Project Statement Initial Draft (Individual)

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Part 1: Relevant Article Summaries

Article #1: Unlocking the Potential of the Human Microbiome for Identifying Disease Diagnostic Biomarkers

I chose this article to gain more background information regarding the human microbiome and current use of biomarkers for disease diagnosis. In the article the authors delve into the comparison of microbiomes to a "fingerprint". Everyone has a unique microbiome that is shaped by their age, genetics, lifestyle, and even environmental factors. This unfortunately creates a complex problem when it comes to trying to link microbiome biomarkers to specific diseases. Your microbiome is ever changing as are the symbiotic or pathogenic relationships contained in them. Human microbiota also plays a huge role in health and disease from homeostasis, immune response, to metabolism and more. It has a significant contribution to an individual's health and disease risk or even contraction. The authors mention that "host immunity might be closely related to the compositional and functional changes of gut flora" (Haijo et al. 2022). Biomarkers are classified as "a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention" (Haijo et al. 2022). It's noted that recent developments with machine learning and artificial intelligence have changed the way these biomarkers are used for detections of diseases and conditions. In the rational, identification of "Ideal biomarkers" is not easy so therefor, in combination with patient information such as metagenomics, disease classification is more accurate. There also have been a few important bacterial metabolites that have been identified as being potential biomarkers for human diseases summarized from data of the Human Metabolome Database (HMDB) version 5.0 as well as the Marker Database (MarkerDB). These bacterial metabolites include short-chain fatty acids (SCFAs), branched-chain amino acids (BCAAS), tryptophan and indole-derivative metabolites, trimethlyamine n-oxide (TMAO), imidazole propionate (ImP), bile acids, and lipopolysaccharides (LP)/endotoxin. Current evidence based research has shown links between diseases such as cancer and the human microbiome still in preliminary stages. Further research and development is necessary for identification of these predictive microbiome-based biomarkers. Those of which will lead to revolutionary treatment and diagnoses of conditions such as irritable bowel syndrome (IBS) and cancer. There is still a lot of work needed to continue facilitating this development of biomarker research.

Continued and expanded collaboration efforts such as open-source databases, and standardized testing methodologies are necessary for this to happen.

Article #2: Application of metagenomics in the human gut microbiome

When delving deeper into role metagenomics plays in the human gut microbiome, this article stood out to me. It's not just about how these concepts separately could relate; it's about how metagenomics is applied in the study of the human gut microbiome currently and how we can improve upon this single-omic approach to really get the full picture of gut microbiome importance in health and disease. The human gut microbiome has a large amount of research data already addressing the role it plays in human immunity, and metabolism, amongst other things. But it wasn't until recently (due to the development of PCR-denaturing gradient gel electrophoresis) that scientists fully understood how complex the gut microbial ecosystem really is. This is due to traditional culturing methods which cultivate only about 10-30% of gut microbiota (Wang et al. 2015). The authors talk about how this new PCR testing in conjunction with "shotgun metagenomics" reveals "who's there" in addition to "what can they do", such important questions that are on the verge of fully being answered. There are quite a few projects that have studied the intestinal microbiome such as MetaHIT and the American Human Microbiome Project who applied metagenomics to their study. This in-depth profiling has revealed postulations that the human gut microbiome consists of three enterotypes "*Prevotella, Ruminococcus and Bactericides* spp" (Wang et al. 2015). Other studies revealed that composition and diversity is affected by factors such as age, diet, location, and other lifestyle factors. Recently metagenomics has been on the forefront of development with "*Escherichia coli (E. coli)* being the most commonly used host for functional metagenomics" (Wang et al. 2015). The article then dives into recent developments in antibiotic-resistance , where some human commensal microbiota have antibiotic-resistance genes (ARGs) leading to human gut-associated resistome. Studies show that participants from France actually had significantly higher levels of ARGs than the samples from Scandinavian participants. Interestingly, it was understood that ARGs can actually be exchanged among gastrointestinal microbes during host stress. The application of metagenomics has revealed some of the functions of this dysbiosis including proteins secreated from and on the surface of Gram-positive bacteria in the human gut playing a role in immune modulation. The unfortunate thing is that there are limitations when applying metagenomics to the study of the human gut microbiome. Things like missing microbial expression, high costs, long time commitments, and the need for extremely high quality DNA samples. Actually, 50-90% of sequences are found to contain human contaminants.

Because methods arent standardized, its hard to compare data across studies as well. Much like the other aritcle, the authors note that in conjunction with other omics, the activity or gene expression of a microbial communtiy may be identified. Although, this will take again significant development of the other omic reference databases such as that of metatranscriptomics.

Part 2: Project Summary

In the articles I understood how metagenomics is integral for future study of human health and disease, even with its limitations. Recently (December 2025) a massive metagenomics dataset has been pusblished solving some of the previous issues such as uniform processing and clean, curated metadata. Implementing this, can antibiotic resistance or disease outcomes be predicted and treated?

Part 3: Project Guiding Questions

1. Creating a proof of concept tool has the ability to change disease and treatment modalities tremendously. Is it fesable to develop and implement such a tool without a large team to consistently maintain and update the underlying reference database?
2. Which metagenomic biomarkers of antibiotic resistance emerge under antibiotic pressure, and where do explooitable weaknesses exist within these mechanisms?
3. What vulnerabilities in resistance pathways could serve as targets for mitigaing ARG persistance in microbial communities?
4. Should scope be narrow for a specific disease when modeling a “proof of concept tool” for changes in microbiomes throughout disease states?
5. What is the most useful output for end users, disease similarity ranking, microbiome state maps, or biomarker feature highlights?

References: (APA FORMAT)

1. Hajjo, R., Sabbah, D. A., & Al Bawab, A. Q. (2022). Unlocking the Potential of the Human Microbiome for Identifying Disease Diagnostic Biomarkers. Diagnostics, 12(7), 1742. https://doi.org/10.3390/diagnostics12071742
2. Wang, W. L., Xu, S. Y., Ren, Z. G., Tao, L., Jiang, J. W., & Zheng, S. S. (2015). Application of metagenomics in the human gut microbiome. World journal of gastroenterology, 21(3), 803–814. https://doi.org/10.3748/wjg.v21.i3.803