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The Human Gut Microbiome: Relationships to Nutrition, Obesity, and Eating Disorders

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Abstract

In this brief communication, studies pertaining to the human gut microbiome were collected and condensed into key points. It was found that the human gut microbiome and human nutrition are correlated, with nutrition impacting the makeup of the gut microbiome and the gut microbiome influencing how an individual metabolizes nutrients. Following this, a link was also established between different gut microbiota characterizations, obesity rates, and eating disorder pathology. Ultimately, further research is required to develop therapies for these diseases, however there exists a solid foundation upon which to base these further explorations.

Keywords: Human gut microbiome; Human nutrition; Brain-gut-microbiota axis; Obesity; Eating disorders

Introduction

The goal of this literature review is to construct a comprehensive view of the relationship between the human gut microbiome, nutrition, obesity, and eating disorders. Many studies have been conducted examining the human gut microbiome, however its relationship with human nutrition and nutritionally derived diseases (obesity and eating disorders) has not been as comprehensively studied. With human patterns of food consumption changing dramatically over the past several hundred years, the way in which humans obtain and process nutrients has also changed. This shift is correlated with a rise in both obesity rates and eating disorders.

By studying the relationship between the human gut microbiome and human nutrition, a better understanding of how our diets, gut bacteria, and health are related may lead to strategies that help assuage the troubling rise in nutritionally related morbidities.

Background

Human nutrition has changed dramatically over the past several thousand years. For much of human history, nutrition has consisted primarily of that which could be obtained through hunting, fishing, and gathering. It wasn't until around 12,000 BCE when an unusually favorable shift in climate allowed the first permanent settlements to appear in the Eastern Mediterranean region of West Asia [1]. As humans shifted from nomadic hunter-gatherers to farmers, nutrition changed as well. Cultivating wild cereals and vegetables and raising livestock increased food security, leading to extended life expectancies and increased fertility.

The next notable shift in human nutrition came with the Industrial Revolution in the latter half of the 18th century [1]. New technologies allowed for revolutionary new ways of producing and preserving foodstuffs. Canning, particularly, introduced the idea of storing large quantities of food for long periods of time [1]. With this new epoch of food consumption, however, came a set of drawbacks. Additives intended to preserve food also compromised the nutritional viability of food, with many vitamins being lost during the canning process. A similar trend can be observed in subsequent centuries, with the advent of ready-made TV dinners in the 1900s, the introduction of fast food, and the popularization of prepackaged, highly processed food. Generally, though the industrialization of food production eased worries regarding food insecurity, it also introduced a great many issues in respect to the health of the general population. Increasing caloric density, food additives, and lack of nutrients in the highly processed foods that are so commonplace today has led to a litany of nutrition-related illnesses and diseases.

Currently, around 42% of Americans are overweight or obese, an increase from 20% in the 1960s ("Obesity and Overweight"). An estimated 9% of Americans suffer from some sort of eating disorder, though this number is likely much higher in reality due to lack of diagnoses and reporting. Though both the medical field and the food science industry have made great strides over the years, research into the human gut microbiome and its interactions with nutrition, body weight, and nutritionally-related diseases is still a relatively new area of study.

Though food production and patterns of consumption has changed rapidly over the past several hundred years, human biology and the mechanics of the gut microbiome remain largely unchanged. This paper seeks to characterize the human gut microbiome and analyze how these microbiota interact with nutrition, obesity, and eating disorders in the modern consumer.

General Characterization of the Human Gut Microbiome

The human gut microbiome is not well-researched, however there does exist a general picture of its composition. It has been theorized that the human gut microbiome can be roughly categorized into three distinct enterotypes [2]. These enterotypes seem to be independent of geographic location, age, sex, and body mass index. The existence of such distinct populations of gut microbiota presents the possibility that, depending on the characterization of an individual's gut

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bacterial composition, he or she might respond differently to diet and pharmaceutical treatment. This theory remains controversial, but does provide valuable insight and framework when discussing a general characterization of the human gut microbiome. Furthermore, as will be later discussed, studies have been conducted across a wide range of human gut microbiomes that support this theory of enterotypes.

Metagenomic studies sequencing 1511 reference genomes has given researchers a clearer view of the makeup of the human gut microbiome. In a more recent study in 2013, researchers [2] mapped 39 human gut microbiome samples from 6 different nationalities to these reference genomes to construct phylogenetic sequences of the bacterial makeup (Figure 1). The results of this genetic mapping allowed researchers to confirm that the microbiota contained within the 39 samples matched previously theorized homologous species of bacteria [2].

Generally speaking, bacteria appear within the gut microbiome as either high abundance or low abundance as a result of environmental pressures to survive. Bacterial species with high abundance typically carry out more robust molecular functions than their less abundant counterparts, although there are a few exceptions to this rule [2]. Importantly, though, abundant bacterial strains within the gut microbiome carry out important biological functions (Figure 2), which will be relevant in discussions pertaining to human nutrition, obesity, and eating disorders.

Though the human gut microbiome is incredibly diverse, comprised of an estimated 300 to 500 bacterial species, there exist repeated clusters of bacterial species that can be categorized into enterotypes (Figure 3). These enterotypes are characterized by repeated clusters of certain bacterial strains, and, though there is not a sharp delineation between

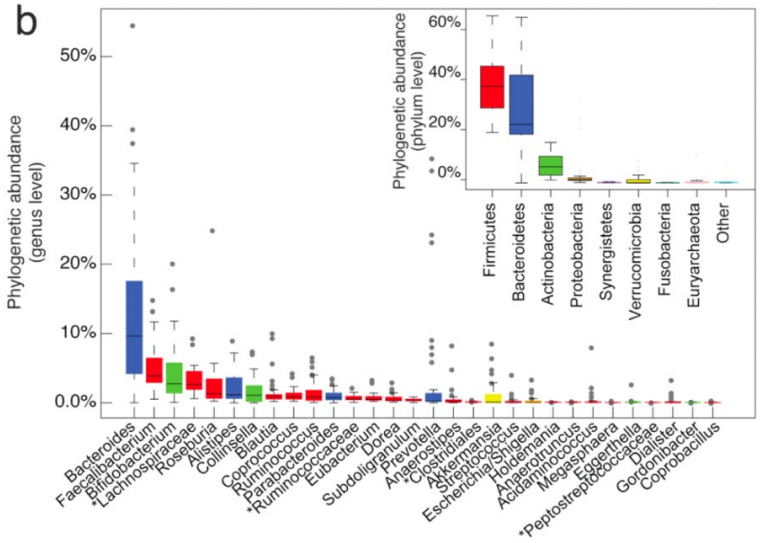

Figure 1: Phylogenetic abundance of the 30 most abundant bacterial species in the human gut microbiome (Arumugam et al. [2]).

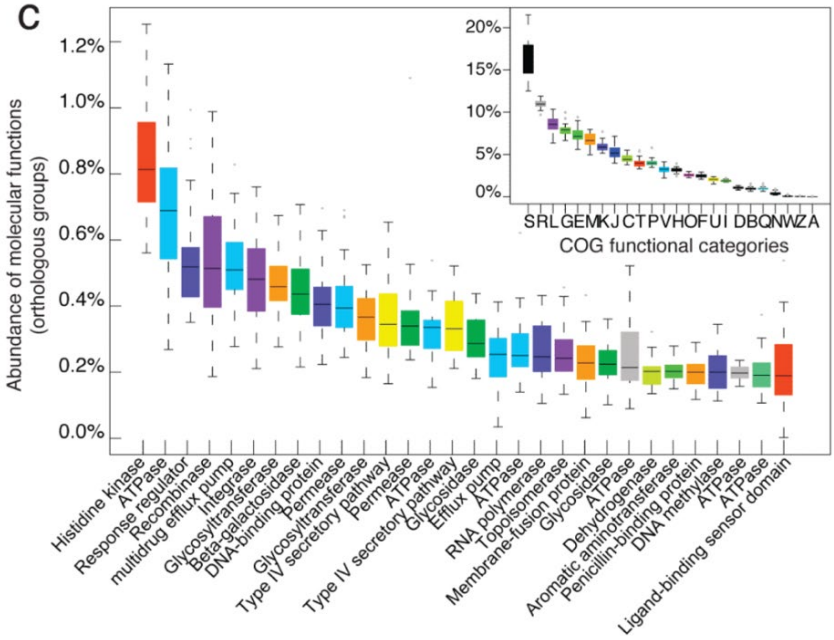

Figure 2: Functions of bacterial species. Functions can be matched to bacterial species in Figure 1 via color-coding (Arumugam et al. [2]).

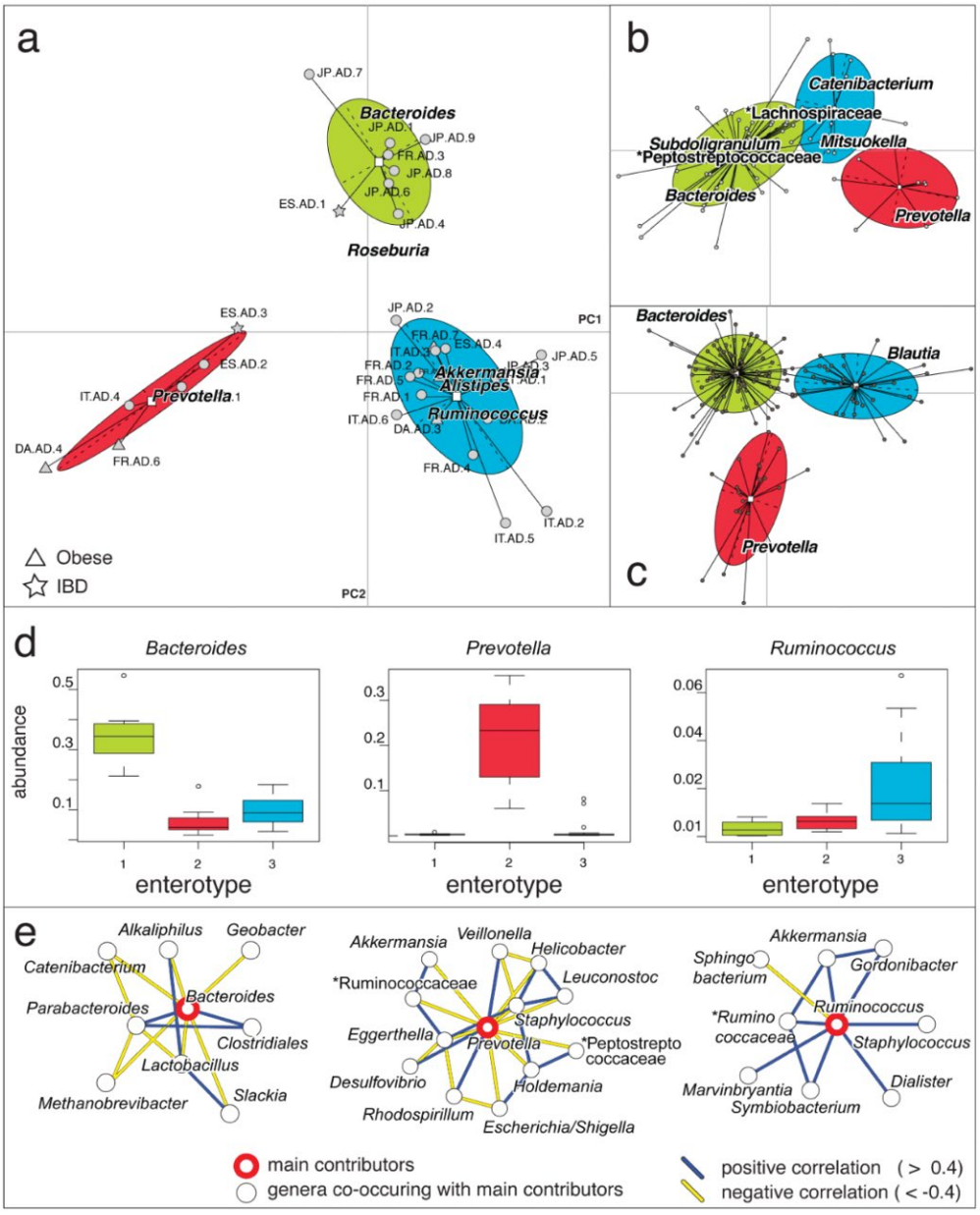

Figure 3: Phylogenetic characterization of the three enterotypes of the human gut microbiome (Arumugam et al. [2]).

the three enterotypes, there are functional differences that can be observed across them.

The enterotypes can be categorized by the relative abundance of dominant bacterial species (Figure 3). Enterotype 1 has high abundance of Bacteroidetes species, which are specialized processors of polysaccharides and proteins [2]. For this reason, individuals with enterotype 1 are especially efficient at extracting energy from carbohydrates and proteins. Enterotype 2 is characterized by a high abundance of Prevotella, whose function is to degrade mucin glycoproteins in the mucus lining of the gut [3]. After degradation, mucin oligosaccharides can then be used as an energy source for other gut-bacterial species. Enterotype 3 is abundant in Ruminococcus species, in particular, the firmicutes species, which is classified as another mucin glycoprotein degrader [2]. This genus is also densely populated with sugar membrane transporters which may help the gut microbiome to more efficiently process saccharides. There does exist some debate regarding whether this third enterotype ought to be included in discussions regarding human nutrition, as the functional differences are most stark between enterotypes 1 and 2 [4]. Thus, it is still a topic of debate of whether this so-called third enterotype ought to be reclassified into either Bacteroidetes or Prevotella enterotypes based off of the relative abundance of these two species.

The functional differences between each of the three enterotypes suggests that individuals may have different pathways of nutrient absorption depending on the clustering of their gut microbiome. For these reasons, nutrition and addressing nutritionally-related diseases and disorders may need to be adjusted depending on the individual and their gut microbiome.

Nutrition

The human microbiome, while internally regulated and compelled to maintain homeostasis, is influenced by a number of external factors. Most relevant among these factors is nutrition – namely, an individual's dietary choices. This interplay goes both directions, with gut microbiome metabolites such as bile acids playing important roles in regulating metabolism.

Though diet is highly variable depending on region, culture, socioeconomic status, and personal proclivities, most studies involving diet and the human gut microbiome divide diet into broad categories – the Mediterranean diet, the Western diet, high fat diets, high fiber diets, to name some examples. In other cases, studies will focus on specific nutrient intake, for example examining the effect of each macronutrient on the gut microbiome. This section of discussion will adhere to these categorizations when discussing variation in diet and nutritional patterns.

Nutritional influence on the gut microbiome begins very early in life, with some studies suggesting that maternal diet may affect her fetus' gut microbiome. In a review published in The British Journal of Nutrition by authors [5], the authors identified two studies linking maternal diet, mode of delivery, and infant gut microbiota. In one study examining the difference between high-fat (43.1% fat intake, experimental) and lower-fat (24.4% fat intake, control) maternal diets, researchers found that Bacteroidetes abundance was inversely proportional to fat intake (Figure 4). The pattern observed here persisted from birth to six weeks of age, after which observation ceased. This relationship may suggest that prenatal consumption of fats may influence an individual's gut bacterial enterotype later in life. In another study, researchers found a positive correlation between fish intake (a hallmark of the Mediterranean diet) and Streptococcus species in infant stool. Though these studies were limited in scope, there is evidence to suggest that manipulating maternal diet may influence infant gut microbiomes.

More robust studies exist that draw a connection between adult dietary choices and the gut microbiome. In a paper published in 2018, researchers [6] investigate the relationships two enterotypes (Bacteroidetes dominant [labeled B-type in the study], and Prevotella dominant [labeled P-type]) with varying diets in an effort to gain further understanding of personalized nutrition. In this longitudinal Danish study, participants were divided into B-type and P-type groups, and asked to follow either a "new Nordic diet" (NDD) or an "average Danish diet" (ADD). NDD participants were prescribed a high-fiber diet, while ADD participants followed a Western diet, characterized by high levels of fat and carbohydrates.

After 26 weeks of dieting, P-type NDD followers lost, on average, 3.5 kg more body weight than their ADD counterparts. For B-type participants, levels of weight loss were similar across both diets (Figure 5). These results indicate that dietary fiber plays a much more important role in regulating body weight in individuals with high levels of Prevotella species, suggesting a Prevotella-dominant specified response to dietary fiber. Researchers believe this is due to increased efficiency of the enzymatic response of P-type individuals for dietary fiber digestion, as well as an improved glucose metabolism in the presence of high levels of fiber.

Interestingly, it seems that, for P-type individuals, dietary fiber factors into not only weight loss, but also the maintenance of body weight. After 26 weeks, all participants were asked to follow an NDD diet. P-type individuals' body weights stabilized at a lower point than their starting weight, while B-type individuals gained weight relative to their starting weight.

The interaction between dietary fibers and P-type individuals is reliant upon the products of Pervotella fermentation. Upon bacterial fermentation, short-chain fatty acids (SCFAs) are produced and are specific to the bacterial strain. Pervotella species are especially prone to producing the SCFA propionate in the presence of dietary fibers. Propionate has been shown to induce weight loss by increasing the amount of peptide YY and glucagon-peptide 1, both of which are appetite inhibitors [7].

This interplay also suggests that early dietary habits may nudge an individual towards one enterotype or the other. Individuals that regularly consume high levels of animal fats and proteins in early life are often associated with the Bacteroidetes enterotype, while individuals with diets high in vegetables, fruits, and dietary fiber often have a gut microbiome consistent with the Prevotella enterotype [4]. Studies have shown that while an individual's enterotype is often "set" between 9 and 36 months of age, shifting dietary habits later in life are not enough to cause a shift in enterotype.

In a study conducted in 2011, researchers [8] subjected 98 subjects to a 10-day controlled feeding where they were subjected to either a high fat/low fiber diet or a high fiber/low fat diet. Each subject's microbiome was phenotyped using 16s DNA tags and clustered, where they fell into three distinct groups representing three enterotypes. Aside from a rapid change in microbiota one day after the beginning of the study, all subjects stayed within their initial clusters, indicating that short-term dietary changes are not enough for an individual's gut microbiota to shift enterotypes (Figure 6).

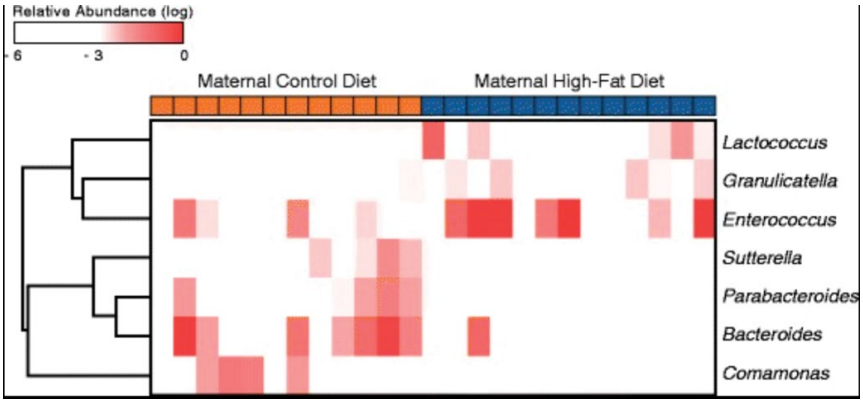

Figure 4: Relative abundance of bacterial species in infant stool (Maher et al. [5]).

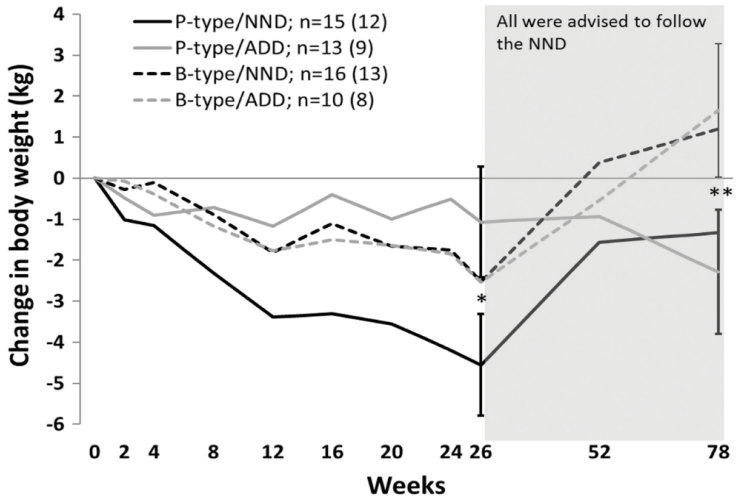

Figure 5: Weight loss of P- and B-type individuals following specified diets (Christensen et al. [6]).

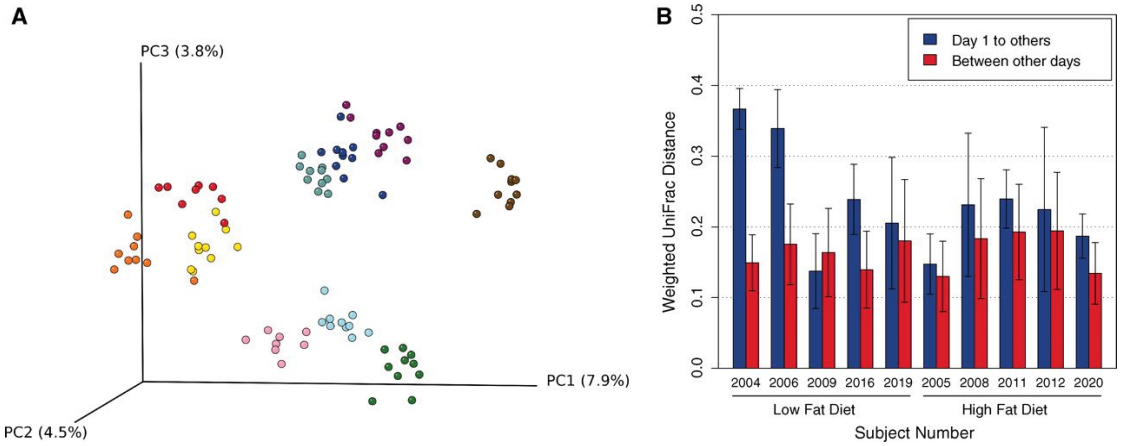

Figure 6: Results of 10 day controlled-feeding experiment (Wu et al. [8]).

Furthermore, a study conducted in 2018 by researchers [9] has indicated that, even after long-term dietary shifts, the gut microbiome tends to revert back to the enterotype established early in life. This longitudinal study recruited 10 volunteers to travel from Beijing to Trinidad and Tobago, where they stayed for six months. Fecal samples were taken from the volunteers at 6 stages: pre-travel (T1), during travel (T2, T3, T4), and post-travel (T5 and T6). Researchers found that the human gut microbiome can be described as "bidirectionally plastic", with volunteer's gut microbiomes changing drastically during their stay, then reverting back to their pre-travel microbiomes one month after returning to Beijing (Figure 7). This plasticity was not dependent on the individual's enterotypes.

One important caveat to this discussion is that, as the industrialization of food has increased and human nutrition becomes more reliant upon processed foods, overall gut microbiota diversity is decreasing. Over time, more individuals are presenting with Bacteroidetes phenotypes, which are less abundant in overall bacterial species than other enterotypes. It is theorized that Bacteroidetes-dominant individuals are less resilient to the rapid environmental changes brough on by the industrialization of foodstuffs due to their relative lack of microbiodiversity. This wide-scale shift in gut microbiota will be especially important as the discussion turns towards the interactions between the human gut microbiome and obesity.

The Human Gut Microbiome and Obesity – Brain-Gut-Microbiome Axis

Obesity is a complex and multifaceted issue, with factors such as mental health and socioeconomic status playing major roles in obesity rates. Furthermore, as food has trended towards becoming more accessible, nutrient-dense, and highly palatable (i.e. containing higher levels of salt, sugar, and fat), the biological imperative to 1) store body fat and 2) consume nutrient-dense foods has contributed to pushing obesity rates upwards. In the scope of this paper, however, obesity will be discussed as the result of hedonistic eating patterns, interactions between the gut microbiome, the brain, and the signaling pathways implicated in feelings of hunger, reward, and satiety.

Important to the discussion surrounding the relationship between the gut microbiome and obesity is an understanding of the brain-gut-microbiome axis and its role in regulating body weight. At a basic level, body weight is regulated by a balance of orexigenic (appetite-stimulating) and anorexigenic (appetite-inhibiting) signaling pathways [10]. Within these pathways are a myriad of signaling molecules, many of which are produced in the gut (Figure 8). In individuals with

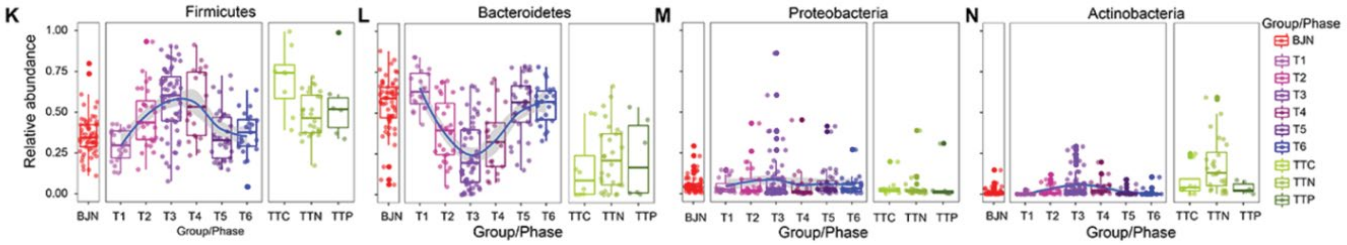

Figure 7: Results of longitudinal travel study (Liu et al. [9]).

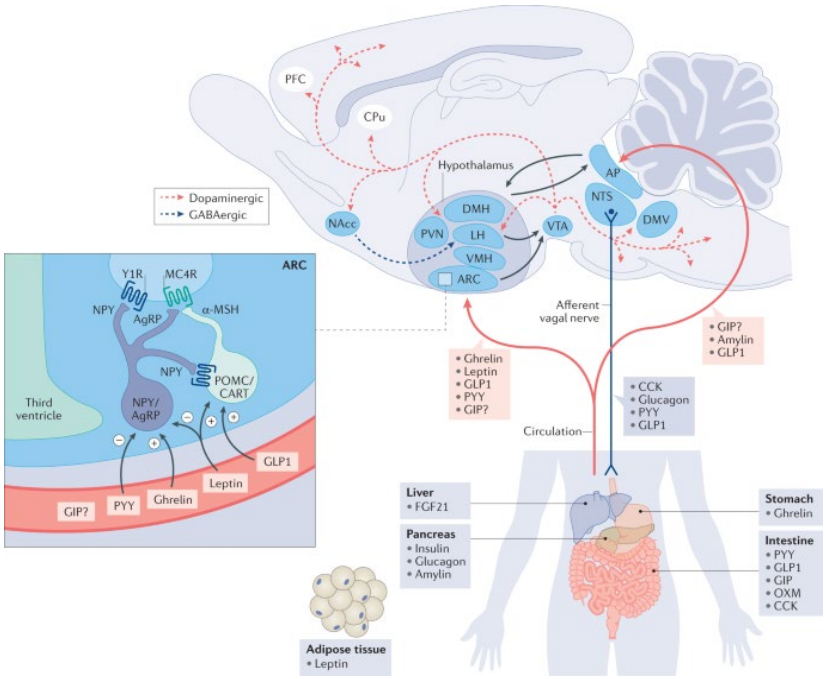

Figure 8: Signaling pathways in regulation of body weight and appetite (Muller et al. [10]).

healthy eating patterns, these two signaling pathways work together in homeostasis to maintain body weight. However, in instances of obesity, an individual may engage in hedonistic eating patterns, overriding satiety cues and continuing to consume highly-palatable foods even after energy requirements have been met [11].

Key orexigenic hormones include ghrelin and insulin, while anorexigenic signals include peptide tyrosine tyrosine (PYY), glucagon-like peptide 1 (GLP1), and leptin. Short-chain fatty acids (SCFAs) have also been implicated in anorexigenic signaling [12].

Ghrelin, a well-known appetite-stimulating hormone, is secreted in the stomach and travels through the bloodstream where it binds with growth hormone secretagogue receptors (GHSRs) in the hypothalamus. Upon binding, appetite is stimulated and one is cued to seek food [10]. Insulin, similarly, stimulates appetite upon secretion by beta-cells in the pancreas. Carried by the bloodstream, insulin binds to insulin receptors on cells and triggers an influx of glucose [10]. This leads to heightened sensations of hunger, and an increase in the drive for an individual to seek out sucrose for consumption.

Conversely, hormones PYY and GLP1 reduce appetite. PYY, upon cleaving into its active form, agonizes neuropeptide-Y type 2 receptors (Y2R) which are located in the ARC in the hypothalamus [10]. These receptors are implicated in dopaminergic signaling pathways, and stimulation of them leads to feelings of satiety, thereby decreasing food intake. GLP1 is secreted by the intestine, and binds to GLP1 receptors in the ARC. This causes a cascade of effects (Figure 9), ultimately resulting in a reduced appetite [10]. SCFAs are also becoming increasingly relevant in discussions of the BGM and body weight regulation, as recent studies have shown that increased production of SCFAs can stimulate the production of GLP1 and PYY [7].

The Gut Microbiome and Obesity – Bacterial Species

One heavily dominant theory surrounding the makeup of the gut microbiome and its relationship to obesity revolves around the Firmicutes to Bacteroidetes ratio (F/B ratio). In a landmark study conducted by [13], researchers discovered that mice with a higher F/B ratio had higher rates of obesity than mice with lower F/B ratios, independent of food consumption and activity levels. Upon investigation, if was found that the obese mice were able to extract an additional 150 kcal of energy from the food they were consuming than their lean counterparts.

Following this study, [14] expanded their investigation to include the human gut microbiome. A sample of 12 obese people was randomly allocated to either a low fat group or a low carbohydrate group, with both groups being calorie-restricted. The participants were subjected to 16s RNA sequences in order to characterize their gut microbiome, and, remarkably, each member of the study were Bacteroidetes and Firmicutes dominant. This observation lends credence to the link

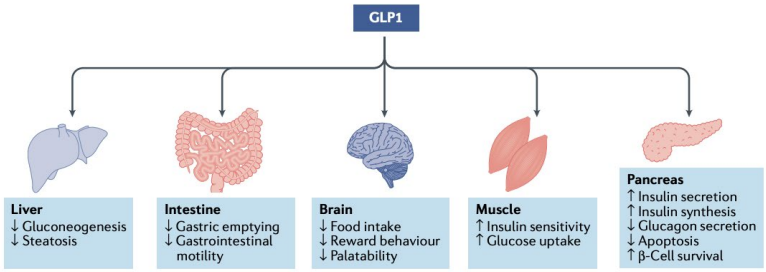

Figure 9: Effects of GLP1 binding to GLP1R (Muller et al. [10]).

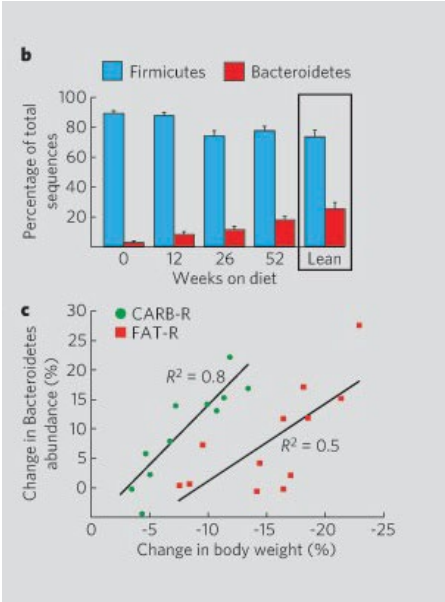

Figure 10: Bacterial population and body weight changes in obese participants following a one-year calorie deficit (Ley et al. [13]).

between rising obesity levels and decreasing diversity amongst human gut microbiomes, particularly if the two-enterotype model is followed rather than the three-enterotype model. Furthermore, each individual had a relatively high F/B ratio, supporting the previous study's findings.

After one year following this diet, participant's F/B ratio decreased, with Bacteroidetes populations increasing as body weight decreased (Figure 10). This negative correlation was independent of the specific diet the participants were following, although the increase of Bacteroidetes was dependent on a higher percent body weight loss in the low-carbohydrate group than the low-fat group.

Researchers attribute this relationship between gut microbial species and body weight largely to the metabolism of indigestible polysaccharides. Gut microbiota are responsible for metabolizing indigestible polysaccharides, for example, cellulose and resistant starch, and produce SCFAs – primarily propionate, acetate, and butyrate - as a byproduct of fermentation. These SCFAs, as previously mentioned, stimulate PYY and GLP1 hormones, reducing appetite. Therefore, individuals who follow and have followed a high-fiber diet may see a reduction in weight loss. This is consistent with the data suggesting that individuals who consume high-fiber diets early in life are predisposed towards the Prevotella enterotype, which may shed light on why the obese patients in the 2006 study were overwhelmingly the Bacteroidetes enterotype.

An interesting aside to this discussion is that obese individuals are actually reported to have higher levels of SCFA in their feces, as well as higher levels of ethanol in their breath than their lean counterparts [12]. This indicates and alternative pathway of microbial metabolism, possibly causing higher levels of energy harvest from food. This would decrease the metabolism of SCFAs, leading to their expulsion in feces. The relationship between the gut microbiome, SCFAs, and obesity is still tenuous, as researchers are still debating what, if any, correlation the three have. However, enough evidence exists to warrant further investigation.

Overall, the characterization of the gut microbiome in obese vs. lean individuals comes down to microbiodiversity, with a host of downstream effects (Figure 11). Individuals who follow high fiber, high nutrient diets (lean) have higher levels of microbiodiversity than individuals who follow low fiber, low nutrient diets (obese). As a result, obese individuals have lower levels of fiber metabolism (possibly leading to decreased anorexigenic signaling via SCFAs) [10].

Reduced diversity in gut microbiota is associated with a thinner gut mucosal membrane, resulting in a phenomenon described as "leaky gut syndrome". When the mucosal membrane becomes too thin, it induces a state called metabolic endotoxemia, wherein bacterial toxins typically contained in the gut enter the bloodstream [10]. While leaky gut syndrome is under debate as an actual disease, a decrease in gut mucosal

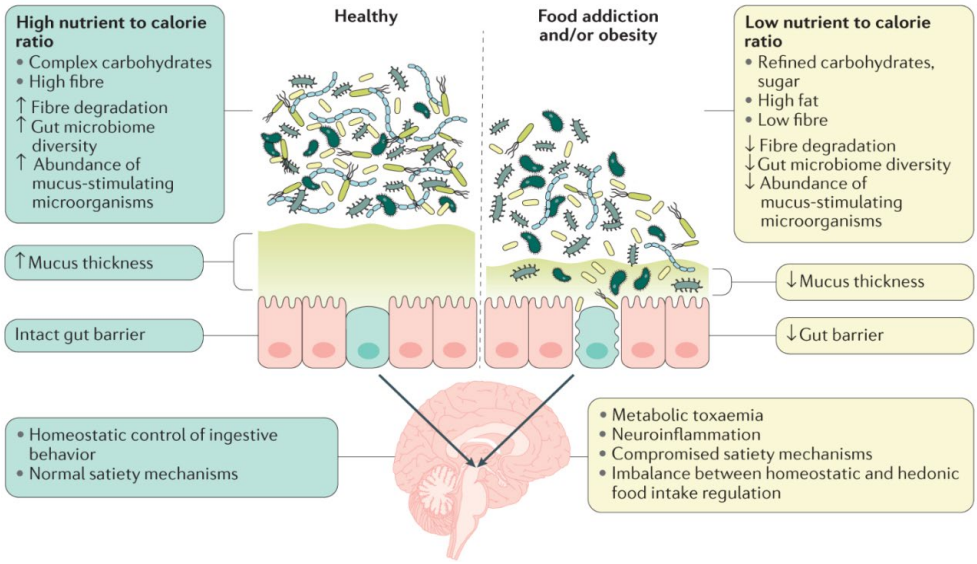

Figure 11: Downstream affects of low nutrient, low fiber diet on microbiota diversity (Gupta et al. [11]).

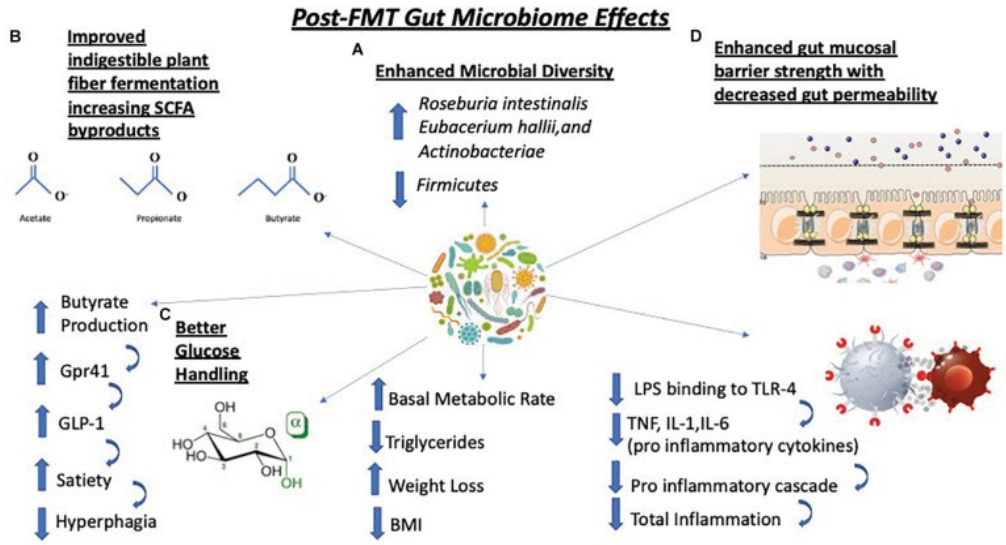

Figure 12: Results of FMT based on small clinical trials (Napolitano and Covasa [15]).

linings has been associated with elevated levels of lipopolysaccharides and inflammatory cytokines in the blood. This state, called metabolic endotoxemia, is associated with obesity by reducing insulin sensitivity and satiety signals.

Several therapies for obesity are in development targeting the BGM, including synthetic analogues for the aforementioned PYY and GLP1 hormones [9]. Another avenue of treatment is fecal microbiota transplantation (FMT). A number of small-scale trials in FMT therapies has shown that, by transplanting microbiota from a lean subject to an obese subject, the obese subject's physiology altered to match that of the lean donor [15]. These physiological adaptations include a thickening of the gut mucosal layer, an increase in SCFAs, increased fermentation of fiber, enhanced microbiota diversity, and an increase in basal metabolic weight (Figure 12). Though early stages show promising results, these changes were not long-lasting, with all physiological adaptations not appearing 18 weeks post-transplant. Despite the short-term nature of these effects, however, there is continuing research into whether FMT therapies, in conjunction with lifestyle changes and other medications, may be a viable treatment for obesity.

The Gut Microbiome in Eating Disorders

Eating disorders are another multifactorial issue, and range drastically in symptoms and severity. The three most commonly recognized eating disorders include anorexia nervosa (AN) – characterized by restrictive eating patterns, bulimia nervosa (BN) – characterized by periods of binge-eating followed by purging, and binge-eating disorder (BED) – an extreme of hedonic eating patterns, wherein the subject uncontrollably eats large amounts of food in a short time. According to a report published [16], AN is the only eating disorder to date that has been investigated in conjunction with the gut microbiota.

A number of studies have been carried out to investigate the relationship between the gut microbiome and restrictive eating disorders. The first major study in this arena was conducted in 2009

by researchers [2], in which they established through RT-PCR that anorexic patients had higher levels of Methanobrevibacter smithii than healthy individuals. M. smithii is a known methanogen, responsible for converting CO_2 to CH_4 in the presence of elemental hydrogen. Excess amounts of methane gas slows intestinal function, causing intestinal discomfort and constipation [17- 21].

Following this study, researchers sought to expand the scope of their investigation, sequencing the entirety of the 16s rRNA genome of AN patients and healthy patients. Stool samples were collected from patients suffering from anorexia nervosa at two separate times: T1 (n=16), collected from patients within an inpatient program, and T2 (n=10), collected from patients after discharge from the inpatient program. At T1, the average BMI of the patients was 16.2 kg/m^2, while at T2 the average BMI had increased to 17.4 kg/m^2. A healthy control group was used as a point of reference, with the average BMI of the group being 21.5 kg/m^2.

It was found that AN patients, both at T1 and T2, had significantly lower levels of microbial diversity than the healthy control group. The samples taken at T2 had a slightly increased level of microbial diversity, indicating that the biodiversity of the microbiome increased with weight restoration in AN patients (Figure 13). Researchers theorize that reduced diversity in the gut microbiome may propagate malnutrition as bacteria adjust to operating in a nutrient-deficient system. This suggests that lower levels of microbial diversity is implicated of the pathology of AN, and may help future investigations into the treatment of AN [22-26].

Patients' moods were also assessed throughout the experiment using the Beck Depression Inventory. It was found that depression levels were negatively correlated with degree of microbial diversity (Figure 14). These findings support the theory of the existence of a BGM axis, though there does exist debate regarding whether bacterial species directly influence feelings of depression and anxiety.

Much of the research regarding eating disorders and the BGM axis focus primarily on the effect of AN pathogenesis on the makeup of the gut microbiome, with most findings concluding that, though malnutrition, the biodiversity of the gut microbiome is compromised. This worsens the symptoms of AN, leading to a cycle of decreased gut microbiota diversity enhancing both the effects of malnutrition as well as the psychological factors contributing to the development of the eating disorder. Little research exists to establish a link between

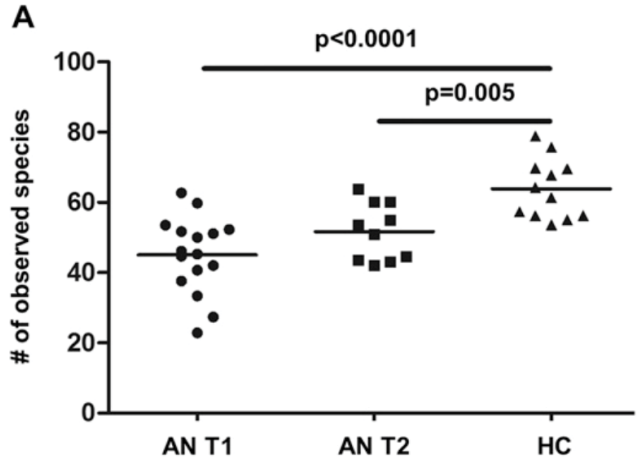

Figure 13: Bacterial diversity among AN patients and healthy controls (Armougom et al. [17]).

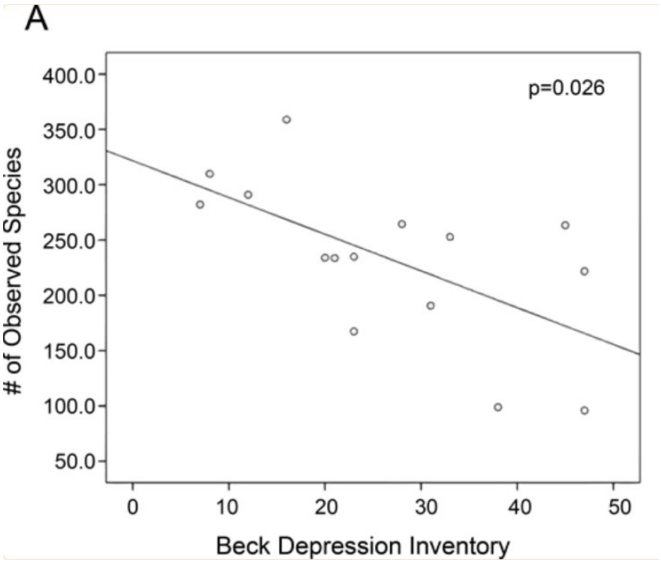

Figure 14: Relationship between bacterial diversity and feelings of depression among AN patients (Armougom et al. [17]).

bacterial makeup and predisposition towards the development of AN, an interesting contrast with the studies regarding the relationship between the gut microbiome and obesity.

Discussion

Throughout this literature review, over 50 papers, paper reviews, and journal articles were reviewed to construct a narrative outlining the relationship between the human gut microbiome, nutrition, obesity, and eating disorders. Of these papers, 31 were selected on the basis of relevance, determined by reading through abstracts, discussions, and conclusions. While the research regarding the human gut microbiome is somewhat fragmented, common threads throughout the studies were identified, with particularly relevant conclusions being referenced directly in the literature review. Though there exists disagreement amongst researchers regarding the human gut microbiome, it can be asserted that the gut microbiome does, in fact, influence nutrition, obesity, and eating disorders.

The human gut microbiome is relatively well characterized in that a basic understanding of the bacterial species present in the gut has been established. Through various experiments sequencing the human gut microbiome, researchers have been able sequence and identify abundant bacterial population species. From these sequences, several repeated clusters of bacterial species has been observed across populations, leading researchers to develop a theory of enterotypes.

Enterotypes have been the subject of debate since their proposal. Because the boundaries between enterotypes are not clearly defined, it is difficult to determine which patterns of clustering warrant categorization into a unique enterotype. This makes it difficult to find cohesive conclusions across different research papers, as different researchers emphasize different enterotypes. Furthermore, the role of enterotypes and their usefulness in providing biomarkers for individuals' propensity towards obesity and ideal nutrition habits is also under debate, with many researchers opting instead to focus on specific abundant species in the gut microbiome. For example, in early obesity studies, the ratio of *Firmicutes* to *Bacteroidetes* was emphasized, rather than a specific enterotype. Despite the uncertainty surrounding this enterotype paradigm, however, it does provide useful framework in

understanding how bacterial species influence nutrition.

In addition to modulating nutrition and metabolism, the gut microbiome may also, itself, be influenced by an individual's dietary choices. Several studies have indicated that high-fiber diets early in life may predispose an individual towards a *Prevotella* phenotype. An arguably more practical discovery are studies that suggest that later changes to diet may temporarily change the gut microbiome. This particular area of research is an opportunity for further investigation, as the implications of consciously modulating the gut microbiome may have useful therapeutic effects.

The discussion surrounding obesity and its relation to the gut microbiome relies heavily on the concept of a brain-gut-microbiome axis. This idea is another that is under debate, however enough studies exist that support the existence of crosstalk between the brain, the gut, and the microbiota within that this is a reasonable framework to work within. Studies relating bacterial species towards obesity rate primarily focus on the F/B ratio, with studies examining the effect of bacterial enterotypes on obesity in human subjects being largely inconclusive. Several studies have established a relationship between a lower F/B ratio and a lower rate of obesity in humans, however the bulk of the research into bacterial species and their influence on obesity rate has been conducted on animals. This, again, is another area for further research.

Therapies targeting obesity through the gut microbiome are another point of interest, with especially promising results coming from FMT treatments. This suggests that by altering the gut microbiome, less-invasive treatments for obesity may be in the near future. For this reason, researchers are continuing to examine the relationship between the gut microbiome and body weight. Future studies, especially examining the longitudinal effects of FMT, may open new pathways for obesity treatment.

The final area of interest for this literature review was the relationship between the gut microbiome and eating disorders. Research surrounding eating disorders, by and large, focuses on the psychological aspect of these diseases. The link between eating disorder and the gut microbiome is only in its infancy, with most studies focusing primarily on anorexia nervosa and its effects on the gut microbiome. For these reasons, the role of the gut microbiome in the pathology of eating disorders is the least robust topic discussed in this literature review. In particular, research into other eating disorders is required and may be helpful in the treatment of eating disorders. Furthermore, the relationship between the gut microbiota and the psychological symptoms of eating disorders is another area where research is lacking. Though it can be observed that lower diversity in gut bacteria is correlated with higher feelings of depression and anxiety, this relationship has not been researched to the point where reliable therapies targeting it have been developed.

Conclusion

Throughout the course of this literature review, I was able to construct a somewhat cohesive narrative of the relationship between the gut microbiome, individual nutrition, obesity, and eating disorders. I also found that though many studies have been conducted on this topic, research remains largely inconclusive. Though many robust theories have been developed on the topic of the gut microbiome, including the existence of enterotypes and a brain-gut-microbiome axis, there is still some question surrounding the extent to which these influence the way in which humans practically engage with nutrition. Much of the research into the gut microbiome and its relationship with nutrition has been conducted in animal studies, in which researchers were able to control for confounding variables. However, humans and their relationship to food is multivariable and depends largely on factors such as location, socioeconomic status, psychological state, and learned behaviors. These factors are difficult to control for, making investigations into the human gut microbiome somewhat nebulous.

Despite these difficulties, however, I feel there are several areas where further research can be conducted to better establish our understanding of the human gut microbiome. Principal among these topics is the correlation between gut bacteria diversity and eating disorder pathology. Though many therapies exist for eating disorders, most focus on psychological treatment and treatment for pressing medical issues. However, the research that exists on the topic of eating disorders and the gut microbiome suggests that by exploiting this relationship, additional modes of therapy may be developed.

The human gut microbiome is a complex and intensely interesting subject. Conducting this literature review gave me a better understanding of the relationship between the gut microbiome and nutrition, and helped me contextualize many of the microbiology concepts I have learned throughout my coursework.

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