

ASSOCIATION OF DIETARY FATS WITH GUT MICROBIOTA PROFILE: HOW DOES PALM OIL FIT IN?

S Y YAP^{*}; P T VOON^{*}; Y K CHEAH^{**}; V K M LEE[†] and SELVADURAY, K R^{*}

ABSTRACT

Diet manipulation alters the gut microbiota composition. Gut dysbiosis is characterised by imbalanced bacteria composition that has been associated with high fat diet. Diets containing high animal fat induce pathogenic bacteria growth and similar bacterial profiles have been identified in obese adults and chronic disease patients. Conversely, diets containing high plant fat increase the abundance of beneficial bacteria. Habitual fat intakes modulate the bacterial species and their metabolites in different geographical locations and ethnicities. Dietary interventions using various degrees of fatty acid saturation reported reduced bacterial diversity in high saturated fatty acid (SFA) diet and increased in high monounsaturated fatty acid (MUFA) diet. However, high polyunsaturated fatty acid (PUFA) diet demonstrated a wide variation in bacterial diversity. These results suggested that the effects of dietary fats on gut microbiota composition are not fully established. Palm oil has almost balanced proportions of saturated and unsaturated fatty acids coupled with unique stereo-specificity fatty acids compositions and nutritional properties, making it the main vegetable oil in the Malaysian diet. However, its effect on the gut microbiota profile is still unknown. This review highlights the abundance of specific bacteria after consuming various dietary fats and proposes potential bacteria profile following the palm oil diet.

Keywords: gut microbiota, dysbiosis, palm oil, dietary fats.

Received: 3 September 2020; **Accepted:** 12 November 2020; **Published online:** 16 February 2021.

INTRODUCTION

The bacterial composition inhabiting the intestine is highly affected by the diet of the human host. The fractions of carbohydrate, fat, and protein in food residue affect the survival of different population of colonic bacteria. These bacteria degrade and ferment colonic food residue to synthesise a wide range of

metabolites that affect the health of the host. The prevalence of a specific type of bacteria could serve as a potential dietary biomarker for diagnosing intestinal health and related systemic health of the host (Mokkala *et al.*, 2019).

In healthy adults, the colonic bacterial composition is dominated by the phyla *Firmicutes* (60%-80%) and *Bacteroidetes* (20%-40%); while only a small amount of *Actinobacteria*, *Proteobacteria*, *Verrucomicrobia* and *Fusobacteria* are present among others (Clavel *et al.*, 2014). The compositions are stable over time and any change in gut environment such as diet modification, and ingestion of probiotics or drugs will result in 'gut dysbiosis' (Leeming *et al.*, 2019). Gut dysbiosis is characterised by the imbalance in the bacteria composition (Kriss *et al.*, 2018), low bacteria diversity as indicated by lower total bacteria counts and Chao number which represents bacteria richness (Tsuji *et al.*, 2018).

^{*} Malaysian Palm Oil Board,
6 Persiaran Institusi, Bandar Baru Bangi,
43000 Kajang, Selangor, Malaysia.
E-mail: syap@mpob.gov.my

^{**} Department of Biomedical Sciences,
Faculty of Medicine and Health Sciences,
Universiti Putra Malaysia, 43400 UPM Serdang,
Selangor, Malaysia.

[†] Department of Family Medicine,
School of Medicine, International Medical University,
Kuala Lumpur, Malaysia.

Diets alter gut microbiota composition as shown in urban and rural populations (Figure 1). Individuals living in urban cities with a diet that is high in animal fat and low in fibre have a significantly ($p < 0.05$) lower abundance of butyrate-producing bacteria compared to individuals living in rural villages that have diet high in fibre and plant-based fats (De Filippo *et al.*, 2010; Ou *et al.*, 2013; Yatsunenkov *et al.*, 2012). Animal fat enriched diet induces gut perturbation by promoting opportunistic pathogenic bile-tolerant bacteria (Figure 1) such as *Alistipes* and *Bilophila* even in a short-term four days dietary intervention (David *et al.*, 2014). This finding agrees with Muegge *et al.* (2011) who had concluded that animal-based fat diets have a very similar gut microbiota profile that is found in carnivorous mammals (Muegge *et al.*, 2011).

Gut microbiota composition of high animal fat intake is correlated with the profile of individuals that are obese and/or have chronic diseases such as Type 2 diabetes, digestion disorder, cardiovascular disease and cancer (Murphy *et al.*, 2015; Illiano *et al.*, 2020; Requena *et al.*, 2018). Hence, bacteria species that overgrows or depletes significantly are proposed as dietary biomarkers for early disease diagnosis.

Cohort studies have attempted to generalise the bacteria profile from constituents adopted different habitual diet. A distinguish variation in gut profile was identified in population depending on various geographical location and ethnicities (Yasir *et al.*, 2015; Jain *et al.*, 2018; Gupta *et al.*, 2017) suggesting that individuals gut microbiota profiles are strongly associated with the host's geographical location. Therefore, extrapolated data collected from different nations is simply too general to be used in the diagnosis of diseases. Researchers should instead use small-scale interpolated data to accurately identify dietary biomarkers and predict metabolic risk (He *et al.*, 2018).

The effect of a high fat diet on the composition of gut microbiome is well known, but there exists little information on the type of geographically-

based habitual fat intake on the profile of gut microbiota. Briefly, edible MUFA such as olive oil and PUFA such as fish oils are a staple in the diet of Mediterranean region (Pauwels, 2011). High PUFA soyabean oil is extensively used by America, Argentina, Brazil, Russia and China (Jia *et al.*, 2020), whereas sunflower oil is mainly used in European diet (Pilorgé, 2020). Palm oil which is balanced in saturated and unsaturated fats has become an increasingly important edible oil in the India, China, European Union, United Arab Emirates and Southeast Asian regions (Parveez *et al.*, 2020).

To date, very few human clinical studies have focused on the effects of positional distribution of fatty acids varying in degree of saturation on the human gut microbiota profile. Therefore, this review highlights the association of dietary fat intakes with the composition of gut microbiota and their metabolites at different geographical locations. Moreover, we also propose a prospective palm oil nutritional research to identify specific genus or species and establish a baseline of gut microbiota profile in the Malaysian diet, which may be a potential dietary biomarker for predicting metabolic health.

THE LINK OF DIETARY FAT SOURCE WITH GUT MICROBIOTA COMPOSITION AND HEALTH

The bioavailability of dietary fats influences the composition of gut microbiota. A plant-based Mediterranean, vegetarian and vegan diets contain a variety of grains, nuts, vegetables, and fruits that provide a variable range of plant fats, phytonutrients and polyphenols (Muralidharan *et al.*, 2019). In contrast, modern diet has been associated with high intake of energy dense- and highly processed foods coupled with red meat consumption (Mozaffarian, 2016).

Effects of high plant-based or animal-based fats on gut microbiota compositions have been summarised into two general pathways (Valdes *et al.*, 2018). High intake of plant-based diet

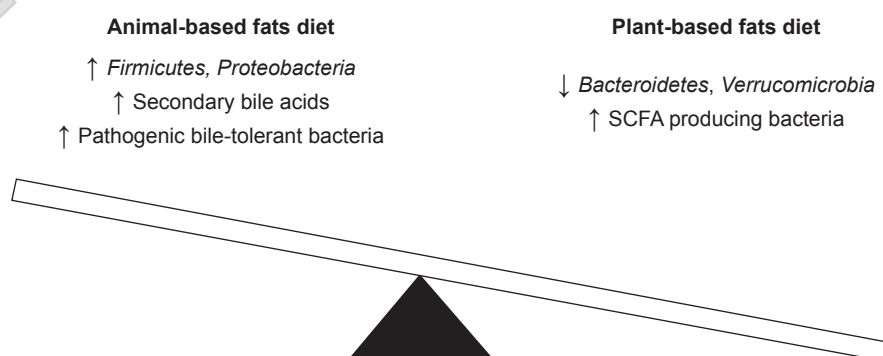


Figure 1. Gut dysbiosis and effects of dietary fat.

stimulates butyrate-producing bacteria (De Filippo *et al.*, 2010) which have been reported to reduce the risk of non-communicable chronic diseases such as hypertension (Silveira-Nunes *et al.*, 2020) and cardiovascular diseases (Ganesan *et al.*, 2018). Animal-based fat intake increases the abundance of pathogenic bile acid-tolerant bacteria (De Filippo *et al.*, 2010) and leads to accumulation of toxins such as deconjugated bile acids and lipopolysaccharides (Requena *et al.*, 2018) in the systematic circulation.

Animal fat promotes the growth of detrimental bile acids tolerant species such as *Clostridium*, *Helicobacter*, *Catenibacterium*, *Fusobacterium*, *Enterobacterium*, *Bacteroides*, *Bilophila* and *Alistipes* (Murphy *et al.*, 2015; Shortt *et al.*, 2018; Tomova *et al.*, 2019; Yang *et al.*, 2020b). These bacteria secrete toxic metabolites such as trimethylamine N-oxide (TMAO) which is derived from dietary choline or L-carnitine, a component of proteins. Bacteria ferment the trimethylamine (TMA) in these proteins to TMAO via flavin-containing monooxygenase 3 (FMO3) enzyme and secrete it into the gut. High concentrations of TMAO in the circulating plasma activates the NF-kappa B pathway and increases the secretion of inflammatory cytokines such as IL-18 and IL-1 β (Yang *et al.*, 2019). These inflammatory markers are found to be elevated in the plasma of insulin-resistant obese adult subjects (Moreno-Indias *et al.*, 2016). Similarly, elevated TMAO levels inhibit the synthesis of bile acid and trigger platelet hyper-reactivity which increases the risk of thrombosis and cardiovascular diseases (CVD) (Yang *et al.*, 2019).

A high fat diet alters the profile of gut microbiota and induces permeability of the intestinal barrier structure in the systematic circulation (Ghosh *et al.*, 2020) and increases the expression of Paneth Cell-Antimicrobial Peptides which trigger intestinal inflammation followed by activation of circulating inflammatory cytokines (IFN- γ and TNF- α) (Guo *et al.*, 2017). This finding sheds light on the importance of gut microbiota profile and metabolites in preventing intestinal tumorigenesis. Overgrowth of detrimental bile acids tolerant bacteria also produces deconjugated bile acid when accumulated and increases the rate of colonic cell proliferation and the risk of colon cancer (Fava *et al.*, 2013; O'Keefe, 2016).

Plant-based fats are generally associated with short-chain fatty acid (SCFA) production. Among the SCFA, acetate and propionate are fatty acids which activate the G-protein coupled receptors 43 (GPR43) in the colon enterocytes and adipocyte. The GPR43 activates cellular signalling events and inhibits colonocytes proliferation (O'Keefe, 2016) as indicated by low Ki-67 proliferation and apoptotic indices. The *ffar2* (*grp43*) and *ffar3* (*gpr41*), receptors of SCFA on glucagon-like peptide 1 (GLP-1) L cells, stimulate the GLP-1 secretion to regulate plasma glucose concentration and maintain glucose homeostasis (Tolhurst *et al.*, 2012). Hence, SCFA that

bind to these receptors may serve as therapeutic treatment for diabetes.

SCFA also demonstrate anti-inflammatory effect by suppressing the production of cytokines and inhibiting actions of the toll-like receptor (TLR) 4 (Mirmonsef *et al.*, 2012). Therefore, SCFA-producing bacteria such as *Prevotella*, *Bifidobacterium* spp. and *Lactobacillus* (Tomova *et al.*, 2019) may have a protective effect against colon cancer as reported in the study on native Africans (Ou *et al.*, 2013).

DIVERSITY OF GUT MICROBIOTA IN DIFFERENT HABITUAL DIETS

High dietary fat intake is associated with a decrease in the *Firmicutes* and *Proteobacteria* phylum but with an increase in *Bacteroidetes* and *Actinobacteria* (Senghor *et al.*, 2018), however contradictory results have also been documented. These contradictory results are likely due to the different ethnicity and lifestyle of populations from different geographical locations (Fontana *et al.*, 2004; Gupta *et al.*, 2017). Later, He *et al.* (2018) observed that variations in bacterial lineages occurred in different locations within the same ethnic group. Following this observation, they recommended establishing a localised baseline to identify gut microbial as dietary biomarkers (He *et al.*, 2018).

The type of food, meal preparation, drinks, and other socio-cultural rituals co-influence the gut microbiota profile of people in different regions (Senghor *et al.*, 2018). The typical gut microbiota profile in urban European and American population, and rural African population have been extensively reviewed (Snijder *et al.*, 2017; Almeida *et al.*, 2019). Therefore, this review focuses on the gut microbiota profile of Asians in geographically different locations (Table 1).

Comparison of Gut Microbiota Profile within Same Country but on Different Diets

Gut microbiota profile differs across geographical locations in urban and rural populations in Asian countries (Table 1). Generally, individuals from rural areas have diverse bacteria species as a result of variety of unprocessed plant-based diet intake; whereas the gut microbiome of urban population is dominated by *Bacteroides*, *Faecalibacterium* and *Ruminococcus* as a consequence of high modern processed food intake (Table 1).

Dietary patterns segregate the gut microbiota profile from different parts in the countries, particularly in Indian and Chinese populations (Table 1). Similar observation was also reported in South Korea, where Jeju Islanders who typically consume more animal lipid have high abundance of *Butyricimonas* than people who lived in Seoul city (Nam *et al.*, 2011).

TABLE 1. GUT MICROBIOTA DIVERSITY IN INDIVIDUALS FROM DIFFERENT GEOGRAPHICAL REGIONS

Country	Region	Study population; Sample size	Diets/ lifestyle	Sequencing method	Gut microbiota compositions	Reference
Saudi Arabia	• Urban	• adults • n=18	• limited food variety, low fruits and vegetables intake compared to French	• 16S rRNA Illumina MiSeq (V3-V4)	• Arabic: ↑ <i>Proteobacteria</i> , <i>Blautia wexlerae</i> , ↓ <i>Verrucomicrobia</i> , <i>Bifidobacterium breve</i> compared to French	Yasir <i>et al.</i> (2015)
	• Jeddah (Urban)	• healthy males • n=18	• limited food variety, fruit, vegetables, fast food and snacks	• 16S rRNA Illumina MiSeq (V3-V4)	• ↑ <i>Bacteroidetes</i>	Angelakis <i>et al.</i> (2016)
	• Bedouins (rural)	• healthy males • n=10	• vegetables, chicken, dairy products, fermented food and rice	• 16S rRNA Illumina MiSeq (V3-V4)	• ↑ <i>Verrucomicrobia</i> • ↑ <i>Spirochaetae</i> <i>Treponema berlinense</i> , <i>T. succinifaciens</i> due to fermented food intake	
	• Arabian Peninsula	• healthy native Arab Kuwaitis • n=25	• meats, dairy products, grains, legumes, nuts, vegetables (leafy greens, herbs), fruits and nuts	• 16S rRNA Illumina MiSeq (V3-V4)	• ↑ <i>Bacteroides dorei/vulgatus</i>	Plummer <i>et al.</i> (2020)
India	• North (Bhopal, Ludhiana, Lucknow, New Delhi)	• n=247	• Details dietary records were not provided	• 16S rRNA Ion Torrent (V3-V4)	• Eastern and Western: ↑ <i>Bacteroidetes</i> • Northern and Southern: ↑ <i>Spirochaetes</i> • ↑ <i>Faecalibacterium</i> and <i>Prevotella</i> genus across the geographic landscape	Shetty (2018)
	• East (Guwahati, Kolkata, Patna)	• n=250				
	• West (Ahmedabad, Ajmer, Mumbai, Nagpur)	• n=263				
	• South (Chennai, Cochin, Mangalore)	• n=226				
	• Ahmedabad (Western India)	• healthy adults • n=80	• fruits, vegetables, wheat, millet, sorghum, dairy products, sprouts, leafy vegetables, rice, pulses, low meat and fish intake	• 16S rRNA Illumina MiSeq (V3-V4)	• ↑ <i>Prevotella</i> , <i>Sutterella</i> and <i>Succinivibrio</i> phylum <i>Proteobacteria</i>	Tandon <i>et al.</i> (2018)
	• Ballabgarh, Faridabad district, sea level	• healthy adults • rural (n=25) • urban (n=24)	• vegetarian, eggetarian, non-vegetarian • mustard oil, soyabean oil and ghee	• 16S rRNA pyro-sequencing (V1-V5)	• Urban: ↑ <i>Lactobacillus</i> • Rural: ↑ <i>Parabacteroides</i> , <i>Blautia</i> , <i>Brevundimonas</i> , <i>Pelomonas</i> and <i>Megamonas</i> • Leh: ↑ <i>Prevotella copri</i> , uncharacterised species of <i>Faecalibacterium</i> and <i>Lachnospiraceae</i> • High ghee intake: ↑ <i>Collinsella</i> • High sunflower oil: ↑ <i>Roseburia</i> and <i>Sporobacter</i>	Das <i>et al.</i> (2018)
	• Leh, Ladakh district, high altitude	• n=35	• lack of dairy intake, high consumption of sunflower oil			
	• Central India (Bhopal) • Southern India (Kerala)	• n=110	• plant-based diet • omnivorous diet	• 16S rRNA sequencing, whole genome shotgun	• Central region: ↑ <i>Prevotella</i> • Southern region: ↑ <i>Bacteroides</i> , <i>Ruminococcus</i> and <i>Faecalibacterium</i>	Dhakan <i>et al.</i> (2019)

Country	Region	Study population; Sample size	Diets/ lifestyle	Sequencing method	Gut microbiota compositions	Reference
	- Ladakh (cold desert) - Jaisalmer (hot-and semi-arid) - Khargone (subtropical to tropical climate)	- healthy adults - n=31	- noodle, whole wheat bread, yak butter, barley, alcoholic beverage - whole wheat bread, spicy curries, lentils, grains and butter milk - lentils, grains, rice, whole wheat bread, vegetables, spices, tea and milk	- whole genome sequencing - Illumina HiSeq-2500	- Ladakh: ↑ <i>Prevotella</i> - Jaisalmer: ↑ <i>Bifidobacterium</i>	Kaur <i>et al.</i> (2020)
Russia	- Saint Petersburg, Saratov, Rostov-on-Don and Novosibirsk (urban) - Tatarstan, Omsk, Tyva and Khakassia (rural)	- healthy adults - n=96	- urban: high processed food intake - rural: high unprocessed natural food intake	16S rRNA SOLiD sequencing	- Overall: ↑ <i>Bifidobacterium</i>, <i>Megamonas</i>, <i>Phascolarctobacterium</i>, <i>Lactobacillus</i> or <i>Akkermansia</i> - Omsk: ↑ <i>Prevotella</i>, <i>Lachnospiraceae</i>, <i>Coprococcus</i> and <i>Faecalibacterium</i> - Tatarstan: ↑ <i>Roseburia</i>, <i>Coprococcus</i>, <i>Faecalibacterium</i> and <i>Ruminococcus</i> genera - Tyva: ↑ <i>Bifidobacterium</i>	Tyakht <i>et al.</i> (2013)
China	- Five locations - Northeast (Harbin) - Central (Zhengzhou) - East (Wuxi) - Southwest (Chengdu) - Ürümqi	- young healthy adults - n=314	details dietary records were not provided but individuals from rural area of each locations practiced typical farming or pastoral lifestyle	16S rRNA pyro-sequencing (V5-V6)	- Overall: <i>Phascolarctobacterium</i> of <i>Firmicutes</i> most predominant - Core genera: <i>Roseburia</i>, <i>Bacteroides</i>, <i>Blautia</i>, <i>Faecalibacterium</i>, <i>Clostridium</i>, <i>Subdoligranulum</i>, <i>Ruminococcus</i>, and <i>Coprococcus</i> from SCFA-producing lineages - Tibetan group has most unique genera compared to all others ethnics - Rural areas: ↑ <i>Prevotella</i> and <i>Xylanibacter</i>	Zhang <i>et al.</i> (2015)
	Babu district, He Zhou (Southern China)	- healthy - n=134 (Han, n=47; Zhuang, n=28; Yao, n=59)	frequencies of 21 types regular food intakes	16S rRNA Illumina MiSeq (V3-V4)	- Overall: ↑ <i>Bacteroides</i> and <i>Prevotella</i> - Hans: ↑ <i>Megamonas</i> significantly (p < 0.05) due to high intake of beans	Liao <i>et al.</i> (2018)
	- Beijing (Northern) - Jinan (Eastern) - Zigong (Southwest)	- healthy adults - n=131	details dietary records was not provided except fruits, yogurt and drink intakes	16S rRNA Illumina MiSeq (V3-V4)	- Overall: ↑ <i>Bacteroides</i> - Core genera: <i>Alistipes</i>, <i>Bacteroides</i>, <i>Blautia</i>, <i>Clostridium</i>, <i>Coprococcus</i>, <i>Escherichia/Shigella</i>, <i>Faecalibacterium</i>, <i>Gemmiger</i>, <i>Parasutterella</i>, <i>Roseburia</i> and <i>Ruminococcus</i>	Zhang <i>et al.</i> (2019)
	Zhejiang (Eastern China)	- healthy - n=10	details dietary records were not provided	16S rRNA pyro-sequencing (V3)	Overall: ↑ <i>Faecalibacterium</i>	Ling <i>et al.</i> (2013)
	Shanghai, Jiangyin (Eastern China)	- healthy, native - n=29	- high fat diet (≥40% of dietary calories were from fat) - low fat diet (>40%) - fats were mainly from cooking oil, data of oil types were not provided	16S rRNA Illumina MiSeq (V3-V4)	- Faecal samples: ↑ <i>Prevotella</i> and <i>Abiotrophia</i> - Colon mucosa tissue ↑ unclassified genus of S24-7 from HDF compared to LFD	Qian <i>et al.</i> (2018)

Country	Region	Study population; Sample size	Diets/ lifestyle	Sequencing method	Gut microbiota compositions	Reference
South Korea	- Seoul (inland) - Jeju Island	- healthy, elderly, n=9 - healthy, elderly, n=10	24 hr diet recall - subjects from Jeju Island consumed significantly ($p<0.05$) more animal lipid than those from Seoul	16S rRNA Ion Torrent (V1-V2)	↑ <i>Catenibacterium</i> ↑ <i>Butyricimonas</i>	Shin <i>et al.</i> (2016)
Korea	NA	healthy, n=20	details dietary records were not provided	16S rRNA pyro-sequencing (V1-V3)	- Overall: ↑ <i>Faecalibacterium</i>, <i>Prevotella</i> and <i>Bacteroides</i> - Core gut microbiota: <i>Bacteroides</i>, <i>Parabacteroides</i>, <i>Prevotella</i>, <i>Clostridium</i>, <i>Eubacterium</i>, <i>Faecalibacterium</i>, <i>Lachnospira</i>, <i>Oscillibacter</i>, <i>Roseburia</i>, <i>Ruminococcus</i>, <i>Subdoligranulum</i>, uncultivated human intestinal clones and <i>Fusobacterium</i>	Nam <i>et al.</i> (2011)
Japan	- Sendai city - Azabu University (Eastern Japan)	- healthy adults, n=32 - healthy adults, n=106	- traditional Japanese diet: soya products, fishes, vegetables, fruit, green tea, seaweed, mushrooms, rice, condiments, soup stock 'Dashi', fermented seasoning (soya sauce, miso, vinegar, mirin and sake) - modern Japanese diet contains deep fried dishes, grilled fishes added salts, soya sauce, butter, chesses, sugars - details dietary records were not provided	16S rRNA Illumina MiSeq (V3-V4) 16S rRNA Ion Torrent, pyro-sequencing, Illumina MiSeq (V1-V2)	- Traditional Japanese diet: ↑ <i>Sutterella</i>, ↓ unclassified <i>Lachnospiraceae</i>, <i>Parabacteroides</i>, unclassified <i>Rikenellaceae</i> ↑ <i>Bifidobacterium</i> ↓ <i>Methanobrevibacter smithii</i>	- Kushida <i>et al.</i> (2019) - Nishijima <i>et al.</i> (2016)
Thailand	NA	- healthy adults - vegetarian - non-vegetarian	- santi-Asoke vegetarian diets: vegetables, fruits - ovo-lacto, ovo, lacto vegetarian diets: include eggs, milk, and yoghurt - non-vegetarian diet: pork, fish and chicken, eggs, yoghurt, milk, fruits	16S rRNA pyro-sequencing (V6-V8)	- Overall: ↑ <i>Faecalibacterium prausnitzii</i> and <i>Gemmiger formicilis</i> - Vegetarian diets: ↑ <i>Clostridium nexile</i>, <i>Eubacterium eligens</i>, and <i>Prevotella copri</i> - Non-vegetarian diets: ↑ <i>Collinsella aerofaciens</i>, <i>Ruminococcus torques</i>, various species of <i>Bacteroides</i>, <i>Parabacteroides</i>, <i>Escherichia</i>, <i>Clostridium</i> and <i>Eubacterium</i>	Ruengsomwong <i>et al.</i> (2016)
Indonesia	Bali	healthy adults, n=41	white rice, bread, fried tofu, chicken, palm oil, tempeh, egg, pork, fish, soto, milk and papaya	16S rRNA Illumina MiSeq (V4)	Overall: ↑ <i>Prevotella</i>-rich (type-P) and <i>Bacteroides</i>-rich (type-B)	Febinia <i>et al.</i> (2020)

Note: n - number of subjects; FFQ - food frequency questionnaire; V - variable region; HFD - high fat diet; LDF - low fat diet; NA - not available; SCFA - short-chain fatty acids; 16S rRNA - 16S ribosomal RNA.

China and India have varying geographical locations and thus, create diverse dietary habits in their people and compositions of gut microbiota. In China, the predominated core genus was *Phascolarctobacterium* from the phylum of *Firmicutes* (Zhang *et al.*, 2015), which is also in high abundance in Russian population (Tyakht *et al.*, 2013). Other core genera in Chinese population include *Roseburia*, *Bacteroides*, *Faecalibacterium* and other bacteria from SCFA-producing lineages (Table 1).

Contrary in India, *Prevotella copri* and *Faecalibacterium prausnitzii* (Pulipati *et al.*, 2020) from the butyrate producing bacteria lineages (Kaur *et al.*, 2020), are the most predominant core bacterial genera as identified in the 'Landscape of Gut Microbiome-Pan India Exploration' (LogMPIE) study results suggesting that the majority of Indian populations are still adhering to the whole grains, legumes and plant-based diet (Kaur *et al.*, 2020). However, this result was not in agreement with the smaller cohort study conducted in unique geographical locations (Das *et al.*, 2018).

Das *et al.* (2018) reported that gut microbiota compositions of non-vegetarian adults in high altitude areas of Leh was predominated by *Provetella* compared with vegetarian or ovo-vegetarian diet from sea level Ballabgarh urban region (Das *et al.*, 2018). These results suggest that *Provetella* has distinct oligo types that mediate the carbohydrate-enzyme activities in different diets (Das *et al.*, 2018; Kaur *et al.*, 2020).

The diversity of gut microbiota in Leh and Ballabgarh populations was significantly associated with the types of dietary fat consumption, especially from cooking oils, butter and milk (Table 1). Individuals from Leh has high sunflower oil intake but low in dairy intake. Hence, *Roseburia* (Devillard *et al.*, 2007) and *Sporobacter* (Pu *et al.*, 2016) which are able to degrade PUFA oil, especially linoleic acids, were identified as the predominated gut bacteria in Leh individuals; but genera such as *Pseudomonas* and *Bifidobacterium* which have been associated with dairy products were rare. Furthermore, *Collinsella* was identified as the most abundant genus in Ballabgarh subjects who have high ghee consumption (Das *et al.*, 2018).

Comparison of Gut Microbiota Profile between Countries but on Similar Diets

Although *Prevotella* has been related with high plant-based diet intake, but the core genera of individuals from different countries following the same diet are different (Table 1). For instance, vegetarian groups from Thailand were high in abundance of *Clostridium nexile*, *Eubacterium eligens* and *Prevotella copri* which was different from residence in Leh, India that made up of *Prevotella*, *Coprococcus*, *Clostridium*, *Ruminococcus*,

Howardella, *Erysipelotrichaceae* and *Peptococcus* (Table 1). Similarly, *Spirochaetae* was enriched in Arabs who consumed fermented foods made from pearl millet flour with starter culture (Angelakis *et al.*, 2016) but absent in Japanese who were also on high fermented food intake from soya (Kushida *et al.*, 2019).

Megamonas was the predominant bacteria in Hans population who have high bean intake (Liao *et al.*, 2018) which is rich with unsaturated fats. *Megamonas* was also of the core species in Russian (Tyakht *et al.*, 2013) and in Ballabgarh, Indian populations (Das *et al.*, 2018). Linear discriminant analysis (LDA) effect size (Lefse) analysis could be used to cluster and identify the potential biomarkers from profile of these gut bacteria of distinct populations (Jain *et al.*, 2018).

These studies provided a good foundation of gut microbiota profile to establish localised baseline from complex dietary patterns in Asia and to predict metabolic disorder in niche community. In Southeast Asia, studies regarding the microbial diversity of healthy adults related to the gut health is limited, but effect of dietary pattern on gut microbiota profile in Bali (Febinia *et al.*, 2020) and a comparison on effects of vegetarian diet on gut microbiota on healthy adults in Thailand (Ruengsomwong *et al.*, 2016) are among the few reported works of healthy adults on habitual diet. More comprehensive studies should be conducted to establish the baseline of gut microbiota profile in this region.

SIGNIFICANCE OF SFA, MUFA AND PUFA ON COMPOSITIONS OF GUT MICROBIOTA COMPOSITION

Dietary fat is composed of 90% triglycerides (TG) that are made up of three fatty acid chains linked to a glycerol backbone. A substantial amount of the fatty acid is released by cleavage of the TG by the lingual lipase in the mouth and gastric lipases in the stomach (Mu and Høy, 2004). The remaining TG are almost completely hydrolysed in the proximal small intestine by the *sn*-1, 3 stereospecific pancreatic lipase and yield two free fatty acids (FFA) and a 2-monoacylglycerol (2-MG) (Rogalska *et al.*, 1990). The ionised FFA and 2-MG mix with the bile acid to form mixed micelles with phospholipids and up to 95% of these fatty acids are absorbed by the epithelial cells in the small intestine. These fatty acids are then randomly re-esterified and re-synthesised through a predominant 2-MG pathway to form new TG in the distal small intestine. These plasma TG are then packed with cholesterol, phospholipids, apoproteins to form chylomicrons and absorbed into the lymphatic and blood circulation systems. The remaining fatty acids reach the colon, where they are metabolised by the community of gut microbiota (Bauer *et al.*, 2005).

Dietary Fats Saturation

Dietary fats have fatty acids that vary in chain length, saturation, and positional distribution of fatty acids. Fatty acids are classified into SFA, MUFA, or PUFA based on their degree of saturation. Population or intervention studies of the effects of SFA, MUFA and PUFA rich diets on gut microbiota composition have either been reviewed systematically and extensively (Mokkala *et al.*, 2019; Yang *et al.*, 2020b).

SFA Rich Diet

Generally, a high SFA intake (18E% of SFA, >35E% of total fat) is inversely correlated with bacteria diversity and richness indices (Fava *et al.*, 2013), and higher *Firmicutes* to *Bacteroidetes* (F/B) ratio (David *et al.*, 2014). High F/B ratio has been associated with obese individuals (Kasai *et al.*, 2015). A study involving monozygotic twins shows that habitual SFA intake resulted in similar *Bacteroides* spp. profiles (Simões *et al.*, 2013) but a higher number of *Faecalibacterium prausnitzii* was demonstrated to reduce intestinal inflammation by inducing goblet cell proliferation and mucus production (Fava *et al.*, 2013) to maintain the epithelial integrity (Wrzosek *et al.*, 2013). Although SFA is frequently correlated with increased incidences of CVD and colon cancer, meta-analysis and systematic reviews do not support this claim (Dehghan *et al.*, 2017; Kim and Park, 2018; Kang *et al.*, 2020).

MUFA Rich Diet

A 24 weeks MUFA rich diet did not result in any significant changes in body mass index (BMI), waist circumference, body fat percentage, blood pressure or insulin resistant in 88 adults with metabolic syndrome (Fava *et al.*, 2013). High MUFA consumption also did not significantly affect bacteria richness as measured by Shannon, Chao1 and abundance based coverage (ACE) indices, the phylum distribution or F/B ratio (Pu *et al.*, 2016).

After a year of adhering to a MUFA-rich Mediterranean diet, 20 obese patients with coronary heart disease showed no significant difference in plasma glucose, and insulin and lipoprotein profile but enhanced significant growth in colonic *Roseburia*, *Oscillospira*, *Faecalibacterium prausnitzii* and *Parabacteroides distasonis* compared to the baseline using 16S rRNA pyrosequencing (454 Roche) (Haro *et al.*, 2016). However, another study reported that a MUFA-rich Mediterranean diet reduced the number of colonic *Prevotella* in obese healthy adults but increased it in adults with metabolic syndrome (Pu *et al.*, 2016). Individuals who had highly adhered

to the Mediterranean diet demonstrated lower *Escherichia coli* counts and increased commercial *Bifidobacteria* to *E. coli* ratio, which is an established healthy gut indicator (Mitsou *et al.*, 2017). The enrichment of these SCFA-producing and beneficial bacteria could also be related to the Mediterranean diet which consists of a high concentration of polyphenols and other phytochemicals found in vegetables and fruits (Muralidharan *et al.*, 2019).

PUFA Rich Diet

PUFA-based diets showed inconsistent results on gut microbiota compositions. Randomised controlled trials have demonstrated that high *n*-3 long-chain PUFA diets did not significantly alter bacterial diversity, richness, or phylum distribution compared to the control diet. The study duration varied from 30 days for adults with metabolic syndrome (Pu *et al.*, 2016), to 42 days for healthy overweight individuals (Rajkumar *et al.*, 2014), and to six months for patients with Type 2 diabetes (Balfegó *et al.*, 2016). A high dose of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) supplements failed to demonstrate any significant impact on the composition of gut bacteria (Watson *et al.*, 2017), although these fatty acids have been associated with lower plasma inflammatory markers such as C-creative protein (CRP) (Yang *et al.*, 2020a).

The effect of PUFA diet demonstrated contradictory results on the compositions of gut microbiota. High habitual intake of PUFA resulted in an increase in bacteria diversity in overweight middle-aged adults (Menni *et al.*, 2017) and this diet also promoted the abundance of *Actinobacteria* but lowered *Firmicutes* in the gut of postpartum women (Mandal *et al.*, 2016). Diets enriched with *n*-3 long-chain PUFA was positively associated with the *Lactobacillus* group, whereas *n*-6 long-chain PUFA was negatively correlated with the abundance of *Bifidobacteria* in 11 healthy and 29 overweight or obese monozygotic twin (Simões *et al.*, 2013). Reyes *et al.* (2016) reported that high habitual intake of unsaturated fatty acid and fibre diet increased the content of *Bifidobacterium longum* in young adults, with the increase being higher in lean participants than in overweight or obese participants (Reyes *et al.*, 2016). In men, the abundance of the genus *Blautia* in serum was negatively associated with *n*-3 and *n*-6 PUFA content (Org *et al.*, 2017). The abundance of *Blautia* was increased in participants with higher BMI (Org *et al.*, 2017; Liu *et al.*, 2019), or higher levels of low-density lipoprotein (LDL) and waist circumference in Chinese adults (Zeng *et al.*, 2014), but inversely associated with visceral fat accumulation in Japanese adults (Ozato *et al.*, 2019).

The discrepancy in PUFA diet studies is probably related to the study duration, variation in

the amount and sources of fats, and the pre-existing health condition of the subjects. This is proven in a study on premature infants that were fed with a mixture of fish oil and safflower oil via enterostomies for nine weeks, and the outcomes were compared to that of infants who had received standard treatment (Young *et al.*, 2017). The fish oil-enriched diet yielded varying gut microbial communities at different points in time between the study groups (Young *et al.*, 2017). Different functional pathways were inferred using microbial gene function analysis, and it revealed that the changes in the diversity of microbiota are associated with pathways related to lipid metabolism, followed by pathways related to butyrate and also specific amino acids metabolism between the intervention groups (Young *et al.*, 2017).

These studies showed inconsistent effects of fatty acid saturation on the diversity of gut microbiota and this could be due to the effect of stereo-specificity of fatty acid chains on TG, the sequencing and bioinformatic analysis methods.

EFFECTS OF STEREOSPECIFICITY ON TG OF PALM OIL AND GUT MICROBIOTA

Recently, palm oil has been identified as one of the most affordable EAT-Lancet diets along with transformation toward sustainable global food system (Hirvonen *et al.*, 2019). Palm oil is a unique oil, in which it has almost equal percentages of saturated and unsaturated fatty acids compositions (Koushki *et al.*, 2015) on the TG backbone. Similar to other vegetable oils, the *sn*-2 position in the TG of palm oil is mainly occupied by unsaturated fatty acids (May and Nesaretnam, 2014; Ong and Goh, 2002). However, in certain animal fats, particularly in lard, the *sn*-2 position is occupied by SFA (Table 2).

Increasing evidence demonstrates that the stereospecificity of fatty acids in TG molecules affect its absorbability (Ramírez *et al.*, 2001). Differing from other vegetable oils, the *sn*-1,3 position of palm oil is predominated by long-chain SFA, C18:0 and C16:0. This is evidenced by a study in which high fat palm oil diet was fed to mice and it was found that a high palm oil diet (45% E fat) resulted in overflow of palm oil into the distal intestine, probably due to lack of absorptivity of long-chain fatty acids which then trigger dysbiosis (Wit *et al.*, 2012) rather than the type of diet itself. Therefore, clinical human study using palm oil at recommended dietary intake level should be conducted to avoid pre-mature claim.

The longer fatty acid chains at *sn*-1,3 position have a low tendency of fat deposition in the adipose tissue compared to high PUFA oils in animal studies (Gouk *et al.*, 2013; 2014). It is hypothesised that at certain threshold concentration, long-chain SFA at the *sn*-1,3 position are poorly absorbed in

the small intestine due to these fatty acids having a higher melting point than the core human body temperature and therefore are more prone to form insoluble calcium soap in the high pH small intestinal environment. However, the effect of fatty acid positional distribution on palm oil intake from the habitual diet composition of gut microbiota in humans is unknown.

FUTURE PROSPECTIVES

Dietary fats alter certain species of gut microbiota and their metabolites following regular diet intake. If dietary fat could alter the gut microbiota compositions alone, the bacteria profile in Malaysians may have similar relative abundance to SFA and MUFA diets, but a lower similarity to PUFA diet. The simplified bacteria profile may consist of high abundance of *Bacteroides* spp. (phylum of *Bacteroidetes*) as identified in high SFA; *Roseburia*, *Oscillospira*, *Faecalibacterium prausnitzii* (phylum of *Firmicutes*), and *Parabacteroides distasonis* (phylum of *Bacteroidetes*) from MUFA diet; and *Actinobacteria*, and *Lactobacillus* (*Firmicutes*) as identified in high PUFA diet. However, more complex bacteria composition is anticipated as Malaysia is a multiracial country comprising of different ethnicities and cultures, each having their unique heritage food, which is also influenced by culinary attributes within Malaysia and neighbouring countries. Diversity in food, ethnicities and culture may give rise to a unique gut microbiota profile in Malaysians. Moreover, palm oil remains the most widely consumed oil in Malaysia (Kushairi *et al.*, 2019), although other imported vegetable oils are available in the Malaysian market. Therefore, the effects of fatty acids saturation and stereo-specificity of various cooking oils on Malaysian population's gut microbiota profiles might be of interest to explore.

High throughput sequencing and analytical technologies coupled with extensive bioinformatics database using analytical software (Zhao *et al.*, 2018; Onywera and Meiring, 2020) had accelerated the process of identifying colonic bacteria and predicting the functional profiles of metabolites in establishing the baseline of gut bacteria profile of Malaysian. The hope is that changes of the identified species or metabolite from the baseline could be used as a non-invasive biomarker for clinical diagnosis of diet-related cardio-metabolic or non-communicable diseases in the early stage.

ACKNOWLEDGEMENT

The authors would like to thank the Director-General of MPOB for permission to publish this article.

TABLE 2. STEREOSPECIFIC POSITIONING OF FATTY ACID (MOL %) IN TRIACYL-*SN*-GLYCEROLS OF PLANT-BASED OIL AND ANIMAL-BASED FAT

Oil/ Fat	Position	Fatty acid (mol %)							
		14:0	16:0	16:1	18:0	18:1	18:2	18:3	20-24
Peanut	TG		9		3	58	23		7
	1		14		5	59	19		4
	2		2		trace	59	39		1
	3		11		5	57	10		15
Soyabean	TG		3		2	26	17	10	43
	1		4		2	23	11		53
	2		1			37	36	6	6
	3		4		3	17	4	20	70
Linseed	TG		9		4	24	54	8	
	1		14		6	23	48	9	
	2		1		trace	22	70	7	
	3		13		6	28	45	9	
Corn	TG	11		2	29	57	1		
	1	1		3	28	50	1		
	2	18		trace	27	70	1		
	3	2		3	31	52	1		
Olive	TG		10		2	76	10	1	
	1		13		3	72	10	1	
	2		1			83	14	1	
	3		17		4	74	5		
Palm	TG		48		4	36	10		
	1		60		3	27	9		
	2		13		trace	68	18		
	3		72		8	14	3		
Cacao butter	TG		24		35	36	3	trace	1
	1		34		50	12	1	1	1
	2		2		2	87	9		
	3		37		53	9	trace		2
Beef	TG	5	27	6	17	33	5	1	
	1	4	41	6	177	20	4	1	
	2	9	17	6	9	41	5	1	
	3	1	22	6	24	37	5	1	
Lard	TG	2	27	3	13	45	9		
	1	1	10	2	30	51	6		
	2	4	72	5	2	13	3		
	3	-	trace	2	7	70	18		
Chicken	TG	1	30	6	6	45	11	1	
	1	1	47	7	8	31	5	1	
	2	trace	13	5	6	55	19	1	
	3	1	31	7	3	49	8	1	
Mutton#	TG	3	22	2	35	36	2		
	1	1	35	2	47	4	-		
	2	4	14	2	15	52	5		
	3	3	16	1	42	26	2		

Note: Trace = <0.5%, TG = intact triacylglycerols, #Results are listed for *cis*-18:1 isomers only; *trans*-18:1 was present in positions *sn*-1, *sn*-2 and *sn*-3 as 5%, 2% and 6%, respectively.

Sources: Brockerhoff and Yurkowski (1991); Brockerhoff *et al.* (1966); Christie and Moore (1971).

REFERENCES

- Almeida, A; Mitchell, A L; Boland, M; Forster, S C; Gloor, G B; Tarkowska, A; Lawley, T D and Finn, R D (2019). A new genomic blueprint of the human gut microbiota. *Nature*, 568: 499-504.
- Angelakis, E; Yasir, M; Bachar, D; Azhar, E I; Lagier, J C; Bibi, F; Jiman-Fatani, A A; Alawi, M; Bakarman, M A; Robert, C and Raoult, D (2016). Gut microbiome and dietary patterns in different Saudi populations and monkeys. *Sci. Rep.*, 6: 32191.
- Balfegó, M; Canivell, S; Hanzu, F A; Sala-Vila, A; Martínez-Medina, M; Murillo, S; Mur, T; Ruano, E G; Linares, F; Porras, N; Valladares, S; Fontalba, M; Roura, E; Novials, A; Hernández, C; Aranda, G; Sisó-Almirall, A; Rojo-Martínez, G; Simó, R and Gomis, R (2016). Effects of sardine-enriched diet on metabolic control, inflammation and gut microbiota in drug-naïve patients with Type 2 diabetes: A pilot randomized trial. *Lipids Health Dis.*, 18: 78.
- Bauer, E; Jakob, S and Mosenthin, R (2005). Principles of physiology of lipid digestion. *Asian-Aust J. Anim Sci.*, 18: 282-295.
- Brockerhoff, H and Yurkowschi, M (1991). Stereospecific analyses of several vegetable fats. *J. Lipid Res.*, 7: 62-64.
- Brockerhoff, H; Hoyle, R J and Wolmark, N (1966). Positional distribution of fatty acids in triglycerides of animal depot fats. *Biochim. Biophys. Acta - Lipids Lipid Metab.*, 116: 67-72.
- Christie, W W and Moore, J H (1971). Structures of triglycerides isolated from various sheep tissues. *J. Sci. Food Agric.*, 22: 120-124.
- Clavel, T; Desmarchelier, C; Haller, D; Gérard, P; Rohn, S; Lepage, P and Daniel, H (2014). Intestinal microbiota in metabolic diseases. *Gut Microbes.*, 5: 544-551.
- Das, B; Ghosh, T S; Kedia, S; Rampal, R; Saxena, S; Bag, S; Mitra, R; Dayal, M; Mehta, O; Surendranath, A; Travis, S P L; Tripathi, P; Nair, G B and Ahuja, V (2018). Analysis of the gut microbiome of rural and urban healthy Indians living in sea level and high-altitude areas. *Sci. Rep.*, 8: 10104.
- David, L A; Maurice, C F; Carmody, R N; Gootenberg, D B; Button, J E; Wolfe, B E; Ling, A V; Devlin, A S; Varma, Y; Fischbach, M A; Biddinger, S B; Dutton, R J and Turnbaugh, P J (2014). Diet rapidly and reproducibly alters the human gut microbiome. *Nature*, 505: 559-563.
- De Filippo, C; Cavalieri, D; Paola, M D; Ramazzotti, M; Poullet, J B; Massart, S; Collini, S; Pieraccini, G and Lionetti, P (2010). Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. *Africa Proc. Natl. Acad. Sci. USA.*, 107: 14691-14696.
- Dehghan, M; Mente, A; Zhang, X H; Swaminathan, S; Li, W; Mohan, V; Iqbal, R; Kumar, R; Wentzel-Viljoen, E; Rosengren, A; Amma, L I; Avezum, A; Chifamba, J; Diaz, R; Khatib, R; Lear, S; Lopez-Jaramillo, P; Liu, X Y; Gupta, R; Mohammadifard, N; Gao, N; Oguz, A; Ramli, A S; Seron, P; Sun, Y; Uba, A; Tsolekile, L; Wielgosz, A; Yusuf, R; Yusufali, A H; Teo, K K; Rangarajan, S; Dagenais, G; Bangdiwala, S I; Islam, S; Anand, S S; Yusuf, S and Investigators, P U R E P S (2017). Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): A prospective cohort study. *The Lancet*, 390: 2050-2062.
- Devillard, E; McIntosh, F M; Duncan, S H and Wallace, R J (2007). Metabolism of linoleic acid by human gut bacteria: Different routes for biosynthesis of conjugated linoleic acid. *J. Bacteriol Res.*, 189: 2566-2570.
- Dhakan, D B; Maji, A; Sharma, A K; Saxena, R; Pulikkan, J; Grace, T; Gomez, A; Scaria, J; Amato, K R and Sharma, V K (2019). The unique composition of Indian gut microbiome, gene catalogue, and associated fecal metabolome deciphered using multi-omics approaches. *GigaScience*, 8: 1-20.
- Fava, F; Gitau, R; Griffin, B A; Gibson, G R; Tuohy, K M and Lovegrove, J A (2013). The type and quantity of dietary fat and carbohydrate alter faecal microbiome and short-chain fatty acid excretion in a metabolic syndrome 'at-risk' population. *Int. J. Obes.*, 37: 216-223.
- Febinia, C; Malik, S; Djuwita, R; Weta, I; Wihandani, D; Maulida, R; Sudoyo, H and Holmes, A (2020). Population stratification in the gut microbiota of Bali is associated with transitional lifestyle. *Research Square General Microbiol.* DOI:10.21203/rs.3.rs-40341/v1
- Fontana, L; Meyer, T E; Klein, S and Holloszy, J O (2004). Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis in humans. *Proc. Natl. Acad. Sci. USA.*, 101: 6659-6663.
- Ganesan, K; Chung, S K; Vanamala, J and Xu, B (2018). Causal relationship between diet-induced gut microbiota changes and diabetes: A novel strategy to transplant *Faecalibacterium prausnitzii* in preventing diabetes. *Int. J. Mol. Sci.*, 19: 3720.

- Ghosh, S S; Wang, J; Yannie, P J and Ghosh, S (2020). Intestinal barrier dysfunction, LPS translocation and disease development. *J. Endocrine Soc.*, 4: 1-15.
- Gouk, S W; Cheng, S F; Mok, J S L; Ong, A S H and Chuah, C H (2013). Long-chain SFA at the *sn*-1, 3 positions of TAG reduce body fat deposition in C57BL/6 mice. *Br. J. Nutr.*, 110: 1987-1995.
- Gouk, S W; Cheng, S F; Ong, A S H and Chuah, C H (2014). Stearic acids at *sn*-1, 3 positions of TAG are more efficient at limiting fat deposition than palmitic and oleic acids in C57BL/6 mice. *Br. J. Nutr.*, 111: 1174-1180.
- Guo, X; Li, J; Tang, R; Zhang, G; Zeng, H; Wood, R J and Liu, Z (2017). High fat diet alters gut microbiota and the expression of paneth cell-antimicrobial peptides preceding changes of circulating inflammatory cytokines. *Mediators of Inflammation*, 2017: 9474896.
- Gupta, V K; Paul, S and Dutta, C (2017). Geography, ethnicity or subsistence-specific variations in human microbiome composition and diversity. *Front Microbiol.*, 8: 1162-1162.
- Haro, C; Rangel-Zúñiga, O A; Alcalá-Díaz, J F; Gómez-Delgado, F; Pérez-Martínez, P; Delgado-Lista, J; Quintana-Navarro, G M; Landa, B B; Navas-Cortés, J A; Tena-Sempere, M; Clemente, J C; López-Miranda, J; Pérez-Jiménez, F and Camargo, A (2016). Intestinal microbiota is influenced by gender and body mass index. *PLoS ONE*, 11: e0154090.
- He, Y; Wu, W; Zheng, H M; Li, P; McDonald, D; Sheng, H F; Chen, M X; Chen, Z H; Ji, G Y; Zheng, Z D X; Mujagond, P; Chen, X J; Rong, Z H; Chen, P; Lyu, L Y; Wang, X; Wu, C B; Yu, N; Xu, Y J; Yin, J; Raes, J; Knight, R; Ma, W J and Zhou, H W (2018). Regional variation limits applications of healthy gut microbiome reference ranges and disease models. *Nature Med.*, 24: 1532-1535.
- Hirvonen, K; Bai, Y; Headey, D and Masters, W A (2019). Affordability of the EAT-Lancet reference diet: A global analysis. *Lancet Glob Health*, 7: 1-8.
- Illiano, P; Brambilla, R and Parolini, C (2020). The mutual interplay of gut microbiota, diet and human disease. *FEBS Journal*, 287: 833-855.
- Jia, F; Peng, S; Green, J; Koh, L; Chen, X and Chen, X (2020). Soybean supply chain management and sustainability: A systematic literature review. *J. Clean Prod.*, 255: 120254.
- Jain, A; Li, X H and Chen, W N (2018). Similarities and differences in gut microbiome composition correlate with dietary patterns of Indian and Chinese adults. *AMB Expr.*, 8: 104.
- Kang, Z Q; Yang, Y and Xiao, B (2020). Dietary saturated fat intake and risk of stroke: Systematic review and dose – response meta-analysis of prospective cohort studies. *Nutr. Metab Cardiovas Dis.*, 30: 179-189.
- Kasai, C; Sugimoto, K; Moritani, I; Tanaka, J; Oya, Y; Inoue, H; Tameda, M; Shiraki, K; Ito, M; Takei, Y and Takase, K (2015). Comparison of the gut microbiota composition between obese and non-obese individuals in a Japanese population, as analysed by terminal restriction fragment length polymorphism and next-generation sequencing. *BMC Gastroenterol.*, 15: 100.
- Kaur, K; Khatri, I; Akhtar, A; Subramanian, S and Ramya, T N C (2020). Metagenomics analysis reveals features unique to Indian distal gut microbiota. *PLoS ONE*, 15: e0231197.
- Kushairi, A; Abdullah, M O; Nambiappan, B; Hishamuddin, E; Zanal Bidin, M N I; Ghazali, R; Subramaniam, V; Sundram, S and Parveez, G K A (2019). Oil palm economic performance in Malaysia and R&D progress in 2018. *J. Oil Palm Res. Vol.* 31: 165-194.
- Kim, M and Park, K (2018). Dietary fat intake and risk of colorectal cancer: A systematic review and meta-analysis of prospective studies. *Nutrients*, 10: 1963.
- Koushki, M; Nahidi, M and Cheraghali, F (2015). Physico-chemical properties, fatty acid profile and nutrition in palm oil. *Arch. Adv. Biosci.*, 6: 117-134.
- Kriss, M; Hazleton, K Z; Nusbacher, N M; Martin, C G and Catherine, A L (2018). Low diversity gut microbiota dysbiosis: Drivers, functional implications and recovery. *Curr. Opin Microbiol.*, 44: 34-40.
- Kushida, M; Sugawara, S; Asano, M; Yamamoto, K; Fukuda, S and Tsuduki, T (2019). Effects of the 1975 Japanese diet on the gut microbiota in younger adults. *J. Nutr. Biochem.*, 64: 121-127.
- Leeming, E R; Johnson, A J; Spector, T D and Roy, C L (2019). Effect of diet on the gut microbiota: Rethinking intervention duration. *Nutrients*, 11: 2862.
- Liao, M; Xie, Y; Mao, Y; Lu, Z; Tan, A; Wu, C; Zhang, Z; Chen, Y; Li, T; Ye, Y; Yao, Z; Jiang, Y; Li, H; Li, X; Yang, X; Wang, Q and Mo, Z (2018). Comparative analyses of fecal microbiota in Chinese isolated Yao

- population, minority Zhuang and rural Han by 16S rRNA sequencing. *Sci. Rep.*, 8: 1142.
- Ling, Z; Liu, X; Luo, Y; Yuan, L; Nelson, K E; Wang, Y; Xiang, C and Li, L (2013). Pyrosequencing analysis of the human microbiota of healthy Chinese undergraduates. *BMC Genomics*, 14: 390.
- Liu, Y; Qin, S T; Song, Y L; Feng, Y; Lv, N; Xue, Y; Liu, F; Wang, S X; Zhu, B L; Ma, J M and Yang, H X (2019). The perturbation of infant gut microbiota caused by cesarean delivery is partially restored by exclusive breastfeeding. *Front Microbiol.*, 10: 598.
- Mandal, S; Godfrey, K M; McDonald, D; Treuren, W V; Bjørnholt, J V; Midtvedt, T; Moen, B; Rudi, K; Knight, R; Brantsæter, A L; Peddada, S D and Eggesbø, M (2016). Fat and vitamin intakes during pregnancy have stronger relations with a pro-inflammatory maternal microbiota than does carbohydrate intake. *Microbiome*, 4: 55.
- May, C Y and Nesaretnam, K (2014). Research advancements in palm oil nutrition. *Eur. J. Lipid Sci. Tech.*, 116: 1301-1315.
- Menni, C; Jackson, M A; Pallister, T; Steves, C J; Spector, T D and Valdes, A M (2017). Gut microbiome diversity and high-fibre intake are related to lower long-term weight gain. *Int. J. Obes.*, 41: 1099-1105.
- Mirmonsef, P; Zariffard, M R; Gilbert, D; Makinde, H; Landay, A L and Spear, G T (2012). Short-chain fatty acids induce pro-inflammatory cytokine production alone and in combination with Toll-like receptor ligands. *Am. J. Reprod. Immunol.*, 67: 391-400.
- Mitsou, E K; Kakali, A; Antonopoulou, S; Mountzouris, K C; Yannakoulia, M; Panagiotakos, D B and Kyriacou, A (2017). Adherence to the Mediterranean diet is associated with the gut microbiota pattern and gastrointestinal characteristics in an adult population. *Br. J. Nutr.*, 117: 1645-1655.
- Mokkala, K; Houttu, N; Cansev, T and Laitinen, K (2019). Interactions of dietary fat with the gut microbiota: Evaluation of mechanisms and metabolic consequences. *Clin. Nutr.*, 39: 994-1018.
- Moreno-Indias, I; Sánchez-Alcoholado, L; García-Fuentes, E; Cardona, F; Queipo-Ortuño, M I and Tinahones, F J (2016). Insulin resistance is associated with specific gut microbiota in appendix samples from morbidly obese patients. *Am. J. Transl Res.*, 8: 5672-5684.
- Mozaffarian, D (2016). Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: A comprehensive review. *Circulation*, 133: 187-225.
- Mu, H and Høy, C E (2004). The digestion of dietary triacylglycerols. *Prog. Lipid Res.*, 43: 105-133.
- Muegge, B D; Kuczynski, J; Knights, D; Clemente, J C; González, A; Fontana, L; Henrissat, B; Knight, R and Gordon, J I (2011). Diet drives convergence in gut microbiome functions across mammalian phylogeny and within humans. *Science*, 332: 970-974.
- Muralidharan, J; Galiè, S; Hernández-Alonso, P; Bulló, M and Salas-Salvadó, J (2019). Plant based fat, dietary patterns rich in vegetable fat and gut microbiota modulation. *Front Nutr.*, 6: 157.
- Murphy, E A; Velazquez, K T and Herbert, K M (2015). Influence of high-fat diet on gut microbiota. *Curr. Opin Clin. Nutr. Metab. Care*, 18: 515-520.
- Nam, Y D; Jung, M J; Roh, S W; Kim, M S and Bae, J W (2011). Comparative analysis of Korean human gut microbiota by barcoded pyrosequencing. *PLoS ONE*, 6: e22109-e22109.
- Nishijima, S; Suda, W; Oshima, K; Kim, S W; Hirose, Y; Morita, H and Hattori, M (2016). The gut microbiome of healthy Japanese and its microbial and functional uniqueness. *DNA Res.*, 23: 125-133.
- O'Keefe, S J (2016). Diet, microorganisms and their metabolites, and colon cancer. *Nat. Rev. Gastroenterol Hepatol.*, 13: 691-706.
- Ong, S H A and Goh, S H (2002). Palm oil: A healthful and cost-effective dietary component. *Food Nutr. Bull.*, 23: 11-22.
- Onywera, H and Meiring, T L (2020). Comparative analyses of Ion Torrent V4 and Illumina V3-V4 16S rRNA gene metabarcoding methods for characterization of cervical microbiota: Taxonomic and functional profiling. *Sci. African*, 7: e00278.
- Org, E; Blum, Y; Kasela, S; Mehrabian, M; Kuusisto, J; Kangas, A J; Soininen, P; Wang, Z; Ala-Korpela, M; Hazen, S L; Laakso, M and Lusi, A J (2017). Relationships between gut microbiota, plasma metabolites and metabolic syndrome traits in the METSIM cohort. *Genome Biol.*, 18: 70.
- Ou, J; Carbonero, F; Zoetendal, E G; Delany, J P; Wang, M; Newton, K; Gaskins, H R and O'Keefe, S J (2013). Diet, microbiota, and microbial metabolites in colon cancer risk in rural Africans and African Americans. *Am. J. Clin. Nutr.*, 98: 111-120.
- Ozato, N; Saito, S; Yamaguchi, T; Katashima, M; Tokuda, I; Sawada, K; Katsuragi, Y; Imoto, S; Ihara, K and Nakaji, S (2019). Association between nutrients

- and visceral fat in healthy Japanese adults: A 2-year longitudinal study brief title: Micronutrients associated with visceral fat accumulation. *Nutrients*, 11: 2698.
- Parveez, G K A; Hishamuddin, E; Loh S K; Abdullah, M O; Salleh, K M; Zanal Bidin, M N I; Sundram, S; Azizul Hassan, Z A and Idris, Z (2020). Oil palm economic performance in Malaysia and R&D progress in 2019. *J. Oil Palm Res. Vol.* 32: 159-190.
- Pauwels, E K J (2011). The protective effect of the Mediterranean diet: Focus on cancer and cardiovascular risk. *Med. Princ. Pract.*, 20: 103-111.
- Pilorgé, E (2020). Sunflower in the global vegetable oil system: Situation, specificities and perspectives. *OCL*, 27: 34.
- Plummer, E; Bulach, D; Carter, G and Albert, M J (2020). Gut microbiome of native Arab Kuwaitis. *Gut Pathogens*, 12: 10.
- Pu, S; Khazanehei, H; Jones, P J and Khafipour, E (2016). Interactions between obesity status and dietary intake of monounsaturated and polyunsaturated oils on human gut microbiome profiles in the Canola Oil Multicenter Intervention Trial (COMIT). *Front in Microbiol.*, 7: 1-14.
- Pulipati, P; Sarkar, P; Jakkampudi, A; Kaila, V; Sarkar, S; Unnisa, M; Reddy, D N; Khan, M and Talukdar, R (2020). The Indian gut microbiota-Is it unique? *Indian J. Gastroenterol.*, 39: 133-140.
- Qian, L; Gao, R; Hong, L; Pan, C; Li, H; Huang, J and Qin, H (2018). Association analysis of dietary habits with gut microbiota of a native Chinese community. *Exp. Ther. Med.*, 16: 856-866.
- Rajkumar, H; Mahmood, N; Kumar, M; Varikuti, S R; Challa, H R and Myakala, S P (2014). Effect of probiotic (VSL#3) and omega-3 on lipid profile, insulin sensitivity, inflammatory markers, and gut colonization in overweight adults: A randomized, controlled trial. *Mediat Inflamm.*, 2014: 348959.
- Ramírez, M; Amatea, L and Gilb, A (2001). Absorption and distribution of dietary fatty acids from different sources. *Early Hum. Dev.*, 65: S95-S101.
- Requena, T; Martínez-Cuesta, M C and Peláez, C (2018). Diet and microbiota linked in health and disease. *Food Funct.*, 9: 688-704.
- Reyes, L M; Vázquez, R G; Arroyo, S M C; Avalos, A M; Castillo, P A R; Pérez, D A C; Terrones, I R; Ibáñez, N R; Magallanes, M M R; Langella, P; Humarán, L B and Espinosa, A A (2016). Correlation between diet and gut bacteria in a population of young adults. *Int. J. Food Sci Nutr.*, 67: 470-478.
- Rogalska, E; Ransac, R and Verger, R (1990). Stereoselectivity of lipases II. Stereoselective hydrolysis of triglycerides by gastric and pancreatic lipases. *J. Biol. Chem.*, 33: 20271-20276.
- Ruengsomwong, S; La-Ongkham, O; Jiang, J; Wannissorn, B; Nakayama, J and Nitisinprasert, S (2016). Microbial community of healthy Thai vegetarians and non-vegetarians, their core gut microbiota, and pathogen risk. *J. Microbiol Biotechnol.*, 26: 1723-1735.
- Senghor, B; Sokhna, C; Ruimy, R and Lagier, J C (2018). Gut microbiota diversity according to dietary habits and geographical provenance. *Human Microbiome J.*, 8: 1-9.
- Shetty, S A (2018). Gut microbiota features of the geographically diverse Indian population. *BioRxiv*, 478586. DOI:10.1101/478586.
- Shin, J H; Sim, M; Lee, J Y and Shin, D M (2016). Lifestyle and geographic insights into the distinct gut microbiota in elderly women from two different geographic locations. *J. Physiol. Anthropol.*, 35: 31.
- Shortt, C; Hasselwander, O; Meynier, A; Nauta, A; Fernández, E N; Putz, P; Rowland, I; Swann, J; Türk, J; Vermeiren, J and Antoine, J M (2018). Systematic review of the effects of the intestinal microbiota on selected nutrients and non-nutrients. *Eur. J. Nutr.*, 57: 25-49.
- Silveira-Nunes, G; Durso, D F; De Oliveira, L R A; Cunha, E H M; Maioli, T U; Vieira, A T; Speziali, E; Corrêa-Oliveira, R; Martins-Filho, O A; Teixeira-Carvalho, A; Franceschi, C; Rampelli, S; Turroni, S; Brigidi, P and Faria, A M C (2020). Hypertension is associated with intestinal microbiota dysbiosis and inflammation in a Brazilian population. *Front Pharmacol.*, 11: 258.
- Simões, C D; Maukonen, J; Kaprio, J; Rissanen, A; Pietiläinen, K H and Saarela, M (2013). Habitual dietary intake is associated with stool microbiota composition in monozygotic twins. *J. Nutr.*, 143: 417-423.
- Snijder, M B; Galenkamp, H; Prins, M; Derks, E M; Peters, R J G; Zwinderman, A H and Stronks, K (2017). Cohort profile: The healthy life in an urban setting (HELIUS) study in Amsterdam, The Netherlands. *BMJ Open*, 7: e017873-e017873.
- Tandon, D; Haque, M M R S; Shaikh, S P S; Dubey, A K and Mande, S S (2018). A snapshot of gut microbiota

of an adult urban population from Western region of India. *PLoS ONE*, 13: e0195643.

Tolhurst, G; Heffron, H; Lam, Y S; Parker, H E; Habib, A M; Diakogiannaki, E; Cameron, J; Grosse, J; Reimann, F and Gribble, F M (2012). Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. *Diabetes*, 61: 364-371.

Tomova, A; Bukovsky, I; Rembert, E; Yonas, W; Alwarith, J; Barnard, N and Kahleova, N (2019). Review article: The effects of vegetarian and vegan diets on gut microbiota. *Front in Nutr.*, 6: 157.

Tsuji, H; Matsuda, K and Nomoto, K (2018). Counting the countless: Bacterial quantification by targeting rRNA molecules to explore the human gut microbiota in health and disease. *Front Microbiol.*, 9: 1417.

Tyakht, A V; Kostyukova, E S; Popenko, A S; Belenikin, M S; Pavlenko, A V; Larin, A K; Karpova, I Y; Selezneva, O V; Semashko, T A; Ospanova, E A; Babenko, V V; Maev, I V; Cheremushkin, S V; Kucheryavyy, Y A; Shcherbakov, P L; Grinevich, V B; Efimov, O I; Sas, E I; Abdulkhakov, R A; Abdulkhakov, S R; Lyalyukova, E A; Livzan, M A; Vlassov, V V; Sagdeev, R Z; Tsukanov, V V; Osipenko, M F; Kozlova, I V; Tkachev, A V; Sergienko, V I; Alexeev, D G and Govorun, V M (2013). Human gut microbiota community structures in urban and rural populations in Russia. *Nat. Commun.*, 4: 2469.

Valdes, A; Walter, J; Segal, E and Spector, T (2018). Role of the gut microbiota in nutrition and health. *BMJ*, 361: k2179.

Watson, H; Mitra, S; Croden, F C; Taylor, M; Wood, H M; Perry, S L; Spencer, J A; Quirke, P; Toogood, G J; Lawton, C L; Dye, L; Loadman, P M and Hull, M A (2017). A randomised trial of the effect of omega-3 polyunsaturated fatty acid supplements on the human intestinal microbiota. *Gut*, 67: 314968.

Wit, N D; Oosterink, E; Bosch-Vermeulen, H; Keshtkar, S; Duval, C N C; Vogel-Van B N J D; Muller, M and Meer, R V D (2012). Saturated fat stimulates obesity and hepatic steatosis and affects gut microbiota composition by an enhanced overflow of dietary fat to the distal intestine. *Mucosal Biol.*, 303: G589-G599.

Wrzosek, L; Miquel, S; Noordine, M L; Bouet, S; Chevalier-Curt, M J; Robert, V; Philippe, C; Bridonneau, C; Cherbuy, C; Robbe-Masselot, C; Langella, P and Thomas, M (2013). *Bacteroides thetaiotaomicron* and *Faecalibacterium prausnitzii* influence the production of mucus glycans and the development of goblet cells in the colonic epithelium of a gnotobiotic model rodent. *BMC Biol.*, 11: 61.

Yang, B; Ren, X L; Li, Z H; Shi, M Q; Ding, F; Su, K P; Guo, X J and Li, D (2020a). Lowering effects of fish oil supplementation on proinflammatory markers in hypertension: Results from a randomized controlled trial. *Food Funct.*, 11: 1779-1789.

Yang, Q; Liang, Q; Balakrishnan, B; Belobrajdic, D P; Feng, Q J and Zhang, W (2020b). Role of dietary nutrients in the modulation of gut microbiota: A narrative review. *Nutrients*, 12: 381.

Yang, S J; Li, X Y; Yang, F; Zhao, R; Pan, X D; Liang, J Q; Tian, L; Li, X Y; Liu, L T; Xing, Y W and Wu, M (2019). Gut microbiota-dependent marker TMAO in promoting cardiovascular disease: Inflammation mechanism, clinical prognostic, and potential as a therapeutic target. *Front Pharmacol.*, 10: 1360.

Yasir, M; Angelakis, E; Bibi, F; Azhar, E; Bachar, D; Lagier, J C; Gaborit, B; Hassan, A M; Jiman-Fatani, A A; Alshali, K Z; Robert, C; Dutour, A and Raoult, D (2015). Comparison of the gut microbiota of people in France and Saudi Arabia. *Nutr. Diabetes*, 5: e153.

Yatsunenkov, T; Rey, F E; Manary, M J; Trehan, I; Dominguez-Bello, M G; Contreras, M; Magris, M; Hidalgo, G; Baldassano, R N; Anokhin, A P; Heath, A C; Warner, B; Reeder, J; Kuczynski, J; Caporaso, J G; Lozupone, C A; Lauber, C; Clemente, J C; Knights, D; Knight, R and Gordon, J I (2012). Human gut microbiome viewed across age and geography. *Nature*, 486: 222-227.

Young, A J; Marriott, B P; Champagne, C M; Hawes, M R; Montain, S J; Johannsen, N M; Berry, K and Hibbeln, J R (2017). Blood fatty acid changes in healthy young Americans in response to a 10-week diet that increased n-3 and reduced n-6 fatty acid consumption: A randomised controlled trial. *Br. J. Nutr.*, 23: 1-13.

Zeng, Q; He, Y; Dong, S Y; Zhao, X L; Chen, Z H; Song, Z Y; Chang, G; Yang, F and Wang, Y J (2014). Optimal cut-off values of BMI, waist circumference and waist: Height ratio for defining obesity in Chinese adults. *Br. J. Nutr.*, 112: 1735-1744.

Zhang, J; Guo, Z; Xue, Z; Sun, Z; Zhang, M; Wang, L; Wang, G; Wang, F; Xu, J; Cao, H; Xu, H; Lv, Q; Zhong, Z; Chen, Y; Qimuge, S; Menghe, B; Zheng, Y; Zhao, L; Chen, W and Zhang, H (2015). A phylo-functional core of gut microbiota in healthy young Chinese cohorts across lifestyles, geography and ethnicities. *The ISME J.*, 9: 1979-1990.

Zhang, W; Li, J; Lu, S; Han, N; Miao, J; Zhang, T; Qiang, Y; Kong, Y; Wang, H; Gao, T; Liu, Y; Li, X; Peng, X; Chen, X; Zhao, X; Che, J; Zhang, L; Chen, X; Zhang, Q; Hu, M; Li, Q and Kan, B (2019). Gut

microbiota community characteristics and disease-related microorganism pattern in a population of healthy Chinese people. *Sci. Rep.*, 9: 1594.

Zhao, D Y; Yuan, B; Carry, E; Pasinetti, G M; Ho, L; Faith, J; Mogno, I; Simon, J and Wu, Q L

(2018). Development and validation of an ultra-high performance liquid chromatography/triple quadrupole mass spectrometry method for analyzing microbial-derived grape polyphenol metabolites. *J. Chromatogr. B. Analyt. Technol. Biomed Life Sci.*, 1: 34-45.

ARTICLE IN PRESS