Module 2 Project Statement Initial Draft

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Article Summaries

Article #1: Ma, Z., Zuo, T., Frey, N., & Rangrez, A. Y. (2024). A systematic framework for understanding the microbiome in human health and disease: from basic principles to clinical translation. Signal Transduction and Targeted Therapy, 9(1), 237. [https://doi.org/10.1038/s41392-024-01946-6]

The article begins with a brief history of microbial research over the past 4-5 centuries. Antoni van Leeuwenhoek was the father of microscopy and credited with documenting microorganisms in the 1600s. After the discovery of the fundamental building blocks of life (DNA), the fields of genetics and microbiology both prospered. Currently, NGS and multi-omics have given rise to clinical and ecological use cases for identifying and understanding the microbial communities in various environments. One important area of study is the human microbiome, which can impact health and disease. Several projects including the Human Microbiome Project (HMP) and Integrative Human Microbiome Prject (iHMP), European MetaHIT project (Metagenomics of the Human Intestinal Tract), American Gut Project (AGP), Dutch Microbiome Project (DMP), have all added to the body of knowledge around Human microbiomes. Dysbiosis has become more popular in regards to health and aging and the term “hologenome” describes the human genome and the genetic content of microbiomes as a single entity. The researchers go on to discuss various studies involving small animal trials and how laboratory animals raised without microbes suffer in various physiological facets, such as issues with the cardiovascular system, digestive system, respiratory system, kidney function, metabolism, and immune system. The authors delve into how microorganisms, which include bacteria, fungi, archaea and viruses, have co-evolved with humans throughout time. Recognizable microbial signatures in humans have been identified at specific life stages (i.e. toddler to adolescent or adult to senior). Microbes are typically found on the outside or mucosal layers, not internally in the body (except the intestinal tract). However, recent studies have shown that microbes have been found in areas of the body that were historically thought to be void of any microbial inhabitants (i.e. liver or blood). Some studies have shown evidence that blood type may correlate to the microbiota found in a human. As the term “gut microbiome” has gained popularity over the past decade, the authors highlight how the human gastrointestinal tract houses a diverse community that performs a variety of tasks related to metabolism, which supplement the human body. Finally, the researches show how the human microbiome may be altered by the use of pharmaceuticals. Many pharmaceuticals have been shown to alter tissues in the human body, which then exhibit selective pressures on the microbial community; varying combinations of medications and doses are also a factor. Microbial organisms have the potential to enhance, diminish, or even cause harmful byproducts to occur from medications. This review provides a great foundation on the human microbiome and key areas of clinical interest that may benefit general understanding of the human microbiome or more specific relationships to disease.

Article #2: Tegegne, H. A., & Savidge, T. C. (2025). Leveraging human microbiomes for disease prediction and treatment. *Trends in pharmacological sciences*, *46*(1), 32-44.

Sequencing, the ability to identify segments of the genetic code (DNA), has opened up many new avenues of research. Tegegne and Savidge (2025) delve into modern bioinformatics approaches to handle microbiome data. High throughput sequencing (HTS) has emerged as a standard tool for microbial research. Combined with polymerase chain reaction (PCR), microbial communities analyses can be geared to more universal or specific approaches (whole genome). Metagenomic approaches, such as 16S rRNA sequencing, can cast a wide net, especially on rarer microbial taxa, however at the cost of shallower sequencing depth compared to whole-genome sequencing (WGS). Another benefit of WGS is the ability to identify bacteria, fungi, viruses and protists in a single sample. This level of sequencing can also benefit researchers, as gene function within these taxa can also be inferred, which can be useful in understanding areas such as metabolic pathways and antibiotic resistance. Metagenome-assembled genomes (MAGs) have become a popular next-step in identification by providing a greater level of certainty, especially when specific microbial strains may be drug-resistant. One example of strain-level identification is the determination if a patient patient is suffering from a Clostridoides difficile infection (CDI). Once verified, fecal microbiota transplants (FMT) can be achieved to provide the patient with an increase in microbial gut biodiversity. This is possible with WGS and strain-level identification. A recent method to increase sample resolution is through high-quality metagenome-assembled genomes (HQMAGs). HQMAGs are given unique identifiers that can then be used to determine if accurate matches are found within the dataset. If various datasets are combined for new analyses, the unique identifiers can be used independently of the dataset to allow for more comparisons. Before clinical significance can be obtained from microbiome samples, confidence in proper identification must be achieved through utilizing pipelines that provide accurate data.

Questions

1. Are there microbiome signatures common in certain diseases?
2. Can bioinformatics be used on large publicly available datasets to identify patterns of microorganisms and characteristics of a population?
3. Is there a link between populations with foods high in preservatives and certain microorganism selection?
4. Can antibiotic resistant strains be detected in patients to prevent the unnecessary administration antibiotics and ensure proper alternatives are used?
5. As microbial diversity appears to decrease in patients as they age, do Blue Zone residents (healthy aging populations) show greater microbial diversity compared to those in poorer health regions of the world?

Summary

The human microbiome has become a popular area of research over the past decade. As sequencing advancements have allowed for more novel studies, new clinical applications and questions arise. Many large publicly available datasets on the human microbiome are now available. This provides a great opportunity for datamining new microbial trends that may impact human health.