Link between Gut Microbiota and Obesity: Effects of Dietary Fats

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INTRODUCTION

“You are what you eat.” This phrase becomes more profound as obesity becomes increasingly recognised as one of the significant health problems that plague society (Nyberg et al., 2018). Obesity increases the risk of heart diseases, diabetes, stroke, asthma, cancer, as well as several other diseases (Guh et al., 2009; Lauby-Secretan et al., 2016). In Malaysia, 33.4% of her 32 million people are overweight while 30.6% are obese (Institute of Public Health, 2015).

Many factors contribute to the risk of obesity. Two of the most significant factors are living a sedentary lifestyle and having an imbalanced diet consisting of processed food and food high in saturated animal fats, refined sugar and salt (Dao and Clément, 2018).

Part of the food that we consume is taken up by the microbiota (gut bugs) that inhabits our intestines. The microbiota is a complex community made up of bacteria, viruses and fungi which form a symbiotic relationship with us (Collins, 2014). One gram of human faecal matter contains approximately $10^{12}$ to $10^{14}$ cells. These microorganisms consume undigested residual food in the gut and produce substances (metabolites) that are either beneficial or harmful to the body (Flint et al., 2015). Our diet shapes the composition of our gut bacteria, which in turn affects the metabolites that are produced, which subsequently govern our health (Lyu and Hsu, 2018) (Figure 1).

Gut bacteria are sometimes called the “hidden organ” in our body because they can cause critical physiological effects. The link between these effects and gut bacteria was not well known until the advent of culture-independent sequencing technologies because gut bacteria are mostly of the anaerobic type which is difficult to culture in a laboratory setting. These new sequencing technologies facilitate the identification and characterisation of the bacterial

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Figure 1. The effect of diet on the composition of gut microbiota and metabolites on health, adapted from Lyu and Hsu (2018).
composition in both healthy and diseased individuals which then enable their comparison.

**IMPORTANCE OF GUT MICROBIOTA**

The link between gut bacteria and obesity has been made apparent in the studies on germ-free mice (Bäckhed et al., 2007; Clarke et al., 2012). Germ-free mice are microbiologically sterile mice that are reared in strict isolation with no exposure to any microorganism. Researchers fed a diet rich in carbohydrates and fats to germ-free mice and to normal gut bacteria-colonised mice. At the end of their studies, they found that the germ-free mice had only minimal body fat and did not gain weight, whereas their colonised counterparts became obese (Figure 2). Thus, from this, we can deduce that obesity induced by a high carbohydrate and fats diet may be linked to the metabolites produced by the gut bacteria.

In another study, Turnbaugh et al. (2006) transferred gut bacteria from regular mice of different body weight categories to germ-free mice. Interestingly, they found that the germ-free mice recipients adopted the body weight category of their donors (Figure 3).

This finding is further reinforced by the work of Ridaura et al. (2013) who transferred faecal microbiota from human twins to germ-free mice. They found that the germ-free mice which received gut microbiota from the obese twin suffered from increased adiposity while those which received gut microbiota from lean twin did not (Figure 4).

More recently, Kulecka et al. (2016) found that when they removed the gut microbiota from lean mice with high-dosage antibiotics, and quickly transplanted colonic bacteria from obese mice into these mice, the lean mice developed an obese body type. Together, these studies emphasise the point that gut microbiota governs the metabolic processes of the host animal to a large extent, and is an essential determinant of our health.

Bacteria that produce beneficial substances are known as gut-friendly bacteria. They extract energy from ingested food and produce many useful compounds (metabolites) such as short-chain fatty acids (SCFA) which have anti-inflammatory properties (Flint et al., 2015), and amino acids (e.g. tryptophan, that is fermented to yield indole). Indole acts as a
signalling molecule in a system that protects the host (Kamada et al., 2014). They also renew intestinal epithelium cells (Tomas et al., 2015), and prevent overgrowth of pathogenic microorganisms. Conversely, pathogenic gut bacteria produce harmful or toxic substances which kill gut-friendly bacteria. Accumulation of these toxic compounds can interrupt the balance of metabolites that our body requires.

CLASSIFICATION OF BACTERIA

Bacteria are systematically classified based on their characteristics and genetic traits. It is a hierarchal type classification in which bacteria that share most common genetic characteristics are grouped into the same rank called taxa. Groups of taxa are given taxonomic rank, and these groups are gathered to form a higher rank, thus creating the taxonomic hierarchy. The classification ranking becomes increasingly specialised, moving from the general group domain to kingdom, then phylum, class, order, family, genus and, finally, species (Figure 5).

![Figure 5. An example of classification of the bacteria Streptococcus mutans using the taxonomy hierarchy.](image)

COLONIC BACTERIA COMMUNITY IN THE HEALTHY GUT

In a healthy adult, about 7 to 10 phyla of microorganisms are typically present in the gut. Out of these, the predominant phyla are Firmicutes (60%-80%) and Bacteroidetes (20%-40%), while Actinobacteria, Proteobacteria, Verrucomicrobia and Fusobacteria are present only in small proportions (Biagi et al., 2010; Wu et al., 2011) (Figure 6).

In the gut, the diversity of colonic bacteria increases as we move from the stomach to the colon with the population increasing by as much as 10³ to 10⁴ bacteria/g in the small intestine, and then by as much as 10¹² bacteria/g in the colon. Each segment of the gut is dominated by a different composition of the microbiota (Sommer and Bäckhed, 2016) (Figure 7), and their interaction and the metabolites produced by all these bacteria are important in maintaining gut health.

DYSBIOSIS AND DISEASES

The importance of gut microbiota is reinforced by findings from a study by Goodrich et al. (2014) who isolated colonic bacteria from more than 1000 twin adults.

![Figure 6. The main phyla of colonic bacteria.](image)

![Figure 7. Segments of the gut, density and type of bacterial species that maintain overall physiological functions. Microbial density and complexity increase from the stomach to the colon [adapted from Sommer and Bäckhed (2016)].](image)
They found that gut microbiota affects the metabolism of the host. Variations in the gut bacteria community and the substances produced (colonic composition) are known as dysbiosis. Changes in the gut microbial composition are associated with age, gender, body mass index (BMI), use of antibiotics, drugs, probiotics, and diet (De Filippo et al., 2010; Rodriguez et al., 2015; Filippo et al., 2017) (Figure 8).

An imbalanced community of gut microbiota, i.e. low diversity of bacteria, alteration in the *Firmicutes/Bacteriodetes* ratio, or low abundance of SCFA-producing genera such as *Roseburia* and *Eubacterium*, can lead to an increase in potential pathogens such as *Fusobacterium nucleatum* (Schwiertz et al., 2010) and the development of carcinogenic secondary bile acids (Hildebrandt et al., 2009; Islam et al., 2011) and toxins such as lipopolysaccharides (LPS) (d’Hennezel et al., 2017) and exopolysaccharides (EPS) (Ciszek-Lenda et al., 2011).

Accumulation of toxic substances increases the risk of health problems such as obesity, Type II diabetes, and neural, colon or heart diseases (Schepersjans et al., 2014; Noble et al., 2017; Battson et al., 2018; Meng et al., 2018). Therefore, a balanced community of gut microbiota is crucial in maintaining gut health.

**IMPORTANCE OF DIET**

Rothschild et al. (2018) examined colonic bacteria from more than 1000 twin pairs in the UK twins study, and found that environmental factors related to diet, drugs and anthropometric measures are more significant determinants of microbiota composition than heritable components such as genetics. The food that we eat shapes the type of gut bacteria and metabolites that circulate or accumulate in our bodies (Figure 9).

Gut dysbiosis can occur when switching from a high-fat, low-fibre diet to a low-fat, high-fibre diet (Figure 9). Independent research groups have found that the change in gut microbiota composition can happen rapidly, within one to five days after the subjects switched from an animal-based diet to a plant-based diet (Wu et al., 2011; David et al., 2014). David and co-workers (2014) found that the gut bacteria of adults who had an animal-based diet consisting of 70% fat, 30% protein and 0% fibre altered as quickly as 48 hr after the diet switch. Specific alterations in the composition of
The colonic bacteria from the lean OBESITY GUT MICROBIOTA AND EFFECTS OF DIETS ON higher population of bacteria from the Firmicutes phylum had a relatively higher population of bacteria from the Bacteroidetes phylum and a proportionally decreased population from the Bacteroidetes phylum.

Several human clinical studies have also reported that a higher proportion of Firmicutes and Actinobacteria phyla, and a lower proportion of Bacteroidetes and Verrucomicrobia phyla, led to body weight gain (Backhed et al., 2004; Ley et al., 2005; Turnbaugh et al., 2009; Simões et al., 2013). De Filippo et al. (2010) compared the gut microbiota of children from Italy who lived in urban areas and who typically consumed modern food with gut bacteria of children from rural Africa (Burkina Faso) who typically consumed large amounts of polysaccharides. They found that the Italian children had a higher proportion of Entebacteriaceae (phylum Firmicutes) and a lower proportion of Bacteroides (phylum Bacteroidetes), whereas the African children had a higher proportion of Bacteroidetes and a lower proportion of bacteria from the Firmicutes phylum (Figure 10) (De Filippo et al., 2010).

Various researchers have also identified a higher proportion of Prevotella and Xylanibacter (phylum: Bacteroidetes) (De Filippo et al., 2010; Claesson et al., 2012) in lean people who followed a plant-based diet. Diets rich in animal fat, red meat and sugar, but low in fibre, were found to result in increased populations of Bacteroides (phylum Bacteroidetes) and Ruminococcus (phylum Firmicutes) (Mukhopadhya et al., 2012; Hold, 2014).

Generally, these studies indicate that lean people tend to have a higher population of Bacteroidetes and a lower population of Firmicutes (Figure 10). Since then, a high ratio of Firmicutes to Bacteroidetes (F/B) has become associated with obesity (Lecomte et al., 2015). Researchers and academics have started to link a high F/B ratio with obesity in humans (Figure 10), and changes in the F/B ratio were used as a general measure of obesity.

However, conflicting findings later came to light as more and more human clinical studies were carried out. These studies unexpectedly found a proportionately higher population of Firmicutes phylum and Bifidobacterium longum (phylum Actinobacteria) in lean, healthy adults (Reyes et al., 2016). Other researchers (Fava et al., 2013; David et al., 2014; Lecomte et al., 2015) found that long-term high animal fat intake resulted in increased body weight but a lower Firmicutes population. These contradictory results called for a meta-analysis of the investigations on gut microbiota in obese adults. The analysis then found that the populations of certain beneficial bacteria from the Firmicutes phylum, such as Lactobacillus, are low in the gut of subjects who adopted high fat diets, resulting ultimately in a lower count of Firmicutes.
Other studies also reported contradictory results on the relative abundance of gut microbiota at the phylum level. These results are summarised in Table 1.

Of particular interest is the observation that a higher relative abundance of Faecalibacterium prausnitzii, Peptostreptococcus anaerobius and Christensenella from the Firmicutes phylum had been measured in lean adults (Simões et al., 2013; Remely et al., 2015; Xu et al., 2015; Beaumont et al., 2016), while Erysipelotrichia, Lactobacillus reuteri and Clostridium ramosum from the same phylum had been measured to be higher in obese adults (Chakraborti, 2015).

Therefore, the F/B ratio is only an arbitrary metric at best, and not an accurate measure of obesity (Sze and Schloss, 2016). A more detailed analysis should be carried out to identify a more robust indicator of obesity, and further investigation down to the lower taxonomic classifications such as genera and species is suggested.

### HIGH FAT DIETS AND GUT MICROBIOTA

Although it is recognised that a high-fat, low-fibre diet alters the community of gut microbiota and increases the risk of obesity, the effects of other nutrient components are also important (Lang et al., 2018).

Recent studies have reported that a high saturated fat diet results in an increased risk of obesity (David et al., 2014; Marchesi et al., 2016; Araújo et al., 2017). This type of diet promotes the growth of pathogenic bacteria which then produce toxic substances such as lipopolysaccharide, peptidoglycan and flagellin that erode the protective layer (mucin) of the gut cells and then penetrate into the gut (Hersoug et al., 2018). A high saturated fat diet also increases the circulation of carcinogenic compounds such as secondary bile acids (Kakiyama et al., 2013) in the intestinal lumen (Figure 11). The accumulation of these toxic compounds then leads to systemic inflammation, obesity, adiposity and insulin resistance (Schroeder et al., 2018).

Gut microbiota that produces these toxins is found to consist of more than one phylum. It typically includes Bacteroides (phylum: Bacteroidetes); Ruminococcus, Faecalibacterium prausnitzii and Listeria monocytogenes (phylum:

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**TABLE 1. RELATIVE ABUNDANCE OF GUT MICROBIOTA AT GENUS AND SPECIES LEVELS FOUND IN OBESE AND LEAN ADULTS (up arrow = high; down arrow = low)**

<table>
<thead>
<tr>
<th>Phylum</th>
<th>Order/ family/ genus/ species</th>
<th>Obese adults</th>
<th>Lean adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinobacteria</td>
<td>Bifidobacteria</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>Firmicutes</td>
<td>Faecalibacterium prausnitzii</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peptostreptococcus anaerobius</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Erysipelotrichia</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lactobacillus reuteri</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clostridium ramosum</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Christensenella</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>Bacteroidetes</td>
<td>Prevotellaceae</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Bacteroidesvulgatus</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alisilocespp</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Bacteroides spp.</td>
<td>↑</td>
<td></td>
</tr>
<tr>
<td>Verrucomicrobia</td>
<td>Akkermansia</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td></td>
<td>Akkermansia muciniphila</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteobacteria</td>
<td>Enterobacteriaceae</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Simões et al. (2013), Chakraborti (2015), Remely et al. (2015); Xu et al. (2015); Beaumont et al. (2016).

![Figure 11. A high fat diet increases the penetrability of the gut mucus layer, thus more toxins can diffuse into the gut [adapted from Schroeder et al. (2018)].](image)
Firmicutes); and Fusobacterium nucleatum (phylum: Fusobacteria) (Mukhopadhyya et al., 2012; Fava et al., 2013; Hold, 2014; Heras et al., 2019). These bacteria are found at elevated levels in subjects who eat high fat diets. Therefore, we must also consider the effect of the type of dietary fats intake on the community of gut microbiota, something which warrants further investigation.

HIGH SFA, MUFA, AND PUFA DIETS AND GUT MICROBIOTA

Dietary fats originate from animal, and plant sources, and are classified as either saturated fatty acids (SFA), mono-unsaturated fatty acids (MUFA) or poly-unsaturated fatty acids (PUFA) according to their chemical structure. Differences in the chemical structure may affect the rate of digestion and absorption which in turn alter the composition of gut bacteria and the type of metabolites produced. The relationship between high SFA, MUFA, and PUFA consumption and the composition of gut microbiota is summarised in Table 2.

From Table 2 we can see that a high SFA diet increases the bacterial population of the Firmicutes, Fusobacteria and Proteobacteria phyla. These bacteria have been associated with the risk of obesity as they were found to have a higher tendency to increase body weight in humans. The effects of MUFA and PUFA diets on the population of beneficial and pathogenic bacteria are less consistent (Table 2).

Irregular pattern of the relationship between dietary fats, especially MUFA and PUFA, and gut bacteria population is due to variations in inter-individual, percentage and type of fat intake, and the duration of the study. To date, published data have been collected from a heterogeneous sample set which include obese patients (BMI >25), infants, diabetics and the elderly (>60 years old) (Turnbaugh et al., 2006; Menni et al., 2017; Yang et al., 2017) who were overfed with a high fat diet (>40% fat in the total energy intake). Data on the relationship between dietary fats and gut microbiota in normal healthy adults are still lacking. Furthermore, the sources of dietary fats used in these studies were not specified. For instance, no distinction was made between SFA, MUFA and PUFA extracted from animal, plant and dairy sources. Lastly, the duration of these studies was also not standardised.

TABLE 2. EFFECTS OF HIGH DIETARY FATS FROM PLANT AND NON-PLANT SOURCES ON THE COMMUNITY OF GUT MICROBIOTA

<table>
<thead>
<tr>
<th>Type of dietary fats</th>
<th>Gut microbiota (species, genus, family, order)</th>
<th>Phylum</th>
</tr>
</thead>
<tbody>
<tr>
<td>High SFA</td>
<td>↑ Clostridium bolteae, Blautia</td>
<td>Firmicutes</td>
</tr>
<tr>
<td></td>
<td>↑ Helicobacter, Escherichia coli,</td>
<td>Proteobacteria</td>
</tr>
<tr>
<td></td>
<td>Bilophila wadsworthia</td>
<td>Fusobacteria</td>
</tr>
<tr>
<td></td>
<td>↑ Leptotrichiaceae, Listeria monocytogenes</td>
<td></td>
</tr>
<tr>
<td>High MUFA</td>
<td>↑ Clostridium bolteae, Blautia</td>
<td>Actinobacteria</td>
</tr>
<tr>
<td></td>
<td>↑ Helicobacter, Escherichia coli,</td>
<td>Bacteroidetes</td>
</tr>
<tr>
<td></td>
<td>Bilophila wadsworthia</td>
<td>Firmicutes</td>
</tr>
<tr>
<td></td>
<td>↑ Leptotrichiaceae, Listeria monocytogenes</td>
<td>Proteobacteria</td>
</tr>
<tr>
<td>High PUFA</td>
<td>↑ Bifidobacterium</td>
<td>Actinobacteria</td>
</tr>
<tr>
<td></td>
<td>↑ Oscillospira, Faecalibacterium,</td>
<td>Firmicutes</td>
</tr>
<tr>
<td></td>
<td>Ruminococcaceae, Isobaculum, and</td>
<td>Proteobacteria</td>
</tr>
<tr>
<td></td>
<td>Lactobacillus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ Clostridium, Streptococcus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ Serratia, Escherichia, Citrobacter</td>
<td></td>
</tr>
<tr>
<td>High n-3 PUFA</td>
<td>↑ Lactobacillus</td>
<td>Firmicutes</td>
</tr>
<tr>
<td>High n-6 PUFA</td>
<td>↓ Bifidobacterium</td>
<td>Actinobacteria</td>
</tr>
</tbody>
</table>


SFA is often labelled as unhealthy, but this is not always necessarily so. This label is far too general and does not differentiate between SFA from animal, plant and dairy sources. First, it must be noted that palm oil has a more balanced saturated and unsaturated fatty acid ratio compared to other vegetable oils (Figure 12).

Second, we must consider that the position of the fatty acid attached to the triglyceride backbone is different for fats originating from an animal, plant or dairy source (Figure 13). For
vegetable (palm) oil, the fatty acid at the second position in the triacylglycerol backbone is predominantly oleic acid (MUFA) or linoleic acid (PUFA), while for animal fat, the fatty acid in the second position of the triacylglycerol backbone is mainly SFA (Ong and Goh, 2002) (Figure 13).

The unique distribution of fatty acid components in palm oil causes it to have a similar effect on blood cholesterol level as olive oil (Voon et al., 2011). Palm oil also has a lower tendency for fat deposition in the adipose tissue compared to high PUFA oils (Gouk et al., 2013; Gouk et al., 2014). Therefore, the nutritional value of palm oil should not be grouped together with that of saturated fats from animal and dairy sources.

To date, the link between dietary fats and metabolites produced by the gut microbiota that increases the risk of obesity is still unclear. There are many confounding factors in experimental designs such as inter-individual variation, dietary source of the fats and the distribution of their fatty acids on the triglyceride backbone, a non-standardised duration of study, as well as obesity status and exercise intensity of the test subjects (John and Mullin, 2016). Furthermore, this relationship is convoluted by the type of metabolites produced by the gut bacteria. Therefore, more comprehensive, long-term studies should be carried out with due consideration given to the effects of content of the fatty acids and the distribution of fatty acid components on normal healthy adults, before any association can be fully established.

CONCLUSION

Colonic microbiota is mostly affected by the type of nutrients consumed by the host. Faecal samples can provide a quick estimate of the diversity of the microbiota in the colon, which relates to gut health. Most of the data reviewed here were obtained from published North American and European studies because only a few studies have ever been carried out in Africa, South America and Asia, and the studies are even sparser in Southeast Asian countries, especially in Malaysia. Hence, more research is required to investigate the relationship between the typical Malaysian diets and gut microbiota, as well as the contribution of nutritionally balanced palm oil on human gut health. The outcome of such studies may reveal the effect of intake of different dietary oils on the type of colonic bacteria present. Furthermore, identified “lean” bacteria can perhaps one day be transplanted into obese individuals as a possible treatment for pandemic obesity.

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