Microbiome Diagnostic Industry Overview

July 01, 20XX

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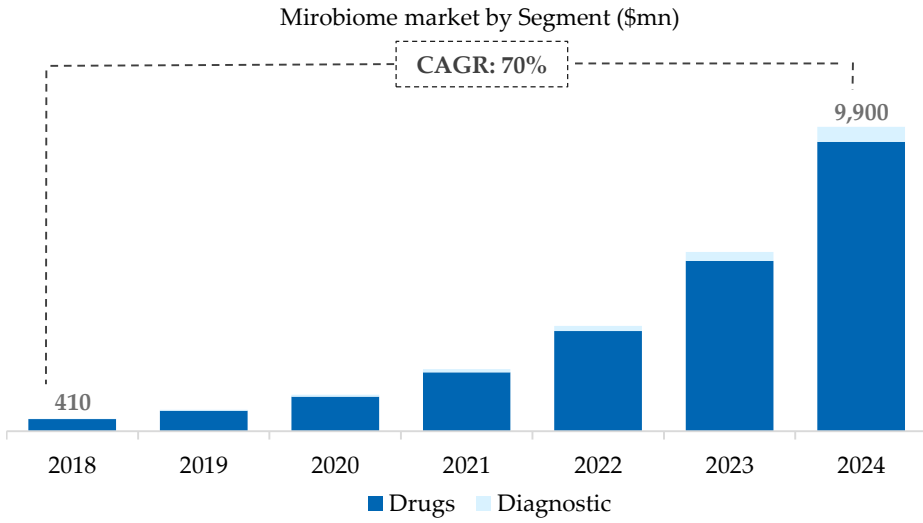
Microbiome Overview[1]

- The collection of microbes that live in and on the human body is known as the microbiota. The microbiome refers to the complete set of genes within these microbes
- The role of the microbiome is so central to the body's operations that it essentially acts as an organ. The microbiome impacts aging, digestion, the immune system, mood, and cognitive function
- Of the 100 trillion that make up the human microbiome (accounting for 1–3% of a person's body weight) half of the microbiome (1–2 kg) reside in the GI tract, which hosts the largest and most diverse collection
- Majority of the microorganisms benefit humans by supplementing them with traits that they do not otherwise possess
    - these include the capability to metabolize complex carbohydrates and prevention of growth of pathogens
- The human microbiome market can be broadly segmented by application into ***therapeutics (including therapeutic and medical foods) and diagnostics***
- The main reason for the growth of the therapeutic market is the need for reliable, precise and quicker treatment of chronic lifestyle diseases and various other disorders

Market Growth[1]



The overall microbiome market is expected to reach $9.9 bn by 2024 (growing at a CAGR of 70%) with 95% of it being the therapeutic market

Microbiome Diagnostic Overview[1]

- There are four major categories for microbiome diagnostics,
    - **Diagnosis or prognosis**: Use of microbiome markers to identify the disease and prognosis of the disease
    - **Treatment selection**: Understanding of the patient's microbiome associated with the disease could lead to selection of right treatment
    - **Disease monitoring**: Analysis of microbiota to predict the outcomes of the microbiome based drugs and also normalization of the microbial flora using microbiome time-series analysis
    - **Microbiome research:** Develop targeted precision medicine using microbiota cocktails to target the affected microflora
- **Salivary Microbiome** - The identification of biomarkers in the saliva would provide a means to easily and quickly obtain actionable information to support disease diagnosis. Advances in this regard include the use of high-throughput sequencing methods to identify pathogenic organisms in the saliva of patients with periodontal disease
- **Gastrointestinal Microbiome** – Research findings regarding the microbiome of the gastrointestinal (GI) tract in healthy and select disease states have the potential to provide noninvasive and accurate methods to diagnosis and choose treatment plans for systemic diseases associated with an altered microbiome. The disease states most studied are cardiovascular disease, IBD, and diabetes
- **Microbial translocation-Associated Disease -** Translocation of the GI tract microorganisms to the systemic circulation is normally prevented by the physiological environment and components that allow normal gut function. However, translocation through and intact barrier and its link to sepsis has been observed. Microbial translocation has also been found to be associated with increased infections in critically ill patients

Company Logo

Sources

1. IP Pragmatics (Link)

Industry Overview: Microbiome Diagnostic

Diagnostic Test Developments

Machine Learning	▪ Machine learning is used to generate customized reports showing the breakdown of a person's gut bacteria ▪ The reports also give advice like which fibrous foods to eat or probiotics to drink to improve good bacteria	**IBD110**	▪ IBD110 is the first noninvasive gut microbiome biomarker surrogate marker of mucosal healing ▪ A microbiome-targeting treatment being developed by Enterome against Crohn's disease
Analytics	▪ The analytical methods and tools for analyzing microbial consortia, such as functional imaging, omics-based interrogation, and cell culture, have been quite primitive compared to those for pure cultures	**Probiotic Food**	▪ Scientists have verified probiotic bacteria play a critical role in helping maintain a good digestive function ▪ Plant-based probiotic kale and broccoli poppers have been introduced by Brad's Plant in the U.S. market
Next-Generation Sequencing (NGS)	▪ These techniques can sequence all the DNA present in a sample, including that of bacteria that may have been killed by preventive treatment with broad-range antimicrobials	**Sequencing & qPCR**	▪ Quantitative PCR (or qPCR), microarrays and RNA sequencing are valuable assays for in-depth gene expression analysis

Applications

- Diagnostic applications of the microbiome can be divided into two categories: diagnosis of infectious diseases and monitoring of microbial components of noncommunicable chronic diseases
- The diagnosis of human infections and selection of antimicrobial agents may be refined in the context of the microbiome. Rather than focusing solely on identification of the etiologic agent(s) of infection, clinical laboratories could evaluate the microbiome at a specific body site of interest
- For example, rapid detection of Clostridium difficile in stool specimens in cases of recurrent C. difficile infection may be tested in parallel with stool-based 16S rRNA gene sequencing to evaluate the extent of dysbiosis or cooccurrence of other enteric pathogens
- Microbial metabolites may provide useful microbial biomarkers to monitor effective treatment in chronic infections such as recurrent C. difficile associated disease
- The development of microbiome diagnostics involves full sequencing and mapping for total bacterial gene content that characterizes the personal metagenome associated with a disease phenotype
- To characterize the microbiome, there are a range of strategies available in the market, the simplest being the marker gene approach using variable regions within the highly conserved 16S ribosomal RNA gene
    - Complimentary approaches including metagenomics (study of all genomes in an ecosystem), metatranscriptomics (characterization of gene expression from all microbes in an ecosystem), metabolomics (characterization of all small molecule metabolites in an ecosystem), and metaproteomics (characterization of all proteins in an ecosystem) provide greater insight into functional potential as well as the expression of microbiome-derived bioactive molecules necessary to understand the diagnostic and therapeutic implications for the microbiome

Industry Overview: Microbiome Diagnostic

Key Development by Companies[1]

Company Logo	▪ The Company has developed a proprietary data analytics platform that enables identification of novel mechanisms in microbe-microbe and microbe-human interactions. ▪ Using these microbial data points, the Company anticipates the issues of dysbiosis present due to the prevalence of metabolic and inflammatory diseases	**Company Logo**	▪ It is a microbiome testing company offering their platform through accredited US healthcare practitioners, with test results explained by the clinician ▪ The company also shares test results with researchers to improve research towards understanding how food and human microbes affect health
Company Logo	▪ The Company currently offers diagnostic DNA sequencing platforms to allow consumers to identify bacteria in their stool samples	**Company Logo**	▪ The Company develops sampling devices through its approved OriCol platform, which is also currently being tested for the validation of Calprotectin as a biomarker for the differential diagnosis of inflammatory bowel diseases
Company Logo	▪ Offers a diagnostic which uses metagenomic sequencing to provide each consumer with a personalized nutrition plan. ▪ The technology is still in the beta testing phase	**Company Logo**	▪ The Company is a biomarker and personalized treatment company offering data-driven mapping of how the gut microbiota affects metabolism to help industry develop the next generation of pharmaceuticals and functional food
Company Logo	▪ The Company is developing biomarker diagnostic tests for chronic conditions linked to changes in gut microbiota such as type-2 diabetes and irritable bowel disorders ▪ These are expected to launch alongside microbiome-based drugs for ulcerative colitis and Crohn's disease	**Company Logo**	▪ The Company is developing a collection kit and an analysis report that describes the microbiome composition in the dental caries sample, expected to be used in conjunction with microbiome drugs for the dental caries infection

Key Development for Women's Health

- For other non-gut microbiome applications, one important diagnostic areas is women's health. The current microbiome diagnostics assays for women's health involve predicting early pre-term labour and prognostic tests for understanding the changes in the vaginal microbiome through the monthly menstrual cycle and through the reproductive life
- It uses specialized analytics to integrate high-throughput and long read-length DNA sequencing data that generates microbiome profiles highlighting imbalance in the vaginal microbiome[1]
- The Company's test, SmartJane, performs STI testing, HPV high- or low-risk strain identification and microbiome profiling all from a sample a woman collects herself and mails to the company lab for testing. It allows women to self-sample at home instead of going into a doctor's office for testing will lead to more women getting care[2]

Industry Overview: Microbiome Diagnostic

Growth Opportunities

Lifestyle Changes	▪ The growing awareness among the consumers about the benefits of probiotics, and increasing demand for probiotic dietary supplements will propel the market to grow at a significant rate in the future	**Increase in Research and Development Activities**	▪ Advances in metagenomics and next-generation sequencing have made microbiome-based testing easier and cheaper, paving the way to carry out rapid analysis of the genomic content of microorganisms from human sample. This has bolstered the development process for microbiome-based diagnostics
Increasing Pool of Venture-cap Funded Startups	▪ The global human microbiome market is mainly driven by the rising investments by angel investors and venture capital firms/individual venture capitalists in the research and development of human microbiome-based therapies	**Rise in Clinical Trials for Gut Health-based Diseases**	▪ The gut microbiota helps to provides essential signals for the development and appropriate functioning of the immune system ▪ Through this critical contribution to immune fitness, the rise in clinical trails for the gut microbiota has a key role in health and disease
Women's Health	▪ Awareness regarding health and hygiene is rising among women and so is the need for products catering to their needs ▪ In October 2016, Becton, Dickinson and Company received U.S. Food and Drug Administration (FDA) market authorization for a first-of-its-kind molecular test to detect the common causes for vaginitis	**Increasing Incidence of Lifestyle Diseases**	▪ With advancements in precision medicine, personalized nutrition is also playing a crucial role ▪ Almost half of the total chronic disease deaths are attributable to cardiovascular diseases, obesity, and diabetes, as they already affect a large proportion of the population. Hence, this increase in the lifestyle diseases across the globe is driving the market for the human microbiome

Challenges

Safety	▪ The escape of engineered microbiomes into the environment may lead to unintentional colonisation of others may be a concern, even though most genetically modified organisms developed in the lab seem to be less fit than wild-type	**Knowledge Gaps**	▪ The companies' active in this space will need to educate the physicians, patients, vets, farmers etc. regarding the use, efficacy and safety of this new class of products and diagnosis
Regulation	▪ Despite the popularity of bioactive dairy products, it has been difficult to gain new health claims for functional ingredients since the European Food Standards Agency (EFSA) tightened labelling regulations around health claims on food products	**Consumer Perception**	▪ Though there is awareness among the public of the "good bacteria" in yogurts etc., there is still relatively little awareness regarding microbiome therapeutics or the beneficial use of nutraceuticals and medical foods, compared to traditional pharmaceuticals

Industry Overview: Microbiome Diagnostic

Market Landscape

Disease Area	Pre Clinical	Phase I	Phase II
Multiple Therapeutic Areas	Kaleido, symbiotix, BiomX, Whole Biome, synlogic, RondinX, Blue Turtle Bio	Caelus Health, Second Genome	Rebiotix
Gastrointestinal and Infectious Diseases	Eligo Bioscience, TargEDys, Biosis Health, Evolve BioSystems, EPIBIOME, Symbiotic Health, SciBac	assembly biosciences, MaaT, Finch Therapeutics	OSEL, Seres Therapeutics, Synthetic Biologics
Dermatology	Dermala, Naked Biome, azitra, Quorum, Xycrobe		AOBiome
Cancer and Autoimmune	Symberix, Inc, Amrita, Vedanta Biosciences, Evelo Biosciences		
Central Nervous System	Axial Biotherapeutics, Kallyope, Holobiome		

Select Company Profiles

July 01, 20XX

COMPANY 1

Company logo

Overview

- Founded in 1987, The Company is a global clinical laboratory, pioneering a systems approach that supports healthcare providers in the personalized treatment and prevention of chronic disease in all 50 states and around the world
- The Company's system-based testing helps physicians develop targeted treatments for their patients and offers easy-to-read color graphic reports that synthesize test results into actionable information and facilitate physician-patient communication
- The Company offers more than 125 specialized diagnostic assessments, covering a range of physiological areas, including digestive, immunology, metabolic function, and endocrinology as well as consultation ,online medical education services and webinar sessions
- It is licensed by CLIA, the federal agency regulating laboratories, and by those states requiring individual licenses
- In addition to their diagnostic services, they also serve primary and specialty physicians and healthcare providers in the United States and internationally
- **Headquarters:** ABC
- **Employees:** XX
- **Revenue:** $Y.Y mn

Medical Education

- The Company has an internationally renowned medical testing facility which provides educational support in a broad array of formats, including complementary phone consultations to healthcare professionals with the Company accounts
- It has created various multimedia universities that house important information related to the product lines, through their University Modules
- It also offers educational resources in the form of health and wellness bookstore to assist clinicians and patients
- Provides supplemental educational materials which are available for assistance in clinical application and interpretation of the Company's tests throughout the site
- The Company help in learning GDX through its audio-visual learning modules which are available to help in understanding and clinically applying the Company's broad array of diagnostic testing
- The Company also organizes webinars for leader in the field to share their experience on diagnostic and therapeutic approaches to common clinical condition

Tests By Product Line

Gastrointestinal Immunology	• Includes the GI Effects Profiles as well as CDSA(Comprehensive Digestive Stool Analysis) 2.0	**Environmental**	• Determines exposures to common classes of toxic and hazardous chemicals that are widespread in the environment and within each class, the measurement of the individual compounds that are frequently found to be problematic
Genomics	• Evaluates common genetic variations known as single nucleotide polymorphisms (SNPs); the presence of specific SNPs may indicate a predisposition for health vulnerabilities and these SNPS may be assessed in multiple functional areas including cardiovascular, detoxification, methylation, immune modulation, and estrogen metabolism	**Endocrinology**	• The Endocrinology product line includes a variety of comprehensive tests designed to evaluate and monitor hormone levels and endocrine glands
		Nutritional	• It is designed to identify and target nutritional imbalances, offering personalized patient recommendations and includes the NutrEval, ION and CardioION profiles

COMPANY 2

Company logo

Overview

- Founded in 2004 , the Company provides Next Generation Sequencing (NGS) services
- It mainly provides two types of services
    - **Analysis Services** - Offers complete NGS project services, from Project Design to Customized Cloud Services for results and, also the Bioinformatics Services
    - **Software development services** – With its Next Generation Sequencing, Cloud Computing and Bioinformatics software, they develop tailored software solutions for the customers
- The Company licenses its developments under the AGPL v3 license
- The Company's computing infrastructure is based on Amazon Web Services
- It provide services to customers from Research Groups, Universities, Hospitals, Biotech and Pharma companies, Bioinformatics facilities, and Contract Research Organizations (CRO)
- **Location** – ABC
- **Employee Count** – XX
- **Revenue** - $Y.Y mn

Platforms

ABC	• Bioinformatics has experience analyzing data from ABC sequencers and in designing many kinds of sequencing projects involving Illumina platforms like: • Metagenomics (Shot-Gun and 16S), Genomics, RNA-seq, etc. • The several ABC sequencer options include: XXXXX
XYZ	• Third Generation Sequencing: XYZ is based on Single Molecule Real Time sequencing (SMRT technology) • The XYZ technology achieves read lengths up to 30,000 bp with a mean size of 4,200 to 8,500 bp • This is currently the only technology able to directly detect all the types of nucleotide modifications
DEF	• The Company analyzes data from DEF machines like for example, the first draft of the E. coli genome from the German outbreak

Services

NGS Projects	• **Bacterial Genomics**: Complete bacterial genomes and amplicons for specific genes • **Metagenomics**: 16S and shotgun approaches • **Transcriptomics**: mRNA and non-coding RNA • **Immunogenomics**: TCR and BCR repertoires • **Software development projects**: Cloud Computing and storage of massive data, tailored software
Bioinformatics Consultancy	• Services range from research contract to addressing a purely scientific question to the development of practical solutions to solving problems related to a product in a biotech company • Bacterial Genomics studies include Comparative genomics, Membrane protein studies, Pathways analysis, Pathogenicity and virulence protein detection, etc.

Collaborations

Collaboration Logos

COMPANY 3

Company logo

Overview

- Founded in 2008, the Company is a microbial genomics platform focused on rapid characterization of microorganisms, pathogens and anti-microbial resistance for infectious disease identification, food safety inspections, pharmaceutical discovery, public health surveillance and microbiome analysis
- It also provides high resolution bioinformatics to facilitate personalized treatment in health care and monitoring of environmental bio threat agents
- The Company uses patented methods and curated databases of more than 65,000 microbial genomes, including bacteria, viruses, fungi, parasites, and antibiotic resistance and pathogenicity markers for identification of pathogens and commensal flora to sub-species or strain level
- The platform uses proprietary sequence analysis algorithms to accurately profile all microorganisms in a metagenomic sample employing next-generation DNA sequencing
- It serves clinics and hospitals, patients and healthcare personnel, pharmaceuticals, the public health sector, industries, and research laboratories
- **Location :** XX
- **Employee :** YY
- **Revenue:** $X.X mn

Service Offerings

Infectious Disease Diagnostic	• Detects multiple organisms and accurately identifies pathogens, their virulence and antibiotic resistance genes, all within a time frame of 24 hours
Healthcare Associated Infections	• Provides high resolution genomic and epidemiological subtyping of pathogens facilitates early detection of outbreaks and helps identify sources of transmission
Pharmaceutical Discovery Research	• Aids in the discovery process by providing translation of microbiome science for the discovery and development of novel products; bioactivation and toxicity screening to identify downstream biochemical byproducts
Public Health	• Hospital surveillance, epidemic control, and outbreak investigation are some of the areas where they aid the public sector
XYZ ***(Database)***	• Offers several curated XYZ databases and also provides data analysis for their clients

Clients

Client Logos

Collaborations

Zymo Research & Microbiome Standards Analysis	▪ It offers accurate and reproducible microbiome measurements with multi-kingdom strain-level resolution and industry leading sensitivity and precision
Plugin	▪ Detects microbes in metagenomic samples -It gives fast, accurate and comprehensive analysis of unassembled next generation sequencing reads ▪ Deeper insight through expert curated reference data Identifies bacteria, viruses, fungi, and protists, as well as, antibiotic resistance and virulence factors in a whole genome shotgun metagenomic sample

COMPANY 4

Company logo

Overview

- Founded in 2016, the Company develops technology and uses genome sequencing & machine learning to modernize infectious disease diagnosis and treatment
- The Company is developing a molecular diagnostic that uses high throughput sequencing and computational techniques to identify, within hours, both the species and the antibiotic resistance profile of a pathogen
- It aims at removing public health crisis created by Antibiotic Resistance by developing a new class of diagnostic that helps physicians to switch from broad spectrum antibiotic therapy
- **Location :** XX
- **Employee :** YY
- **Revenue** :$Z.Z mn

Sequencing Based Diagnostic Testing

- The Company is developing **high-throughput sequencing** which enables individuals to sequence DNA and RNA overnight and at lower costs
- The Company uses a combination of two different types of next-generation sequencing technologies: **illumina** and **nanopore**
    - **Illumina** uses an approach called 'sequencing by synthesis' wherein an optical detection technology takes short snippets of DNA, replicates them, and reads out the sequencing
    - **Nanopore** uses electric currents to read long DNA strands and helps get very long reads very quickly and in an order of magnitude longer than that using illumine
- Microbiological culture, which would take three to five days to sequence samples takes three to five hours at the Company to generate these sequence able samples
- It matches genomic data utilizing its Keynome™ algorithm with its proprietary database of microbial resistance profiles, called MicrohmDB™ which enables it to pinpoint genome-specific resistance and generate accurate treatment solutions

Key Executives

President & CEO		**Scientific Co-founder**	
CTO, Co-founder		**Scientific Co-founder**	

COMPANY 5

Company logo

Overview

- Founded in 2004, the Company is an early stage molecular diagnostics company that develops in-vitro diagnostics, screens tests, and health assays that leverage breakthroughs in next-generation DNA sequencing, computational systems biology, and human microbiome sciences
- It researches DNA sequencing, computational systems biology, and human microbiome sciences
- The Company introduced a new type of microbiomic diagnostic test for early detection and monitoring of polymicrobial and immunological diseases such as inflammatory bowel disease, colon cancer, HIV infection, alcoholic liver disease
- It works in collaboration with some of the leading universities and medical institutions across the United States and Canada to analyze various gastrointestinal diseases
- **Location :** XX
- **Employee :** YY
- **Revenue** : $Z.Z mn

Technology

- Develops and patents DNA Sequencing Technology that is the preferred Method of the NIH Human Microbiome Project
- The patented technology uses high-throughput next-generation sequencing for clinical research, diagnosis, prognostication, and monitoring of disease progression in inflammatory bowel disease (IBD), polymicrobial, and immunological diseases
- The xx platform provides a means of applying high-throughput DNA sequencing methods such as pyrosequencing to metagenomics research, clinical research and diagnostic testing
- The sequencing is done by adding unique barcodes for identifying a hundred or more individual patient samples in a single high-throughput DNA sequencing run
- The technology being used enables the use of DNA sequencing with advanced bioinformatics and comparative statistical analysis to economically perform clinical trials and diagnostic testing of individual patients

Management Team

Chairman & CEO		**VP Business Development and Sales**	
President & COO		**Chief Medical Officer**	

COMPANY 6

Company logo

Overview

- Founded in 2015 , The Company develops and operates a web-based platform that provides actionable health improvement and disease prevention solutions based on gut microbiome
- The Company's products include additional microbiome-based diagnostic and therapeutic solutions
- It also provides its services through a smart phone application
- The product offered by the Company for personalized health, is based on a five year research conducted by
- The research was funded solely by the Weizmann Institute of Science and upon its completion, the research technology was licensed to the Company
- **Location** – XX
- **Employee Count** – YY

Key Executives

Board Member, Co-Founder	
Chairman, Co-Founder	
CEO, Co-Founder	

Product Features

Stool Sample	• Once the registration process is completed, the company send an easy-to-use stool sample kit • The kit includes a small tube, toilet accessory and scoop • The stool sample helps to identify the information about the gut microbiome • They also ask to fill out a short questionnaire and ask for a simple HbA1c blood test result
Predicting Food	• The samples are examined and analyzed through their patent pending algorithm • A scoring system is used to rate thousands of different foods and food combinations based on the gut microbiome analysis and lifestyle factors • The Company's algorithm is based on a patent pending technology, licensed from Weizmann Institute of Science
DNA Sequencing	• The company uses its technology to profile the composition and diversity of an individual's gut microbiome at genetic level • This is done because of the gut microbiome diversity. For example the the gut microbiome of obese people is different than that of non obese individual
Personalized Nutrition App	• It prepares unique personalized nutrition recommendations for each and every individual and a consultation with the Company's dietitian to guide through the app, the gut results, and meal planning • Based on the results they provide recommendations specific to the gut make-up, like Top Meals for breakfast, lunch and dinner

1. LinkedIn (Link)

Industry Overview: Microbiome Diagnostic

Company	Geography	Employee Count	Revenue ($mn)	Key Offerings
Company 1 logo	All 50 states of US and around the world	201-500	X.X	Offers over 125 diagnostics assessments to help physicians develop targeted treatments for their patients and offers easy-to-read color graphic reports that synthesize test results into actionable information
Company 2 logo	Multiple locations across US	11-50	Y.Y	The Company services, cloud computing and bacterial genomics
Company 3 logo	Rockville, MD	11-50	Z.Z	Genome databases and gene analytics for personalized healthcare
Company 4 logo	Boston, MA	2-10	A.A	Developing a molecular diagnostic that uses high throughput sequencing and computational techniques to quickly identify , both the species and the antibiotic resistance profile of a pathogen
Company 5 logo	Various Centers across US	2-10	B.B	Microbiome diagnostic test for early detection and monitoring of polymicrobial and immunological diseases such as inflammatory bowel disease, colon cancer, HIV infection, alcoholic liver disease, etc.
Company 6 logo	NA	11-50	C.C	Personalized nutrition app based on an individual's gut microbiome