made nutrition based on microbiome profile is the next frontier
- Environment is the next frontier of microbiome, healthy publication and grant scores indicate that the science is building VC funding can be expected to follow soon
- Therapeutics in GI, infection have uniform scores across the board, reflecting progress. Potential in Cancer, Immune, and Neuro are likely to be the next wave. Skin has garnered reasonable scores in funding, indicating potential in personalized skin care and therapeutics
- Diagnostics, life science tools and informatics are the blood line of this space and has shown steady scores across the board, indicating continued progress and investment

Some Leading Companies

- 1 IndigoAg 
- 2 Perfect Day 
- 3 Karius 
- 4 Kallyope 
- 5 Enterome 
- 6 Finch Therapeutics 
- 7 Pivot Bio 
- 8 Seres Therapeutics 
- 9 Emulate 
- 10 PanTheryx 
- 11 Metabolon 
- 12 Pendulum 

- 13 AgBiome 
- 14 Vedanta Biosciences 
- 15 Viome 
- 16 Joyn Bio 
- 17 GI Innovation 
- 18 Arranta Bio 
- 19 Newleaf Symbiotics 
- 20 Concentric Ag 
- 21 DayTwo 
- 22 Second Genome 
- 23 Axial Biotherapeutics 
- 24 Locus Bioscience 

- 25 Nuritas 
- 26 Trace Genomics 
- 27 BiomX 
- 28 Thetis Pharmaceuticals 
- 29 SniprBiome 
- 30 MicroGen Biotech 

 = Agriculture	 = Personal care + Food & Beverage
 = Food & Beverage	 = Consumer Dx
 = Clinical Dx	 = Therapeutics CDMO
 = Therapeutics	 = Environmental

NOTE: this is not a ranked list

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Trace Genomics

Analyzing the soil microbiome using NGS and machine learning



Trace Genomics has built the first scalable soil microbiome test to help farmers predict soil disease, soil health, and crop quality, using high-throughput DNA sequencing and machine learning.

With a growing, proprietary knowledge base, Trace Genomics can identify previously unknowable microbial species occurring in agricultural soils and provide farmers with information about which microbes could be impacting production. Farmers can use this information to make decisions about which seeds to use, what rotations to deploy and which biological agents and other inputs to apply.

TOTAL FUNDING TO DATE:

~\$60M

INVESTORS:

FMC Ventures, Foodshot Investment Partners, S2G Ventures, Ajax Strategies, Illumina, Alexandria Venture Investments, Cavallo Ventures, WP Global Partners, Beast Ventures, DST Global, HBM Partners, AgFunder, Fall Line Capital, Refactor Capital, SVG Ventures, Viking Global Investors

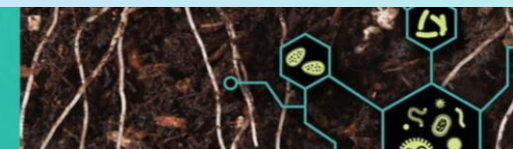
INFORMED SOIL INSIGHTS. SMARTER CROP DECISIONS.
 Harness the power of soil science and machine learning to increase profitability.

ELIMINATE GUESSWORK

We turn your soil samples into meaningful insights, so you can take action. Reach a new level of understanding that eliminates guesswork at every phase with our data-driven, evidence-based recommendations.

Digitize

First, we digitize the living soil. We analyze the soil's biology by applying proprietary soil DNA extraction and sequencing to index and quantify millions of microbes in your soil.



Decode

Next, we decode the soil data. Harnessing machine learning, we conduct high-speed, cost-efficient data analysis to compare against a large and growing set of soil data.

Decide

Then, we combine your soil biological data with your soil chemical data and surface tailored insights to help you take action. Our soil science experts work with you to enable data-driven, evidence-based recommendations so you can decide the best action to take on your growers' fields.



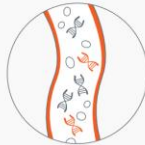


Genomic Insights for Infectious Diseases

The Karius® Test is a blood test based on next-generation sequencing of microbial cell-free DNA. It can identify and quantify over 1,000 clinically relevant pathogens including bacteria, DNA viruses, fungi, and parasites. Applications include complicated pneumonia, infections in immunocompromised patients, and endocarditis.

By using genomics and AI to map a patient's microbial landscape from a single blood draw, Karius moves closer to a vision of a world where infectious disease is no longer a major threat to human health.

We use genomics and AI to advance infectious disease diagnostics.



Microbial cell-free DNA

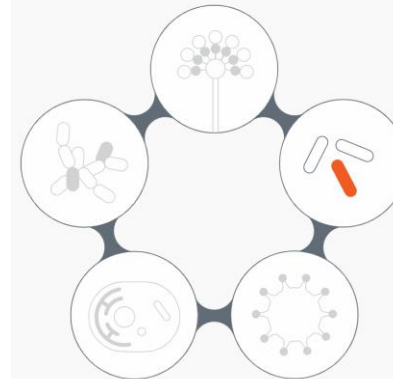
Karius provides unique genomic insights by detecting **microbial cell-free DNA (mcfDNA)** circulating in the bloodstream from pathogens causing an acute infection. Proprietary technology efficiently extracts mcfDNA directly from blood and depletes the strong human background signal and environmental contaminants.



Karius AI technology

Advanced machine learning algorithms allow analysis of complex genomic data in real-time. Proprietary reference genome databases are constantly refined as more data becomes available.

Over 1,000 clinically relevant bacteria, DNA viruses, fungi, and pathogens detected by the Karius Test with a single blood draw.



900+

Bacteria detected

Highlighted Bacteria:

- Nocardia species (72)
- Legionella species (42)
- Rickettsia species (18)
- Actinomyces species (15)
- Mycoplasma species (12)
- HACEK organisms (including *Kingella kingae*, *Aggregatibacter actinomycetemcomitans*, *Aggregatibacter aphrophilus*, *Aggregatibacter segnis*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Haemophilus aegyptius*, *Haemophilus parainfluenzae* and *Kingella denitrificans*)
- Streptobacillus moniliformis*
- Mycobacterium tuberculosis* complex
- Mycobacterium avium* complex (MAC)
- Mycobacterium chimaera*

TOTAL FUNDING TO DATE:

~\$245M

INVESTORS:

aMoon Fund, Casdin Capital, Data Collective, General Catalyst, HBM Healthcare Investments, HBM Partners, Innovation Endeavors, Khosla Ventures, Lightspeed Venture Partners, Pacific 8 Ventures, S28 Capital, SoftBank Investment Advisers, Spectrum Venture Capital, StartX, Tencent Holdings

Perfect Day

The “Impossible Foods” of dairy



Producer of animal-free milk substitutes and proteins intended to offer protein nutritionally identical to that of cow's milk. The company's production process involves yeast fermentation of plant-based sugars and includes ingredients that are sustainable, vegan and devoid of antibiotics, cholesterol and lactose, providing customers with nutrient-dense and environmentally safe dairy alternatives.

Perfect Day genetically engineers microflora to convert plant sugars into the milk proteins casein and whey that are essential in most dairy products..

Made With Microflora

We chose to use microflora (a microorganism such as bacteria, yeast, or in our case, fungi) to make our proteins because they have a long history of safe use making ingredients in many foods you eat today, and because microflora are particularly good at producing animal proteins.

We gave our microflora the genetic “blueprint” corresponding to whey and casein proteins, giving it the ability to produce real milk proteins — identical to what cows produce.

Now, as our flora grazes on simple plant-based inputs, it naturally produces milk proteins.

Fermentation Tanks

To maximize the amount of protein we can produce (and for the most sustainable process), we grow our flora in large tanks at the optimal temperature, pH, and salinity. By following a strict cleaning regimen for our tanks and ensuring they're a closed system isolated from the outside world, we can ensure we're making the purest, safest milk proteins in the world.

Pure Protein

Our proteins have proven to be identical to the ones found in milk. They are Generally Recognized as Safe (GRAS) by the FDA and are some of the purest proteins in the food industry.

As a result, you won't find even a trace of lactose, cholesterol, hormones, antibiotics, or anything else that typically comes along for the ride in cow's milk.

FDA Approves Perfect Day's Animal-Free Whey Protein as Safe to Eat

TOTAL FUNDING TO DATE:

~\$363M

INVESTORS:

ADM Ventures, B37 Ventures, Canada Pension Plan Investment Board, Collier Capital, Continental Grain Company, CPT Capital, Green Monday Ventures, Horizons Ventures, ICONIQ Capital, Lion Ventures, Nationale Postcode Loterij, RebelBio, Sonny Vu, Temasek Holdings, Verus International

Kallyope

A systems biology approach to create a comprehensive map of gut-brain circuits

KALLYOPE

Kallyope is a platform biotechnology firm committed to unlocking the therapeutic potential of the gut-brain axis. It combines cutting-edge technologies in computational biology, sequencing, neural imaging, human genetics, and cellular and molecular biology to give an understanding of gut-brain biology, which further leads to transformational therapeutics that enhance human health.

It identifies circuits connected in physiology and disease and targets these circuits with gut-restricted molecules. Altering the brain through the gut is a novel approach for multiple diseases for which direct targeting of the CNS has been unsatisfactory.

TOTAL FUNDING TO DATE:

~\$245M

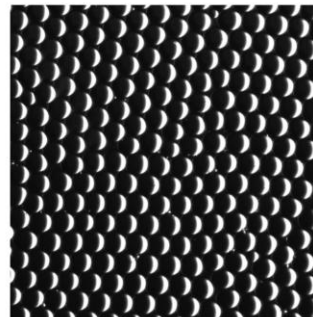
INVESTORS:

Lux Capital, The Column Group, Polaris Partners, Illumina, Alexandria Venture Investments, Two Sigma Ventures, Illumina Ventures, Euclidean Capital, Bill Gates, Greenspring Associates, Casdin Capital

Harnessing the Gut-Brain Axis

Our Platform

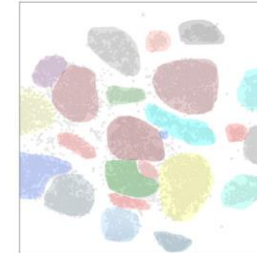
We are integrating cutting-edge technologies to build a comprehensive map of gut-brain circuits and interrogating the functions of these circuits to identify therapeutic targets that can be modulated with gut-restricted molecules. Components of our state-of-the-art platform include single-cell sequencing, computational biology, circuit mapping technologies. We are also using optogenetics and chemogenetics to elucidate the link between circuits and physiology/disease. Implementation of this platform has led to new insights into gut and gut-brain biology that enable a rationale, well-informed approach to targeting gut-brain circuits.



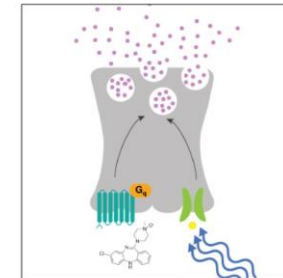
Water-in-oil droplets are loaded with cells and barcoded beads in order to capture the RNA from thousands of individual cells in parallel

SINGLE-CELL SEQUENCING

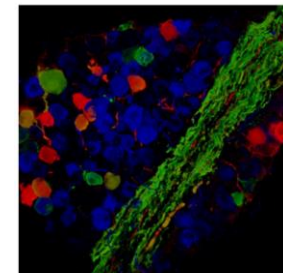
Heterogeneity is a ubiquitous feature of biological systems. The gut-brain axis - a network of cells from the gastrointestinal epithelium, enteric nervous system, vagus nerve, and brainstem - consists of many different cell types, each with unique functions. To identify and characterize each of these cell types we rely on single-cell RNA sequencing. Recent advances in technology have made it possible to routinely profile thousands of individual cells and to identify the RNA transcripts present in each single cell. Coupled with computational biology, this allows us to identify the many different cell types of the gut-brain axis and gain insight into their functions.



Single-cell atlas of murine enteroendocrine cells (EECs)



We activate gut cells using chemogenetics (left) and optogenetics (right) to modulate physiology and behavior



Vitaly-labelled nodose ganglia and associated vagal nerve

COMPUTATIONAL BIOLOGY

At Kallyope we are using computational biology to rationalize target discovery by applying a convergence of new methods from machine learning, next-generation sequencing, network biology, proteomics, knowledge representation, and artificial intelligence. Working closely with our internal sequencing team, the computational group has constructed a comprehensive understanding of the distinct cell types, and their transcriptional profiles, that comprise the gut-brain axis. To accomplish this, we have used proprietary software that extends the state of the art in the genomic alignment of sequencing reads and the high-dimensional, unsupervised clustering of single cells. To date we have identified several novel cell types and molecular targets with the potential to potently modulate systemic physiology, behavior, and disease.

MAPPING CIRCUITS TO FUNCTION

To understand how gut-brain circuits alter behavior and physiology, we are stimulating unique cell types within a gut-brain circuit and observing the physiological responses. We first gain control of a cell type of interest by genetically expressing proteins that can be selectively activated either with light (optogenetics) or with a targeted small molecule (chemogenetics). We can then use these tools to systematically engage each gut-brain circuit, determine its function, and identify promising pathways for treating disease.

CIRCUIT MAPPING

Technical advances in the neurosciences over the past decade have dramatically increased our ability to address previously unapproachable questions such as how do individual cell types respond to inputs and how are those cells integrated into circuits? Genetically-encoded activity sensors enable the interrogation of specific cellular responses throughout the body, and trans-synaptic tracers can determine which neurons are interconnected. Kallyope applies these advances to link the activation of components of the gut-brain axis to neural circuits implicated in processes ranging from metabolic regulation to behavioral control.

Arranta Bio

Consistent and scalable production of drug from a mixture of bacterial strains



Arranta specializes in producing therapies known as live biotherapeutic products (LBPs) that target the human microbiome.

The company has completed construction on a new "commercial-ready" manufacturing facility in Watertown, Massachusetts, as part of a \$100 million expansion effort spread across 2020. The CDMO's plans include building the new plant, which can handle late-stage clinical and commercial clients, as well as expanding capacity at its early clinical-stage facility in Gainesville, Florida.

Partnership agreement with Thermo, will give access to Thermo's products and services and in turn Arranta will provide materials to Thermo Fisher for use in gene-therapy production



12+

years of expertise



>145

species produced



230,000

sq feet of facilities



Arranta Bio announces the acquisition of Captozyme™, creating a Center of Excellence for microbiome development and clinical supply

TOTAL FUNDING TO DATE:

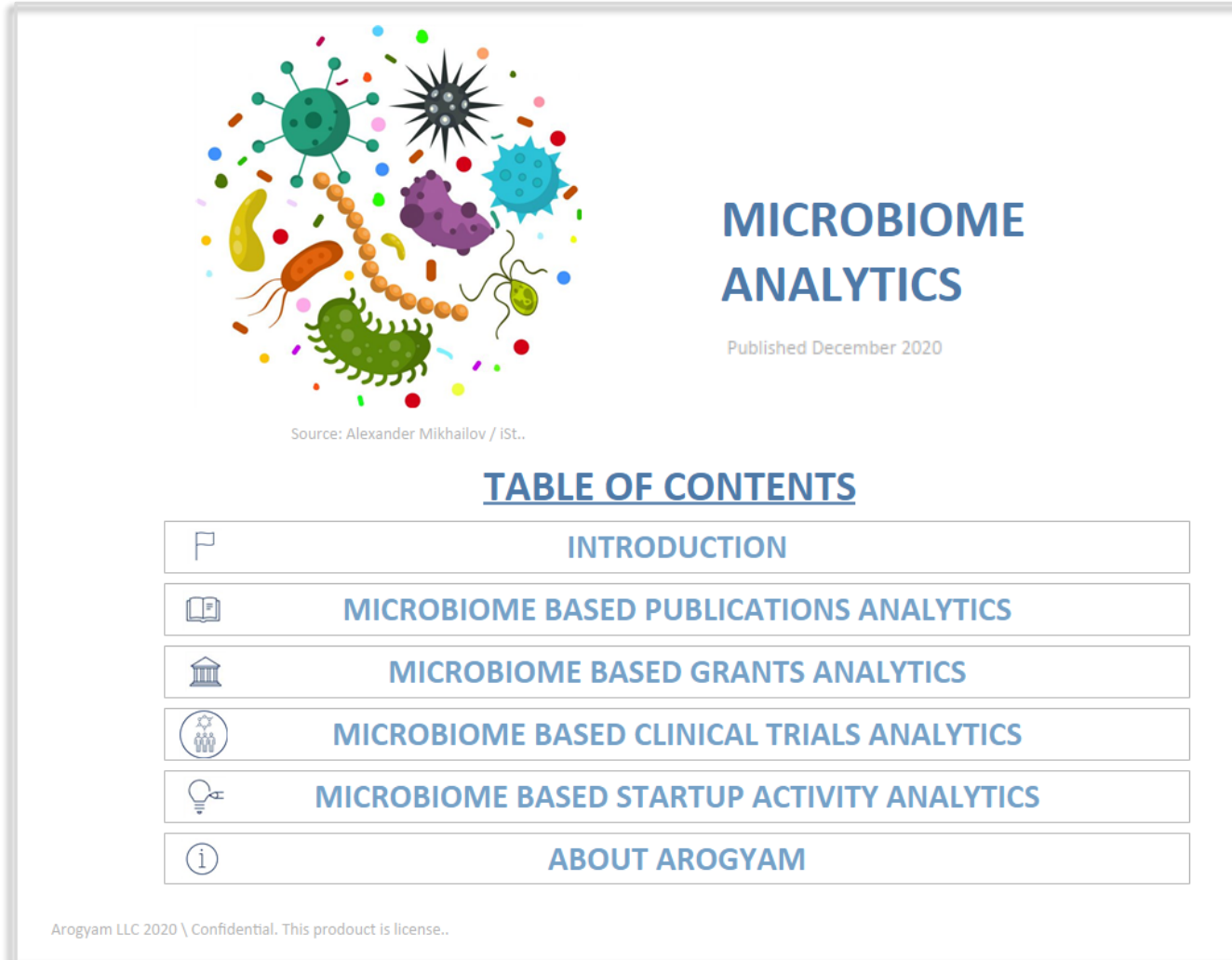
~\$85M

INVESTORS:

Thermo Fisher Scientific, Hockey Stick Investments, and Ampersand Capital Partners

Where is this Data From?







Arogyam Microbiome Market Intelligence Report



The cover of the 'MICROBIOME ANALYTICS' report features a vibrant illustration of various microorganisms including bacteria, viruses, and fungi. The title 'MICROBIOME ANALYTICS' is prominently displayed in blue, with the publication date 'Published December 2020' below it. A source credit 'Source: Alexander Mikhailov / iSt..' is visible. The 'TABLE OF CONTENTS' section lists six items: Introduction, Microbiome Based Publications Analytics, Microbiome Based Grants Analytics, Microbiome Based Clinical Trials Analytics, Microbiome Based Startup Activity Analytics, and About Arogyam. Each item is accompanied by a small icon. At the bottom, a copyright notice reads 'Arogyam LLC 2020 \ Confidential. This product is license..'.

Source: Alexander Mikhailov / iSt..

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	ABOUT AROGYAM

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GLOBAL COVERAGE

DYNAMIC DATA DRIVEN DASHBOARDS



 + a b l e a u

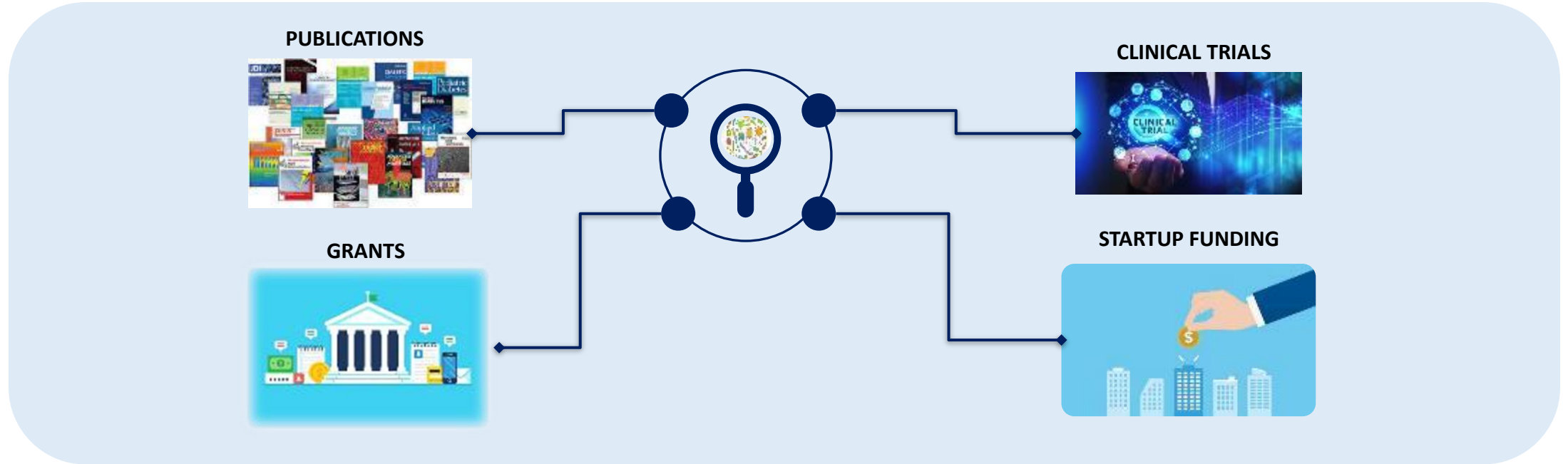
<https://www.arogyam.biz/shop>



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Four Pillars of Market Intelligence for Emerging Markets



- *Volume trends*
- *Funding trends*
- *Distribution by region and countries*



- *Mapping by therapy areas, conditions*
- *Top 5 to 50 agencies, institutions, researchers, sponsors, investors, and companies*
- *And more section specific trends*

Why Monitor the Pillars?

Actionable business insights

PUBLICATIONS



- Close representation of the research market demand
- Identify key thought leaders that can be key influencers and promoters of your products
- Leading institutions that can serve as key leads for sales, collaborators for R&D or key influencers for your product

CLINICAL TRIALS



- Drive revenue growth by finding and winning new business targets faster
- Leading investigators, disease areas, and sponsors better inform planning and understanding of the market landscape
- Identify optimum locations for patient enrollment

GRANTS



- Dollars spent on research is the research market opportunity
- Analyzing grants will point out key institutions, funding bodies, and researchers that are indicators of awareness, could become key beta sites, partners and promoters.
- Distribution by countries and regions to inform the focus of your marketing campaign

STARTUP FUNDING



- Investment funding reflects market growth potential, market need and validity of a solution
- Understand competitive fund-raising activity
- Follow the activity of leading investors and their bets



To understand how the market opportunity and potential growth can be derived from these insights, visit the Arogyam [blog](#)

Market Intelligence Research Methodology



Approach

Use keywords specific to the emerging market that is being analyzed in databases specific for scientific publications, research grants, clinical trials, and startup funding



Data Acquisition

Using keywords specific to the emerging market being analyzed, databases that house scientific publications, grants, clinical trials and startup funding activity are queried.

This trend information along with a range of useful attribute data powers downstream analysis

Natural Language Processing

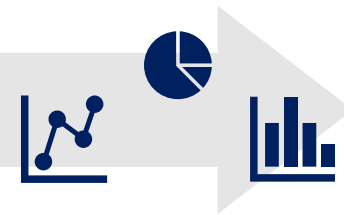


Precise Search Algorithms




Data Validation

Using a combination of automated and manual approaches, the data output is validated to ensure the highest accuracy possible



Data Visualization

Raw data is pushed into enhanced dashboards. The dashboards are carefully crafted to enable users to identify trends and insights from the data. They are intuitive and a powerful way to interact with the data

powered by  + a b | e a u

A Thorough Understanding of Your Target Market Starts Here



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Blog: [“The Art of Market Intelligence for Emerging Markets”](#)