

METAGENOMICS SEQUENCING: “ CURRENT STATUS AND THE ROAD AHEAD ”

Dissertation Submitted to



The IIHMR University, Jaipur
for the partial fulfilment for the award of the
degree of Master of Business Administration
(MBA)

in

Hospital and Health Management

by

Ayushi Kashyap

Under the Supervision and Guidance of

Dr Sheenu Jain

2022

METAGENOMICS SEQUENCING: “ CURRENT STATUS AND THE ROAD AHEAD

Dissertation Submitted to



The IIHMR University, Jaipur
for the partial fulfilment for the award of the
degree of Master of Business Administration
(MBA)

in

Hospital and Health Management
by

Ayushi Kashyap

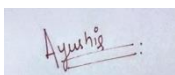
Under the Supervision and Guidance of

Dr Sheenu Jain

2022

DECLARATION

I hereby declare that this dissertation titled is METAGENOMICS SEQUENCING: “CURRENT STATUS AND THE ROAD AHEAD” the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

A small rectangular image showing a handwritten signature in blue ink. The signature appears to be 'Ayushi Kashyap' written in a cursive style.

(Signature)

Ayushi Kashyap

Date:- 27/06/22

CERTIFICATE

This is to certify that dissertation titled **METAGENOMICS SEQUENCING: “CURRENT STATUS AND THE ROAD AHEAD ”** is a record of the research work undertaken by Ayushi Kashyap in partial fulfilment of the requirements for the award of the degree of MBA -Hospital and Health Management from the IIHMR University, Jaipur under my guidance and supervision and her approach to the research study has been sincere, scientific, and analytical.

Faculty Guide

IIHMR University, Jaipur

Date

School Dean

IIHMR University, Jaipur

Date

ACKNOWLEDGEMENTS

I express my thankfulness to my mentor Dr Sheenu Jain, who helped me a lot with her professional guidance and valuable support whenever required. I am thankful for their constant support and providing me the necessary data and briefing me with all the projects throughout my training. I thank them for the patience and forbearance throughout the training, for their sincere guidance and constructive criticism, which helped me to work towards success.

I owe my deepest regards to my family and friends who have motivated me, kept patience and supported me throughout my project work.

At last but not the least I express my heartfelt gratitude to almighty.

Date: 27th June 2022

Place: Jaipur

Ayushi Kashyap

Table of Content

S.NO.	Name of Chapter	Page Number
	Acronyms/Abbreviations	8
Chapter 1	Introduction	9
Chapter 2	Review of Literature	10-23
Chapter 3	Methodology	24
Chapter 4	Results and Discussions	25- 37
Chapter 5	Conclusion and Recommendations	38-39
	References	40

List of Figures

S. No	Name of Figure	Page No.
4.1	Importance of Metagenomics	26
4.2	Drivers, Restraints, Opportunities and Restraints	30

List of Tables

S. No	Name of Table	Page No.
2.1	Review of Literature	10
4.1	Market Segmentation	28
4.2	Key players operating in the metagenomics market	33
4.3	Strategic Overview	34
4.4	Product Launches	36
4.5	Deals	37
4.6	Expansions	37

ABBREVIATIONS

ACGS	Association For Clinical Genomic Science
DBT	Department of Biotechnology
DNA	Deoxyribonucleic Acid
IBAB	Institute of Bioinformatics and applied biotechnology
NCBI	National Center For Biotechnology Information
JGI	Joint Genome Institute
NHGRI	National Human Genome Research Institute
NIH	National Institutes of Health
PMPC	Personalized Medicine Partnership for Cancer
WHO	World Health Organisation

Abstract

Metagenomic sequencing is among the new approaches in genomic analysis, which involves the sequencing and analysis of genetic materials obtained from environmental samples without the prior isolation and cultivation of individual species.

The research includes competitive mapping for significant players in the market. The study reviews the drivers, restraints, opportunities and challenges associated with the market. All the significant developments including, product launches, partnerships, and acquisitions are included in the study.

Metagenomics is the trending technique around the globe and this market has a significant impact on the future. This technique is highly efficient in analysing unculturable, or previously unknown microbes present in rich microbiota, hence gaining acceptance and opening new avenues in various fields.

CHAPTER 1- INTRODUCTION

Metagenomic sequencing is among the new approaches in genomic analysis, which involves the sequencing and analysis of genetic materials obtained from environmental samples without the prior isolation and cultivation of individual species. This technique is highly efficient in analysing unculturable, or previously unknown microbes present in rich microbiota, hence gaining acceptance and opening new avenues in various fields.

The study of the structure and use of complete nucleotide sequences that have been extracted and examined from all the species in a bulk sample is known as metagenomics. Metagenomics is frequently used to investigate a particular population of microbes, such as those found in soil, water, or human skin.

Metagenomics, like genomics, is both a study topic and a collection of research methods that includes numerous related concepts and methods. In this way, the study of all organisms and its application to many other fields, such as epidemiology, clinical microbiology, virology, agriculture, forestry, fisheries, biotechnology, and microbial forensics, has been revolutionised by genomics, a science created to advance biomedicine and our understanding of our species. To define environments by the actualized and potential biochemical and geochemical activities of the genes that are present, as well as the intricate patterns of interactions within and between cells that control their responses to changes in their physical and biological surroundings, we should move straight to the genes.

Metagenomics provides a way to address pressing issues that humanity is currently facing. Unlocking the mysteries of a few of the planet's innumerable microbial populations will show how to overcome a variety of difficulties in biomedicine, agriculture, and environmental stewardship. Earth sciences, life sciences, biomedical sciences, bioenergy, bioremediation, biotechnology, agriculture, biodefense, and microbial forensics are among the most significant possible contributions.

CHAPTER 2- REVIEW OF LITERATURE

Table 2.1: Review of Literature

S. No.	Tittle	Author	Year	Findings
1.	Metagenomics - a guide from sampling to data analysis	• Torsten Thomas, • Jack Gilbert, • Folker Meyer	2012	This study gives practical assistance and advice on sample processing, sequencing technology, assembly, binning, annotation, experimental design, statistical analysis, data storage, and data sharing. It also covers the most recent metagenomics opinions. The availability of standardised processes and shared data storage and analysis becomes more crucial as more metagenomic datasets are produced so that the results of different research may be evaluated and compared.
2.	16S rRNA- Based Taxonomy Profiling in the Metagenomics Era	• MatteoRamazzotti • GiovanniBacci	2018	The paper discusses how metagenomics, phylogenetic markers, and next-generation sequencing (NGS) have enhanced our comprehension of how microbial communities form, function, and

				develop. Targeted and untargeted methods can both produce a cohesive taxonomic framework. For a very long time, targeted techniques have dominated meta-analyses, offering valuable insights into the dynamics and structure of microbial populations.
3.	The metagenomics worldwide research	• Jose Antonio Garrido-Cardenas • Francisco Manzano-Agugliaro	2017	The authors of this article review the history of metagenomics, examine and compare the various massive sequencing platforms used for metagenomic assays, review the literature that is currently available on the topic, and discuss potential future issues that researchers who choose to delve deeper into this area may encounter. The researcher's prior knowledge will help him approach his investigation in this way.
4.	The Road to Metagenomics: From	• Alejandra Escobar-Zepeda,	2015	This review's objective is to walk the reader through the key events

	Microbiology to DNA Sequencing Technologies and Bioinformatics	• Arturo Vera-Ponce de León • Alejandro Sanchez-Flores		and turning points that paved the way for contemporary metagenomics. In this article, the impact of high-throughput sequencing technology on microbiology and bioinformatics is discussed, along with methods for overcoming the inherent computational difficulties brought on by the DNA sequencing revolution.
5.	Review on Metagenomics and its Applications	Asiya Nazir	2016	Metagenomic libraries are a crucial tool for the identification of novel enzyme activities that facilitate genetic monitoring for all future biotechnological applications. The history of metagenomics will be analysed in this overview, along with its more current applications in microbial ecology and biotechnology.
6.	Biotechnological applications of functional metagenomics in	• Laura M. Coughlan • Paul D. Cotter	2015	The latest functional metagenomic techniques are outlined in this review paper, along with

	the food and pharmaceutical industries	• Colin Hill • Avelino Alvarez-Ordóñez		their potential for mining as-yet-unexplored environments for new genes with biotechnological applications in the food and pharmaceutical industries.
7.	Application of metagenomics in the human gut microbiome	• Wei-Lin Wang • Shao-Yan Xu • Zhi-Gang Ren - Liang Tao • Jian-Wen Jiang • Shu-Sen Zheng	2015	The goal of this review is to show how metagenomics can be a potent method for researching the human gut microbiota with promising results. There is also discussion about how to get around metagenomics' limits. The study of the human gut microbiome is also briefly mentioned in relation to metatranscriptomics, metaproteomics, and metabolomics.
8.	The metagenomics worldwide research	• Jose Antonio Garrido-Cardenas • Francisco Manzano-Agugliaro	2017	The authors of this article review the history of metagenomics, examine and compare the various massive sequencing platforms used for metagenomic assays, review the literature that is

				currently available on the topic, and discuss potential future issues that researchers who choose to delve deeper into this area may encounter. The researcher's prior knowledge will help him approach his investigation in this way.
9.	Metagenomics and antibiotics	• L Garmendia • A Hernandez • M B Sanchez • J L Martinez	2012	The use of several metagenomic methodologies is discussed in this study in order to analyse the distribution of antibiotic resistance genes in various environments, understand how antibiotics affect microbial populations, and create new antimicrobial chemicals. These methods include descriptive metagenomics, which is used to track the existence and abundance of already known antibiotic resistance genes in various ecosystems, as well as functional metagenomics, which is

				used to discover new antibiotics or antibiotic resistance genes.
10.	Microbial source tracking using metagenomics and other new technologies	Shahbaz Raza Jungman Kim Michael J Sadowsky Tatsuya Unno	2021	The study discussed how improvements in qPCR and next-generation sequencing (NGS) technologies have moved conventional culture-based MST techniques towards culture independent technologies, where community-based MST is emerging as the preferred strategy. Metagenomic technologies can provide significant insight into finding host specific faecal markers and their relationship with various environments, which may be helpful to overcome some of the limitations of community-based MST methods. Combining metagenomic-based MST techniques with machine learning (ML) algorithms will create a platform that is statistically reliable and automated. Additionally,

				ML-based techniques offer precise resource optimization. It's feasible that these techniques will serve as the standard for disease prediction, outbreak investigation, and medication prescription with the effective implementation of ML based models.
11.	Metagenomics methods for the study of plant-associated microbial communities: A review	• Ayomide Emmanuel Fadiji • Olubukola Oluranti Babalola	2020	The study discussed how improvements in qPCR and next-generation sequencing (NGS) technologies have moved conventional culture-based MST techniques towards culture independent technologies, where community-based MST is emerging as the preferred strategy. Metagenomic technologies can provide significant insight into finding host specific faecal markers and their relationship with various environments, which may be helpful to overcome some of the limitations of

				community-based MST methods. Combining metagenomic-based MST techniques with machine learning (ML) algorithms will create a platform that is statistically reliable and automated. Additionally, ML-based techniques offer precise resource optimization. It's feasible that these techniques will serve as the standard for disease prediction, outbreak investigation, and medication prescription with the effective implementation of ML based models.
12.	Metagenomics and probiotics	• M Gueimonde • M C Collado	2012	Metagenomic research on the human gut microbiome has been made possible by the development of in-depth sequencing techniques. Our understanding of the makeup and function of the gut microbiota has greatly enhanced as a result, making it possible to identify microbiota aberrations linked to various diseases. The

				creation of probiotics meant to rectify these abnormalities has these as its aims. Probiotics are frequently used to alter gut flora. However, there are still very few metagenomic investigations into the impacts of probiotics. Metagenomics promises to advance our knowledge of probiotic action in the near future.
13.	Benchmarking Metagenomics Tools for Taxonomic Classification	• Simon H Ye • Katherine J Siddle • Daniel J Park • Pardis C Sabeti	2019	The authors examined current methods for metagenomic analysis and assessed 20 metagenomic classifiers' performance using simulated and real datasets. They outline the main performance indicators, provide a framework for evaluating new classifiers, and talk about the prospects for metagenomic data analysis in the future.
14.	Novel Strategies for Applied Metagenomics	• Jessica M Moore-Connors • Katherine A Dunn, Joseph P Bielawski	2016	The authors of this review covered the use of next-generation sequencing in microbiome research

		Johan Van Limbergen		and stressed the significance of modelling microbiome structure and function for future advancements in the study of and treatment of inflammatory bowel disease.
15.	Metagenomic Assembly: Overview, Challenges and Applications	- Jay S Ghurye - Victoria Cepeda-Espinoza - Mihai Pop	2016	The authors of this survey discussed the new potential and problems presented by this emerging subject while concentrating on the key algorithmic approaches for genome and metagenome assembly. The authors also discuss several ways that metagenome assembly has been applied to solving intriguing biological issues.
16.	Metagenomics: key to human gut microbiota	- Simone Maccaferri - Elena Biagi - Patrizia Brigidi	2011	The potential of the most recent high-throughput, culture-independent methods for characterising the human gut microbiome in health and disease is highlighted by the authors. Presenting recent and encouraging

				findings highlights the possibilities and potential for future study in the field of human gut microbial ecology.
17.	Metagenomics and novel gene discovery: promise and potential for novel therapeutics	Eamonn P Culligan Roy D Sleator Julian R Marchesi Colin Hill	2014	In order to find novel genes, the scientists evaluated both sequence-based and functional metagenomic techniques. They also discussed some of the drawbacks of each type of approach as well as possible remedies. Finally, scientists explained how the identification of novel genes may be exploited to produce bioengineered probiotics. They also discussed the potential for metagenomic biotherapeutic discovery, with a special focus on the human gut microbiome.
18.	An Introduction to Whole-Metagenome Shotgun Sequencing Studies	• Tyler A Joseph • Itsik Pe'er	2021	Here, the authors discuss the three main metagenomics research fields of assembly, community profiling, and functional profiling to provide an overview

				of whole-metagenome shotgun sequencing investigations, a widely used method for analysing microbial populations. These topics include a significant portion of the metagenomics literature, however they are not all-inclusive. The authors went into great detail on each topic, including the problems that whole-metagenome shotgun sequencing presents and the methods crucial to each topic's answers. They then identified topics for future research that looked particularly promising. Even though the focus is on the human microbiome, the techniques are generally transferable to other study systems.
19.	Metagenomics as a Tool for the Investigation of Uncultured Microorganisms	• N V Ravin • A V Mardanova • K G Skryabin	2015	The main methodological approaches employed in metagenomic investigation of microbial communities are discussed in this review, along with

				successes in the discovery of novel, uncultured microorganisms, the deciphering of their genomes, and an explanation of their function in ecosystems.
20.	Computational tools for viral metagenomics and their application in clinical research	• L Fancello • D Raoult • C Desnues	2012	This review's first section is devoted to a description of earlier work in viral metagenomics, with a focus on viral ecosystems linked with humans (eukaryotic viruses and bacteriophages). The authors detailed the computational difficulties faced by the analysis of viral metagenomes in the second section, and we show the issue of sequences without homologs in public databases and potential methods to characterise them.
21.	The Role of Metagenomics and Next-Generation Sequencing in	• Steve Miller • Charles Chiu	2021	The authors emphasise numerous factors that have an impact on diagnostic performance while outlining the

	Infectious Disease Diagnosis			laboratory approach to mNGS testing. Additionally, they provide an overview of recent research on the diagnostic performance of mNGS assays for a range of infection types and suggest additional research to assess the enhancement of clinical outcomes and cost-effectiveness of mNGS testing.
--	------------------------------------	--	--	---

Chapter 3- Research Methodology

- Research Question:-
 - i. What is the role of metagenomic sequencing globally?
 - ii. What will be the future of the metagenomic sequencing market globally?
- Research Objectives:-
 - i. To define and describe the importance of metagenomics.
 - ii. To provide detailed information regarding the primary factors influencing the metagenomic sequencing market.
 - iii. To enlist the drivers, opportunities, restraints and challenges associated with the current use as well as future usage of metagenomics sequencing.
 - iv. To profile key players in the metagenomic sequencing market and analyze competitively developments were undertaken by major players in the metagenomic sequencing market, which include product launches and enhancements; expansions; partnerships; collaborations and agreements.
- Methodology:-

The data was collected through extensive secondary research. The research study involved extensive secondary sources, directories, and databases such as D&B Hoovers, Bloomberg Business, and Factiva along with government databases to identify and collect information useful for this technology-based, market-oriented and commercial study of the metagenomic sequencing market. Secondary sources referred to for this research study include publications from organisations such as the World Health Organisation (WHO), Institute of Bioinformatics and applied biotechnology (IBAB), National Institutes of Health (NIH), Joint Genome Institute (JGI), National Human Genome Research Institute (NHGRI), National Center For Biotechnology Information (NCBI), Personalized Medicine Partnership for Cancer (PMPC), Association For Clinical Genomic Science (ACGS), and Department of Biotechnology (DBT).

- Study design: Descriptive cross-sectional study

Chapter 4 – Results & Discussions

Importance of Metagenomics

Metagenomics is the study of microbial community genomics without regard to culture. Prokaryotes and viruses can be studied in the environment using metagenomics, which analyses DNA taken directly from environmental samples. In metagenomics, the DNA of all the bacteria in a population is taken into account. In addition to identifying the kind of microorganisms that are present, it can also shed light on their functional characteristics and metabolic processes. This approach combined with functional activity is a potent tool for identifying novel functional genes in uncultured microorganisms.

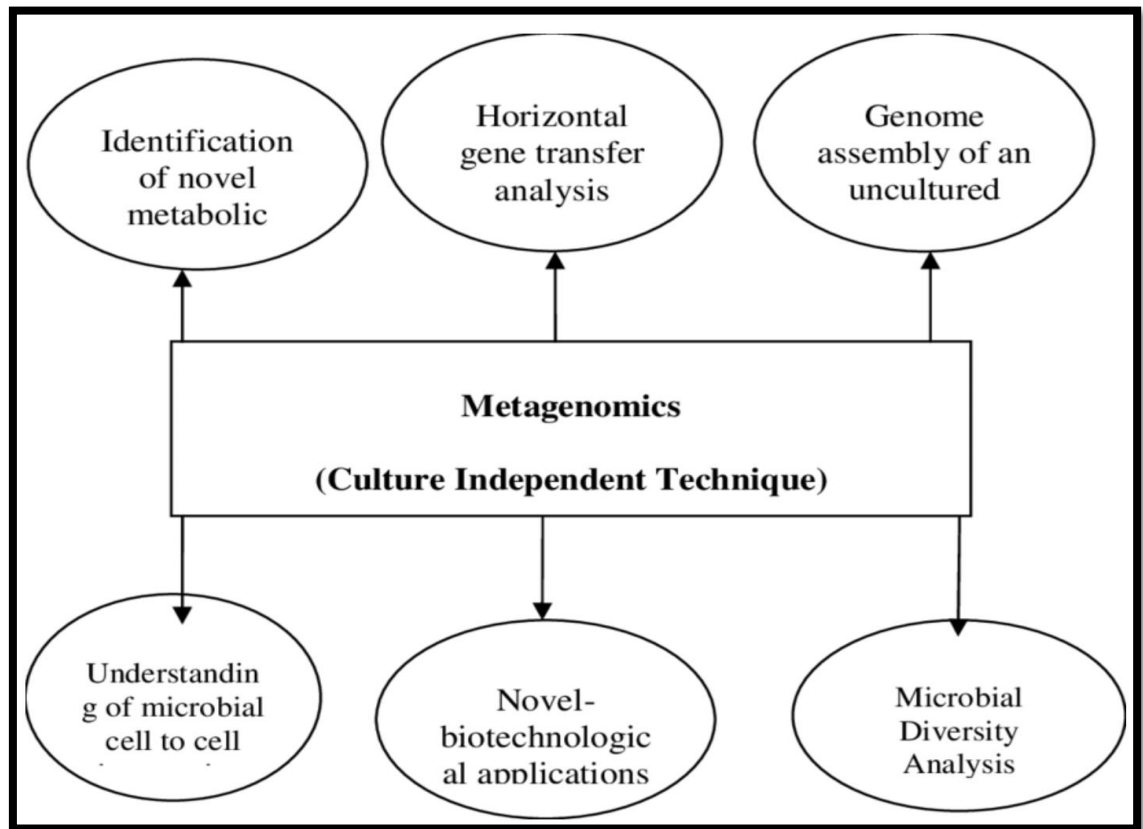


Figure 4.1: Applications of Metagenomics

- Metagenomics could have a significant impact on industrial productivity. Metagenomics research has revealed the existence of unusual bioactive substances including indirubin, violacein, and terrines. The basic research on the soil microbiome led to the development of streptomycin, turbomycin, and other antibiotics. Descriptive metagenomics tracks the existence and quantity of known antibiotic resistance genes in various contexts, while functional metagenomics analyses changes in the microbiome's composition to discover new antibiotics or novel antibiotic resistance genes. Metagenomics techniques have produced new genetic data on industrial enzymes such lipases, proteases, lyases, amylases, and nitrilases.
- Metagenomics has recently been used to locate an unidentified pathogen in disease outbreaks. Pathogens in clinical samples can be found and identified using shotgun metagenomics. RNA obtained from a sample must typically first be transformed to cDNA in order to study RNA viruses. Metagenomics has largely been used to identify viruses and bacterial pathogens, but not parasite infections. For instance, the metagenome of Egyptian mummies contained

genomes for the parasites Plasmodium and Toxoplasma. Recovery of genomic-epidemiological data and assessment of the impact of parasites on the microbial ecology in the gut are two potential uses of metagenomics in parasitology.

- Clinical microbiota investigation using 16S/18S/ITS amplicon sequencing is a sophisticated and cost-effective method. It enables the monitoring of human health and wellbeing and can be used to identify gut bacteria species and their abundance. The creation of probiotics is explained by metagenomics. Monitoring bacterial communities that are linked to humans enables the development of control strategies to improve human health. There is a product called personalised metagenomics that may be bought. Always choose prevention over treatment. Personal genomics, epigenomics, and metagenomics may all work together to provide the basis for future health care.
- Microbial ecology and next-generation sequencing provide useful viewpoints and resources for analysing and tracking the health of wildlife. The health, nutrition, physiology, and immune systems of hosts are significantly impacted by the microbial populations that live inside of animals and plants. We can distinguish between and within hosts' microbiomes thanks to DNA sequencing technology. Microbial communities are sensitive to changes in the outside environment, and habitat quality and microbial diversity are correlated. As a result, considering microbial host and biogeographic variation holds considerable promise for assessments of forest corridors and efforts at reintroduction. In addition, microbial pathogens pose a serious threat to the health of wildlife.

⇒ **Primary factors influencing the metagenomic sequencing market.**

For understanding the factors, the market is segmented into 5 segments.

Table 4.1: Market Segmentation

WORKFLOW	PRODUCT & SERVICE	TECHNOLOGY	APPLICATION	REGION
Sample processing & library preparation	Reagents	16S rRNA Sequencing	Drug Discovery	North America (US & Canada)
Sequencing	Instruments	Shotgun Metagenomic sequencing	Clinical Diagnostics	Europe (Germany, UK, France, & ROE)
Data Processing & Analysis	Services	Whole-genome Sequencing & De Novo assembly	Soil Microbiome applications	Asia Pacific (Japan, China, India, & ROAPAC)
	Analysis & Data	Metatranscriptomics	Industrial Applications	Latin America
			Ecological & environmental applications	Middle East & Africa
			Other Applications	

By Workflow

Based on workflow, the market has been segmented into sample processing & library preparation, sequencing, data processing & analysis. According to various studies and papers, sample processing & library preparation has the largest market share among all others.

By Product & Service Segment

Based on products & services, the market is segmented into reagents & consumables, instruments, services, and analysis & data interpretation solutions. According to various studies and papers, the reagents & consumables segment has the largest market share. Factors such as the development and commercialization of high-quality reagents and kits and the continuous requirement of sequencing reagents by end-users are expected to drive the growth of this segment in the market.

By Technology

Based on technology, the market is segmented into 16S rRNA sequencing, shotgun metagenomic sequencing, whole-genome sequencing & de novo assembly, and metatranscriptomics. According to various studies and papers, the 16S rRNA sequencing segment has the largest market share. The high accuracy and affordability offered by 16S rRNA sequencing, advancements in bioinformatics solutions, and the growing number of metagenomic research activities to identify and classify various bacterial strains are the major factors driving the growth of the 16S rRNA sequencing market.

By Application

Based on applications, the market is segmented into drug discovery, clinical diagnostics, soil microbiome applications, industrial applications, ecological & environmental applications, veterinary applications, and other applications. According to various studies and papers, the drug discovery segment has the largest share of the market. The large share of this segment can be attributed to the increasing research activities for novel drug discovery and growing collaborations between market players, academic institutions, and pharmaceutical companies for drug development.

By Region

According to various studies and papers, North America has the largest share of the market. Factors such as the increasing applications of metagenomics in diagnostics and genomics research, the availability of research funding, and the development of NGS data analysis solutions are driving the growth of the market in North America.

⇒ **Drivers, opportunities, restraints and challenges associated with the current use as well as future usage of metagenomics sequencing**

DRIVERS • Technological innovation in NGS platforms. • Initiatives and funding from government & private bodies for large-scale sequencing projects. • Declining costs of genome sequencing. • Significant applications of metagenomics in various fields.	RESTRAINTS • End-user budget constraints in developing countries.
CHALLENGES • Challenges associated with metagenomic NGS	OPPORTUNITIES • NGS Data analysis using big data.

Figure 4.2: Drivers, Opportunities, Restraints, Challenges

DRIVERS

- **Technological innovation in NGS platforms.**

The development of effective, portable, and simple-to-use NGS platforms with better turnaround times has been made possible by the ongoing technological advancements in sequencers. Due to the instant competitive advantage that the introduction of such products and technology gives businesses, well-known corporations are increasingly concentrating on R&D in order to increase their market positions and share.

For instance, the Sequel II System was introduced by Pacific Biosciences of California, Inc. (US) in April 2019. When compared to the prior Sequel System, the new solution cuts project costs and schedules by almost eight times the amount of data produced. PromethION 24 and PromethION 48 were introduced by Oxford Nanopore Technologies plc (UK) in January 2019. These systems provide modular high throughput, long read, and direct nanopore sequencing data. Thermo Fisher Scientific's Ion GeneStudio S5 System and Illumina's iSeq 100 are two more ground-breaking platforms that guarantee great sequencing efficiency at lower costs.

RESTRAINTS

- **End-user budget constraints in developing countries.**

Academic R&D in poor nations is primarily reliant on outside financing. Despite ongoing efforts by governments and private organisations to offer funding for research globally, many research and academic institutions suffer financial restrictions when it comes to the purchase and usage of cutting-edge and expensive equipment and technologies. NGS sequencers are still expensive even if NGS sequencing costs have decreased. The cost of the two most sophisticated sequencing platforms from Illumina, the NovaSeq 5000 and 6000, is USD 850,000 and USD 985,000, respectively. These sequencers are around 70% quicker than most of Illumina's current platforms, and they can be made even faster with system and software updates.

Another major competitor in the NGS market, Pacific Biosciences of California, offers the PacBio RS II for USD 750,000 and the Sequel system, its most recent sequencing platform, for USD 350,000. Even though low-cost sequencing platforms like the iSeq have entered the market, many end users in developing APAC and LATAM nations still find their price to be prohibitive. As a result, the adoption of related NGS products for metagenomics is being hampered by the limited use of cutting-edge technologies, such as NGS, in academic and research institutions in underdeveloped nations.

OPPORTUNITIES

- **NGS Data analysis using big data.**

The amount of data generated during whole-genome sequencing often ranges in the terabyte range. The management of such massive amounts of data is a top problem for NGS-based metagenomic sequencing end users. Due to inconsistent data formats and a lack of industry-wide standardisation for data output from various NGS platforms, data storage requirements can be rather complex. The yield of NGS runs has, however, been greatly boosted by the use of big data technologies and AI for NGS analysis and the management of workflows.

With improvements in sequencing technology, more data is generated during a sequencing run. Approximately 743 terabytes (743,000 gigabytes) of data are generated by the sequencing of a single human genome as of July 2017, compared to 16.2 gigabytes at the start of the Human Genome Project in 2001, according to a report from the National Human Genome Research Institute. Because the volume of generated genetic data exceeds the capabilities of human analysis, there is a chance to use cutting-edge computational techniques for evaluation and analysis. Accordingly, a number of businesses are integrating cutting-edge computational technology into their sequencing solutions. For example,

- Illumina (US) introduced Illumina Connected Analytics (ICA) in January 2021, a fresh and comprehensive bioinformatics tool for managing, examining, and exploring enormous amounts of multi-omics data
- In 2020, Illumina (US) introduced the TruSight Software Suite, which enables sample-to-report analysis for the diagnosis of genetic diseases,

offers a comprehensive solution, and provides insightful data through simpler genomic sequencing.

- The market for metagenomic sequencing will see significant growth as improved NGS solutions built on big data analytics and cloud computing are developed for handling, storing, and retrieving the massive amounts of data created.

CHALLENGES

- **Challenges associated with metagenomic NGS**

NGS has a lot of potentials, but there are still a lot of barriers to overcome before this technology is widely used in laboratories. Interpreting results, such as separating contamination and colonisation from actual infections, choosing and validating databases utilised for analysis, and forecasting antibiotic susceptibilities present significant problems. The need to remove enormous amounts of human nucleic acid during sequencing preparation and the post-analytic procedure in some circumstances can reduce the sensitivity in comparison to focused PCR approaches for many organisms, even if NGS is analytically more sensitive than typical culturing methods.

Given the greater analytical sensitivity of NGS compared to conventional culture methods, contamination of materials during specimen collection is a major concern. Every stage of the quality-control process, from determining reagent purity to determining sufficient genome coverage controls, needs to be supported by a validated process. To guarantee that high-quality and validated genomes are available with few database mistakes, bioinformatic quality controls are required. Most clinical microbiological laboratories do not have bioinformatics professionals on staff to analyse sequencing findings for each test, which is ideal. In order to guarantee that the results of the most recent NGSs are accurate and reliable, the Federal Drug Administration (FDA) worked with other federal agencies to curate a database called FDA-ARGOS (FDA-database for regulatory-grade microbial sequences). However, these resources need to be updated. Since the majority of the nucleic acids in clinical samples come from the host, the host genome predominates in sequence reads, which is another important NGS constraint. As a result, infections existing at a relatively low load may be harder to detect analytically. NGS testing could potentially play a significant part in the microbiological diagnostic workflow in the future as sequencing and

bioinformatic processing capacity advance. However, this technique is extremely complicated and has questionable therapeutic relevance in the current landscape of medical practice.

⇒ **Key players in the metagenomic sequencing market and analyze competitive developments undertaken by major players in the metagenomic sequencing market, which include product launches and enhancements; expansions; partnerships; collaborations and agreements.**

Table 4.2: key players operating in the metagenomics market

S. No.	Key Players
1.	Illumina, Inc. (US)
2.	Thermo Fisher Scientific, Inc. (US)
3.	Qiagen N.V. (Netherlands)
4.	PerkinElmer, Inc. (US)
5.	Oxford Nanopore Technologies (UK)
6.	Pacific Biosciences (US)
7.	BGI group (China)
8.	Psomagen, Inc. (South Korea)
9.	Eurofins Scientific (Luxembourg)
10.	Zymo Research Corporation (US)

Players in the global metagenomic sequencing market have employed various strategies to expand their global footprint and market shares. The key strategies adopted by the top players in this market have employed various strategies to expand their global footprint and market shares. The key strategies adopted by the top players in this market include product launches, expansions, partnerships, collaborations, agreements, and acquisitions.

Table 4.3: Strategic Overview For Key Players In The Metagenomics Market

Company Name	New Product Launches	Collaborations	Partnership
Illumina, Inc. (US)	Launched the TruSight Software Suite, a turn-key data analysis solution to accelerate and facilitate the adoption of whole-genome sequencing for the identification of genetic diseases.	Entered into a collaboration agreement with Roche to accelerate the availability of distributable NGS- based IVD tests on Illumina's diagnostic (Dx) sequencing systems.	Entered a 15-year partnership with QIAGEN to broaden the availability and use of NGS-based IVD kits, including companion diagnostics, for patient management.
Thermo Fisher Scientific, Inc. (US)	Launched ion torrent carrier seq ECS kit, an NGS- based solution for expanded carrier screening research.	Collaboration with AstraZeneca to codevelop NGS-based companion diagnostics.	Partnership with First Genetics JCS to develop NGS-based diagnostics in Russia.

Qiagen N.V. (Netherlands)	Launched QIAcube connect a next- generation automation solution for sample processing in research labs.	Collaboration with INOVIO expanded to develop NGS companion diagnostics for INOVIO'S VGZ-3100 for advanced cervical dysplasia.	Partnership with Verogen to offer solutions for human identification, including NGS.
Oxford Nanopore Technologies (UK)	Launched PromethION 24 and PromethION48. They offers high throughput, long-read, real- time, direct nanopore sequencing data.		
Pacific Biosciences of California, Inc. (US)	Launched the sequel II system. The system includes the new SMRT Cell 8M, as well as chemistry instrument control software, and the SMRT Link software package.		

Competitive Scenario

This segment studies the growth strategies adopted by market players in the last three years. Several players in this market have adopted various strategies to expand their global presence and increase their market share. Product launches, expansions and acquisitions are a few major strategies adopted by market players to grow in the metagenomic sequencing market.

Table 4.4: Product Launches

Month & Year	Company Name	Product Name	Product Type
April 2019	Pacific Biosciences of California, Inc. (US)	Sequel 2 system	System
June 2019	BGI Genomics (China)	BGI-Xome	Services
February 2020	Thermo fisher scientific, Inc. (US)	Ion-Torrent Carrier Seq ECS Kit	Kits
July 2020	Illumina, Inc. (US)	TruSight Software Suite	Software
October 2020	QIAGEN N.V. (Netherlands)	QIAseq Human Exome TR Insights Solution	Kits and software

Table 4.5: Deals

Year and Month	Development Type	Company 1	Company 2
2020 June	Acquisition	Illumina, Inc. (US)	BlueBee (Netherlands)
2021 January	Collaboration	Illumina, Inc. (US)	Helix opco llc (US)
2021 January	Collaboration	Oxford Nanopore Technologies, Ltd. (UK)	NVIDIA (US)
2021 July	Strategic Alliance	QIAGEN N.V. (Netherlands)	Sysmex Corporation (Japan)
2021 September	Collaboration	Thermo Fisher Scientific, Inc. (US)	AstraZeneca (UK)

Table 4.6: Expansions

Year and Month	Company Name	Development Type	Region of Expansion
November 2019	QIAGEN N.V. (Netherlands)	Expansion	US
October 2020	QIAGEN N.V. (Netherlands)	Expansion	US

Chapter 5 – Conclusion & Recommendation

One of the research fields with the quickest growth is metagenomics. For a better understanding of the connection between microbiota and host health or disease, it is necessary to investigate the human microbiome as an entire ecosystem. Because of this, robust strategies are needed to examine these ecosystems on a global scale, with metagenomic techniques being crucial for further research into the human microbiome. However, while interpreting the findings, it is important to take into account inter-individual variability, methodological bias, and sampling bias. Because it is realistic to expect that communities will differ based on the presence of inter-individual variations, standard operating procedures and meta-analysis studies are crucial for defining the average human microbiome.

A general and more balanced microbiota would be associated with biomarkers of wellbeing in the future thanks to this type of approach, or metagenomics. The relationship between ourselves and our microbiomes and the significance of this interaction for health can also be better-understood thanks to metagenomics.

As a way to identify pathogens in situations of suspected infection, metagenomic next-generation sequencing (mNGS) is becoming more and more accessible. High-throughput sequencing techniques are used in mNGS to evaluate the nucleic acid content of patient samples in order to find and identify microorganism DNA or RNA. This may result in a better ability to diagnose patients, although contamination and the finding of non-clinically significant organisms still raise questions.

The assessment and exploitation of microbial assemblages from harsh and inhospitable habitats, such as solfataric hot springs, hypersaline basins, and ice, were made possible by the advent of enhanced DNA isolation technologies, cloning tactics, and screening approaches. Environmental sequence data sets became more and more complicated with the introduction of next-generation sequencing techniques, which in turn sparked the creation of a number of bioinformatics tools for the analysis and comparison of these data sets with regard to taxonomic and metabolic diversity. More than 210 distinct metagenomes have been sequenced to this point from a wide range of habitats, including soil, the oceans throughout the world, the human gut, and faeces. Today, metagenomics is used in forensic or medical investigations. The Human Microbiome Project was established in 2009. The goal of this project is to map the microbial

populations related to the human gut, mouth, skin, or vagina. In addition, metagenomic methods have been used to investigate extinct animals like the woolly mammoth and Neanderthals. Improved integrated analysis techniques and extensive databases are required to fully utilise this wealth of knowledge.

To supplement DNA-based metagenomic analysis, studies of the gene expression and protein synthesis of microbial communities have arisen recently. Approaches like metatranscriptomics and metaproteomics may help us comprehend the functional dynamics of microbial communities. These methods hold great potential for improving the measurement and prediction of in situ microbial responses, activity, and productivity of microbial consortia when combined with metagenome DNA analysis. Additionally, investigations of the resulting extensive data sets offer a hitherto unheard-of potential to shed light on how microbial communities function in ecosystems and how evolutionary processes work.

References

1. Metagenomics [Internet]. Genome.gov. 2022 [cited 29 June 2022]. Available from: <https://www.genome.gov/genetics-glossary/Metagenomics>
2. Applications N. Why Metagenomics? [Internet]. Ncbi.nlm.nih.gov. 2022 [cited 29 June 2022]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK54011/>
- 3.
4. Thoendel M. Targeted Metagenomics Offers Insights into Potential Tick-Borne Pathogens. 2022.
5. Parry R, James M, Asgari S. Uncovering the Worldwide Diversity and Evolution of the Virome of the Mosquitoes *Aedes aegypti* and *Aedes albopictus*. 2022.
6. Batovska J, Mee P, Lynch S, Sawbridge T, Rodoni B. Sensitivity and specificity of metatranscriptomics as an arbovirus surveillance tool. 2022.
7. Metagenomics: Current Innovations and Future Trends [Internet]. Caister.com. 2022 [cited 29 June 2022]. Available from: <https://www.caister.com/metagenomics-advances>
8. Greninger A. The challenge of diagnostic metagenomics. 2022.
9. Metagenomics [Internet]. NGS Analysis. 2022 [cited 29 June 2022]. Available from: <https://learn.gencore.bio.nyu.edu/metagenomics/>
10. Applications N. Why Metagenomics? [Internet]. Ncbi.nlm.nih.gov. 2022 [cited 29 June 2022]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK54011/>