**American Journal of Life Sciences**
2021; 9(6): 162-172
http://www.sciencepublishinggroup.com/j/ajls
doi: 10.11648/j.ajls.20210906.12
ISSN: 2328-5702 (Print); ISSN: 2328-5737 (Online)

# Dietary Fiber, Gut Microbiota, Short-Chain Fatty Acids, and Host Metabolism

**Linyue Hou†, Yuneng Yang†, Baosheng Sun†, Youlin Jing†, Weixi Deng***

Department of Modern Agriculture, Zunyi Vocational and Technical College, Zunyi, China

**Email address:**
sxauLynn@163.com (Linyue Hou), 63114177@qq.com (Yuneng Yang), xinxiaobao85@163.com (Baosheng Sun), 846326673@qq.com (Youlin Jing), 574230619@qq.com (Weixi Deng)

*Corresponding author

† Linyue Hou, Yuneng Yang, Baosheng Sun and Youlin Jing are co-first authors.

**To cite this article:**
Linyue Hou, Yuneng Yang, Baosheng Sun, Youlin Jing, Weixi Deng. Dietary Fiber, Gut Microbiota, Short-Chain Fatty Acids, and Host Metabolism. *American Journal of Life Sciences*. Vol. 9, No. 6, 2021, pp. 162-172. doi: 10.11648/j.ajls.20210906.12

**Received**: October 13, 2021; **Accepted**: November 5, 2021; **Published**: November 12, 2021

**Abstract:** With the rapid development of gut microbiological research and high-throughput sequencing technology, we have gained a better understanding of the effects of the gut microbiota and its metabolites such as short-chain fatty acids (SCFAs) on the metabolism of hosts. This effect was found closely related with the consumed dietary fiber by hosts. Dietary fiber has been proven to be very important for hosts. However, hosts such as human, chickens and other monogastric animals cannot digest dietary fiber due to a lack of endogenous fiber-degrading enzymes; therefore, they must rely on gut microorganisms who own endogenous fiber-degrading enzymes such as carbohydrate-active enZymes (CAZymes) encoded by gene. Excellent fiber-degrading bacteria include members of Bacteroidetes phylum such as *Bacteroides* and *Prevotella* and members of Firmicutes phylum including *Ruminococcus*, *Fibrobacter*, *Butyrivibrio*, *Ruminiclostridium* and so on. These fiber-degrading bacteria degrade fiber into monosaccharides via different degrading mechanisms. For instance, Bacteroidetes degrade a dozen kinds of plant fiber using its unique arm-polysaccharide utilization locus (PUL). In contrast to Bacteroidetes, members of the Firmicutes use gram-positive PULs (gp PULs) to process fiber. Some members of the Firmicutes can degrade cellulose and hemicellulose through the cellulosome pathway. And then some oligosaccharides and glucose produced by dietary fiber degradation can be used as carbon and energy sources for microbial growth, thus increasing the diversity of microorganisms. Dietary fiber is the substrate of gut microorganisms. The left monosaccharides are fermented into short-chain fatty acids (SCFAs) by SCFA-producing bacteria including *Bifidobacterium*, *Phascolarctobacterium*, *Faecalibacterium* and so on via different pathways. SCFAs mainly include acetate, propionate and butyrate. SCFAs can further regulate the host's metabolism including energy metabolism, host appetite, liver metabolism and the glucose balance via SCFA receptors including GPR41 and GPR43 or other mechanisms. Therefore, gut microorganisms are also called our “second genome” or “forgotten organs”. In this paper, we provide an overview of the interactions among dietary fiber, gut microbiota, SCFAs and host metabolism.

**Keywords:** Dietary Fiber, Gut Microbiota, Short-Chain Fatty Acid, Host Metabolism

## 1. Dietary Fiber and Gut Microbiota

### *1.1. Dietary Fiber and Gut Microbial Diversity*

Gut microbial diversity is a hot topic in research on gut microorganisms, and it is also the focus of the Metahit and HMP projects [1, 2]. The decrease in food diversity is the main factor related to the decrease in gut microbial diversity for people in modern society [3]. The decrease in dietary fiber in food is another important factor. Research has shown that the gut microbial diversity of mice fed a low-fiber diet is lower than that of mice fed a high-fiber diet. Diversity loss intensifies and species become almost extinct in each subsequent generation of mice raised on a low-fiber diet [4]. Among the gut microorganisms lost in mice are Bacteroidetes species, which have an excellent ability to degrade fiber. This leads to the starvation of other microorganisms that cannot degrade fiber because they cannot share the monosaccharides produced from the degradation of fiber by Bacteroidetes [5]. Moreover, a severe loss of gut microorganisms will result in

chronic diseases in the host [6]. In the absence of dietary fiber, *Bacteroides thetaiotaomicron* and *Bacteroides caccae* degrade the mucus layer instead of dietary fiber to obtain a carbon source, resulting in a thinner mucus layer in the gut [7]. In contrast, the intestinal mucus layer of mice fed a fiber-rich diet is thicker, meaning that they are least likely to be infected by *Citrobacter rodentium* [7]. Similarly, a previous study found that the gut microbial diversity of the hunter-gatherer Haza people, who consume more fibrous plants, is 30% higher than that of the Italian urban population, who consume a low-fiber diet [8]. This highlights the fact that dietary fiber supplementation is necessary for the maintenance of gut microbial diversity. However, notably, monogastric animals must rely on fiber-degrading bacteria to degrade dietary fiber due to a lack endogenous fiber-degrading enzymes.

### *1.2. Dietary Fiber and Fiber-Degrading Bacteria*

#### *1.2.1. Bacteroidetes*

Bacteroidetes is the most abundant gram-negative bacteria phylum in the rumen and human large intestine. It is also the most well-known gut bacteria. Bacteroidetes species are "generalists" that degrade dietary fiber polysaccharides [9]. Excellent fiber-degradation Bacteroidetes bacteria include the *Bacteroides* and *Prevotella* genera.

***(i) Bacteroides***

*Bacteroides* is a typical genus of Bacteroidetes, which contains many excellent fiber-degrading species. Among them, *Bacteroides caecigallinarum* can hydrolyze dietary polysaccharides [10], and *Bacteroides ovatus*, *Bacteroides fragilis*, *Bacteroides intestinalis*, *Bacteroides eggerthii*, and *Bacteroides uniformis* [11] can degrade xylan to xylose.

*Bacteroides thetaiotamicron* is one of the best carbohydrate-degrading bacteria. It was the first member of *Bacteroides* to be genome sequenced. Its genome revealed that it is a highly adaptive saccharifying bacteria that can adjust more than one-quarter of its own genes to be in an active state to degrade polysaccharides [12]. *B. thetaiotaimicron* can degrade rhamnogalacturonan-II (RG-II), which is the most complex glycan known at present [13], and it can cleave 20 of the 21 different glycoside bonds in RG-II. It also targets α-mannoside in the host glycoprotein N-glycan [14]. *B. thetaiotaimicron* and *B. ovatus* can also release outer membrane vesicles (OMVs) containing glycoside hydrolases [15], which can degrade fructan and inulin remotely to support the growth of other *Bacteroides* species that cannot degrade these polysaccharides [16, 17]. The mutual benefits among gut microorganisms are very important for the maintenance of microbial diversity.

***(ii) Prevotella***

*Prevotella* is also an excellent fiber-degrading Bacteroidetes genus. It can produce xylanase to decompose plant fiber [18]. When fructooligosaccharides, sorghum, and corn arabinoxylans were provided as substrates, the total yield of short chain fatty acids of the *Prevotella* enterotype was found to be greater than those of the *Bacteroides* enterotype, which indicated that *Prevotella* has a stronger ability to utilize fiber [19]. *Prevotella* is prevalent in people who consume a fiber-rich diet [20]. The study concluded that compared with Italian children, who consume a low-fiber diet, African children, who consume a high-fiber diet, have unique *Prevotella*, *Xylanibacter,* and *Treponema* species. These bacteria contain genes that degrade cellulose and xylan, which can maximize the amount of energy obtained from plant polysaccharides [21]. *Prevotella* became the most diverse and dominant genus in the intestines of pigs when they were fed a solid diet [22].

#### *1.2.2. Firmicutes*

In contrast with Bacteroidetes, Firmicutes species are regarded as "specialists" in fiber degradation. They act specifically on plant polysaccharides (starch and fructose) and oligosaccharides [23]. Among the members of Firmicutes, the Ruminococcus, Fibrobacter, Butyrivibrio, Clostridium and Roseburia genera are excellent fiber-degrading genera.

***(i) Ruminococcus***

The *Ruminococcus* genera includes the excellent cellulose-degrading species *Ruminococcus albus* and *Ruminococcus flavefaciens*. They can produce a lot of cellulase and hemicellulase to degrade fiber. *Ruminococcus flavus* can also degrade fiber through the cellulosome.

***(ii) Fibrobacter***

Fibrobacteres is a gram-negative, anaerobic, cellulose-degrading phylum. Its sole genus, *Fibrobacter*, is one of the most active and important cellulose-degrading bacteria [24]. The genome sequence of the representative strain *Fibrobacter saccharogenes S85* highlights its specificity for cellulose degradation [25]. It was found that *F. saccharogenes S85* could degrade more cellulose when co-cultured with *Ruminococcus flavefaciens* [26]. *Fibrobacter saccharogenes* was first isolated from the rumen by Hangate [27]. At present, *Fibrobacter succinogenes* and *Fibrobacter intestinalis* are the two well-described *Fibrobacter* species.

***(iii) Butyrivibrio***

*Butyrivibrio fibrisolvens* is a gram-positive species that can hydrolyze xylan in the rumen. It plays a key role in fiber digestion and can degrade hemicellulose and ferment it to produce pentose [28]. The genome of *Butyrivibrio proteoclasticus B316T* encodes a large number of polysaccharide-degrading enzymes, which can use hemicellulose (xylan), pectin, and other polysaccharides to produce butyrate [29]. *Butyrivibrio* can utilize pectin [30].

***(iv) Ruminiclostridium***

*Ruminiclostridium thermocellum* can produce cellulosomes composed of cellulase and hemicellulase to rapidly hydrolyze cellulose substrates [31]. The three cellulase subunits of *Ruminiclostridium josui* include the full-length scaffold protein CIPA, endoglucan cellulase RjCel5B, and endoxylanase RjXyn10C. A gene cluster found in its genome encodes 11 proteins, which form cellulosomes [32].

## 2. Mechanisms of Dietary Fiber Degradation by the Gut Microbiota

### *2.1. Adhesion*

Adhesion to a substrate is the first stage in the degradation of plant-cell-wall polysaccharides by gut microorganisms. Bacteria usually enter digestible tissues from the pores or damaged parts of plant tissues and begin to degrade them from the inside to the outside. After adhesion, gut microorganisms form active digestive symbionts in the attached area, and nutrients are released with the degradation of the substrate. The molecular mechanism of major anaerobic gut microorganisms involved in substrate adhesion remains unclear, but it may involve different substrates, binding modules, and carbohydrates on glycoproteins in enzymes and structural proteins. In research on the cellulose degrading bacterium *F. succinogenes*, 13 kinds of cellulose proteins have been found [32].

### *2.2. Carbohydrate-Active enZymes (CAZymes) Released by the Gut Microbiota*

Usually, fiber-degrading bacteria degrade dietary fiber through Carbohydrate-Active enZymes (CAZymes) encoded by their genomes. The genome of members of Bacteroides encode an average of 137.1 CAZymes, so they can utilize a wide range of dietary polysaccharides from plants and complex carbohydrates from hosts, such as mucopolysaccharides [33]. In contrast, most members of the Firmicutes phylum encode an average of 39.6 carbohydrate-active enzymes per genome [34]. Compared with the gut microbial genome, the human genome only encodes 97 glycoside hydrolases (GHs), and a maximum of 17 of these 97 enzymes only degrade starch, sucrose, lactose, and other polysaccharides, but not dietary fiber polysaccharides [35] It is also amazing that no genes encoding for cellulosic or hemicellulosic digestive enzymes were found in the giant panda genome in a study conducted in 2010 [36].

CAZymes are divided into six families, including glycoside hydrolases (GHs), glycosyltransferases (GTs), polysaccharide lyases (PLs), carbohydrate esterases (CEs), carbohydrate binding modules (CBMs), and accessory module enzymes (AAs). Cellulase and xyloglucosase are mainly distributed in the GH5, GH6, GH9, and GH12 families [37]. Xylanases are limited to the GH10 and GH11 families, while pectinases are found in the GH28, GH88, PL1, and PL2 families. GH3 and GH43 mainly include β-glucosidase and β-xylosidase respectively. The GH13 family includes many α-glucosidases that degrade starch.

Gut microorganisms break the main chain or complex sugar structure of sugars to obtain polysaccharide fiber using GHs. Because of the size and complexity of the substrate, bacterial GHs are usually produced extracellularly. GHs hydrolyze and cleave glycoside bonds, while PLs cleave complex carbohydrates through a β-cleavage mechanism [38]. Degradation of complex plant-cell-wall polysaccharides, such as xylan and pectin, usually requires the synergy of a large number of different glycosidases. For example, *B. thetaiotaimicron* encodes up to 25 separate enzymes to degrade the most complex glycan-rhamnogalacturonan-II (RG-II) [10]. Among them, nine enzymes are used to degrade the main chain of L-Rha-D-Galacturonic Acid (D-GalA), which contains only two glycoside bonds. The key degradation enzyme is polysaccharide lyase PL9, which is located on the cell surface [10].

Dietary fiber mainly includes cellulose, hemicellulose, and pectin. Most of the enzymes involved in the degradation of cellulose and hemicellulose belong to the GH family. Among them, cellulase is a multi-component enzyme system that can degrade cellulose into glucose, which is divided into endo-β-1,4-glucanase, exo-β-glucanase, and β-glucosidase. The mechanism of cellulose degradation by microbial cellulase is as follows: firstly, it specifically adsorbs cellulose through the cellulose binding domain (CBD). Then, endo-lucosidase hydrolyzes the β-1,4 glycoside bonds in cellulose molecules to produce many new chain ends. Exo-cellulase acts on the chain ends activated by the endo-enzymes and hydrolyzes the β-1,4 glycoside bonds in the chain to produce cellobiose. At last, β-glucosidase decomposes cellobiose into glucose.

Hemicellulase is the general name for xylanase, xyloglucosanase, mannanase, arabinase and other enzymes. Xylan is the principal carbohydrate in hemicellulose and the second-largest structural polysaccharide found in nature. Due to its heterogeneity, complete hydrolysis of xylan requires different enzymes, including xylanase, β-xylosidase, α-glucuronidase, and α-L-arabinofuranosidase [10]. *B. intestinalis* can secrete a unique bifunctional endoxylanase/arabinofuranosidase which, in combination with other secretory enzymes, attacks the polysaccharide outside the cell to remove its side chain, exposes the xylan skeleton which is degraded into xylooligosaccharides and xylose, and then transports these products to the cell and degrades them into fermentable sugars by β-xylanase [24].

Lignin-degrading enzymes mainly include lignin peroxidase, manganese peroxidase, and laccase.

### *2.3. The Unique Degradation Mechanism of Dietary Fiber by Bacteroidetes*

The abnormal ability of Bacteroidetes to degrade a dozen kinds of plant and host polysaccharides is due to its unique discrete gene cluster, called the polysaccharide utilization locus (PUL). PUL encodes carbohydrate/polysaccharide binding proteins, extracellular polysaccharide degrading enzymes, outer membrane transporters, hybrid two-component systems (HTCs) containing polysaccharide-sensing modules, and a series of GHs that degrade oligosaccharides into fermentable sugars in the cytosols of cells [25]. The PUL of Bacteroidetes encodes a large number of surface proteins [39]. Therefore, compared with Firmicutes, the range of substrates targeted by Bacteroidetes is greater, and polysaccharides are even more obvious, because these require extracellular hydrolysis before they are transported to the cytosol.

The presence of PUL has been confirmed in all Bacteroidetes members, including *Bacteroides thetaiotaomicron* and *Bacteroides ovatus*, which contribute about 18% of their genomes to these gene clusters [40, 12]. The genome of a Bacteroidetes species may contain dozens of different PULs. Each PUL can target a specific complex carbohydrate as its preferred carbon source. Recently, it was found that the degradation of pectin rhamnogalacturonan-I (RG-I) by *Bacteroides thetaiotaomicron* is accomplished through the cooperation of multiple PULs. Different PULs encode glycoside hydrolases in different families to depolymerize the RG-I skeleton and remove the pectin domain attached to RG-I [41].

The first PUL best described is the starch utilization system (Sus) of *Bacteroides thetaiotaomicron* [42]. After the starch utilization system PUL, many PUL have been named. The process of degradation of polysaccharides by the Bacteroidetes PUL system is similar to that of the starch utilization system (Sus). That is, extracellular complex polysaccharides are recognized and bound to by cell surface glycan binding proteins (SGBPs), such as the outer membrane lipoproteins (SusD-like, SusE-like and SusF-like) [43], and then cleaved into oligosaccharides by SusG-like glycoside hydrolase. These oligosaccharides are immediately transported to the periplasmic space by associated transporters in a TonB-dependent manner through the Sus-like channel [32]. They are then are degraded into monosaccharides by SusA-like and SusB-like enzymes, and the monosaccharides are taken up into the cytosol through the inner membrane. When recognizing an intermediate product in the process of polysaccharide decomposition, each PUL also encodes a regulator, which strictly controls the transcription of genes in the PUL. There are three types of PUL regulator: ECF-σ/anti-σ, the SusR type and HTCSS [44].

In 2014, researchers identified the degradation mechanism of xyloglucan by *Bacteroides ovatus* as being realized through xylan utilization loci (XyGULs) [45]. The XyGULs are expected to encode an outer membrane glycobinding protein (SusD-like), a TonB-dependent glycoreceptor/transporter (SusC-like), an inner membrane mixed bicomponent sensor, and eight GHs. *Bacteroides ovatus* cut xyloglucosan into short xyloglucan oligosaccharides (XyGOs) using extracellular xyloglucan endonuclease BoGH5A, and then XyGOs are transported to the periplasm. In the periplasm, α-xylosidase BoGH31A removes α (1,6)-xylose residues from the non-reducing end of XyGOs [45]. The XyGOs are then hydrolyzed by β-glucosidase and β-galactosidase. Finally, the monosaccharides are absorbed by the cytosol as nutrients or for energy. In 2017, researchers purified and published the first three-dimensional atomic structure of SusCD using X-ray crystallography and created a model of substrate transport [46].

### *2.4. The Unique Degradation Mechanism of Dietary Fiber by Firmicutes*

#### *2.4.1. Gram-Positive PULs*

The degradation and transportation of dietary polysaccharides by Firmicutes is far less complex than that of Bacteroidetes, which is largely due to their lack of an outer membrane barrier. In contrast to Bacteroidetes, members of the Firmicutes phylum rarely rely on extracellular polysaccharide degradation but use a variety of transporters to introduce small sugars into cells for processing. For example, *Bifidobacterium* species rely on a set of carbohydrate transporters to transfer xylooligosaccharides into cells and then degrade them by the intracellular enzymes xylosidase and arabinosidase [47]. The transporters encoded by operons recognize the structures of polysaccharides, which include a regulatory protein, extracellular or intracellular enzymes, and one or more specialized transporters.

Unlike PULs of gram-negative Bacteroidetes, Firmicutes species have gram-positive PULs (gp PULs) [48]. The gp PULs are similar to the glycan degradation system of PULs. The target substrate is bound by extracellular carbohydrate binding proteins, partially degraded by CAZymes, and then transferred into the cytosol through transporters for further depolymerization. The gp PULs encode a series of ATP-binding cassette (ABC) transporters, cation co-transporters, transporters from the major facilitators superfamily (MFS) and PEP phosphotransferase system (PTS), regulatory proteins, and CAZymes [48]. ABC transporters can transport ATPase on the bacterial plasma membrane. They use ATP hydrolysis to drive transport. It dimerizes by binding to ATP, depolymerizes after ATP hydrolysis, and transfers bound substrates such as glucose to the other side of the membrane through conformational changes. Moreover, it has an extracellular substrate binding protein that recognizes specific sugars. *Lactobacillus acidophilus* relies on ABC transporters to transport prebiotics [49]. The core apparatus that *Roseburia Intestinalis* utilizes xylan to produce glucose also includes an ABC transporter [48]. MFS, as a co-transporter, uses an ion gradient (usually $H^+$ or $Na^+$) to drive transport. The combination of the PTS system and facilitated diffusion phosphorylates the substrate as it enters, which increases the subsequent metabolic efficiency [50]. PTS transports a variety of monosaccharides and disaccharides, especially hexoses, such as glucose [51]. *F. prausnitzii*, a member of Firmicutes, is good at utilizing smaller carbohydrates. It has a PTS system for transporting glucose [50].

#### *2.4.2. The Cellulosome*

Some members of the Firmicutes phylum, such as *Ruminococcus flavus*, also can degrade cellulose and hemicellulose through the cellulosome pathway. The cellulosome is a multienzyme complex composed of a variety of cellulases and hemicellulases produced by anaerobic cellulose-degrading bacteria through an anchoring adhesion mechanism [52]. It is a nanomachine for bacteria to degrade cellopolysaccharides and can efficiently degrade cellulose, hemicellulose, and other lignans. Cellulosomes are divided into domains and catalytic domains. One of the most important catalytic subunits in the domain is called the "scaffold protein". The cohesin in the domain specifically binds to the dockerin on the catalytic domain, allowing it to

bind to carbohydrates and/or anchor the cell wall. The catalytic domain includes various cellulases, hemicelluloses, and pectinas that are necessary for the degradation of the plant cell wall.

# 3. Dietary Fiber, Gut Microbiota and Short-Chain Fatty Acids

The monosaccharides produced from the degradation of dietary fiber by fiber-degrading bacteria enter the cytosol and are then fermented into short-chain fatty acids (SCFAs) by SCFA-producing bacteria. SCFAs are also known as volatile fatty acids. They are organic fatty acids with 1-6 carbon atoms, mainly including acetate, propionate, butyrate, isobutyrate, isovalerate and valerate. Acetate, propionate, and butyrate account for about 90–95% of SCFAs. SCFAs mainly come from the digestion of carbohydrates such as dietary fiber by intestinal bacteria. Branched-chain fatty acids (BCFAs), such as isobutyrate and valerate, come from the decay of protein. When the microbial diversity is high and the diet contains a variety of complex carbohydrates, microorganisms can easily consume a relatively high proportion of complex carbohydrates. The consumption of a complex diet may lead to increases in various types of SCFA and an increase in the diversity of gut microbiota [16].

## *3.1. Production Pathway of SCFAs*

SCFA-producing bacteria produce SCFAs including acetate, propionate, butyrate and some branched-chain fatty acids (BCFAs) through different pathways.

### *3.1.1. Acetate and Acetate-Producing Bacteria*

The gut microbiota usually produces acetate from pyruvate through acetyl-CoA or the Wood–Ljungdahl pathway [53]. Acetate is synthesized through two branches: (1) the C1 body branch reduces $CO_2$ to formate; and (2) the carbon monoxide branch reduces $CO_2$ to CO, and CO further combines with a methyl group to produce acetyl-CoA [54]. Researchers have found a new pathway of acetate synthesis [55]. Moreover, *Bifidobacterium* transforms monosaccharides into acetate and lactate through the "*bifid-shunt*" pathway [56]. Acetate-producing bacteria can produce acetate from $H_2$, $CO_2$, or formate and carbohydrates.

### *3.1.2. Propionate and Propionate-Producing Bacteria*

Only a few bacteria use the acrylate pathway to produce propionate [57]. Most bacteria use the succinate–propionate pathway to convert succinate into malonyl-CoA, and then generate propionate [58] and more ATP. They can also generate propionate using deoxyhexose (such as fucose and rhamnose) as the substrate through the propylene–glycol pathway [58]. Propionate is finally converted into succinyl-CoA and enters the gluconeogenesis pathway through the tricarboxylic acid cycle. Succinyl-CoA is essential for the synthesis of lysine and methionine. *S*uccinate can be used to produce propionate by *Phascolarctobacterium faecium*, *Propionibacterium*, *Selenomonas,* and *Veillonella* [59]. *Propionibacterium* mainly produces propionate, acetate, succinate, and $CO_2$ [60].

### *3.1.3. Butyrate and Butyrate-Producing Bacteria*

The classic pathway of butyrate synthesis is the polymerization of two molecules of acetyl-CoA to acetoacetyl-CoA, which is transformed into butyryl-CoA through the intermediates L(+)-β-hydroxybutyryl-CoA and crotonyl-CoA. Crotonyl-CoA is subsequently transformed into butyrate through butyrate kinase or butyryl-CoA and acetate-CoA transferase [61]. Butyryl-CoA can also be converted into butyrate by the butyryl-CoA–acetate-CoA transferase pathway. *Clostridium prausnitzii*, *Eubacterium recale,* and *Roseburia intestinalis* all rely on the butyryl-CoA–acetate-CoA transferase pathway to synthesize butyrate [62]. A metagenomic data analysis also showed that butyrate can be synthesized from proteins through the lysine pathway [63, 64].

Many known butyrate-producing bacteria belong to *Clostridium* clusters IV and XIV in the Firmicutes phylum [65]. *Clostridium* cluster IV includes *Ruminococcus* and *Faecalibacterium*; *Clostridium* cluster XIV includes *Eubacterium*, *Roseburia*, *Coprococcus* [66], and *Anaerostipes*. There are two ways to produce butyrate: one is through the direct fermentation of glucose and other monosaccharides by bacteria; the other way is through the production of butyrate by lactate or acetate. This can be done by *Anaerostipes cacca*, *Faecalibacterium prausnitzii* [66], and *Roseburia intestinalis* [67], which can prevent the accumulation of lactate, thereby stabilizing the intestinal environment. *Clostridium prausnitzii* is one of the most abundant and important butyrate-producing bacteria in the gut microbiota of healthy people. It can ferment glucose into acetate and butyrate [68]. The number of *Faecalibacterium* species in the cecal microbiota of naked necked chickens reared on grassland and fed with commercial yeast cell wall prebiotics was shown to be considerably increased [69]. *Roseburia*, *F. prausnitzii,* and others can use acetate and lactate to produce butyrate [70].

### *3.1.4. Branched-Chain Fatty Acids (BCFAs) and BCFA-Producing Bacteria*

About 30% of fermented proteins are transformed into SCFAs, most of which are branched-chain fatty acids (BCFAs), with isobutyrate, isovalerate, and valerate accounting for 16–23% of these [71]. It was found that the abundance of *Alistipes* and *Biliophila* in people who eat a meat-containing diet is significantly higher compared with vegetarians [72]. A significant positive correlation was found between *Alistipes* and BCFAs-isobutyric acid. BCFAs are formed by the metabolism of branched-chain amino acids such as valine, leucine, and isoleucine [64]. It should be noted that harmful metabolites ammonia, amine, stink and indole are also produced in the process of protein decay. Branched BCFAs can promote growth factors related to cellulose-decomposing bacteria and cellulose digestibility in rumen [73], and valerate can significantly inhibit the growth of *Clostridium difficile* [74].

### *3.2. SCFA Transport and Receptors*

There are two ways for SCFAs to be absorbed by the intestine: non-free SCFAs pass through the intestinal epithelial barrier through simple diffusion, while free SCFAs require the monocarboxylate transporter-1 (MCT-1) and sodium-coupled monocarboxylate transporter-1 (SMCT-1) for transport [75]. These SCFAs are bound by the specific G protein-coupled receptors (GPCRs) on the cell membrane. Because these receptors sense free fatty acids, they are also called free fatty acid receptors (FFARs). GPCRs of SCFAs include GPR43 (now renamed FFA2) [76], GPR41 (renamed FFA3) [77], and GPR109A (also known as NIACR1).

So far, studies on GPR41 and GPR43 have mainly focused on humans and mice. Researchers have also identified the SCFA receptors GPR41 and GPR43 in pig and rabbit genomes. These receptors are highly conserved among humans, cattle, mice, and other species. At present, it seems that there are no research reports on SCFA receptors in chickens. Although GPR41 and GPR43 show a 52% sequence similarity, they have different preferences for the lengths of SCFA ligands. Studies have found that GPR43 prefers acetate and propionate with shorter fatty chains, while GPR41 preferentially binds propionate, butyrate, and valerate [74], but this affinity varies among different species.

## 4. SCFAs and Host Metabolism

SCFAs enter the cells to produce the second messenger and initiate the intracellular signal transduction pathway. SCFAs regulate the physiological activities of the cell and affect the energy, appetite, and liver metabolism of the host through GPR41 or GPR43 signaling or inhibiting histone deacetylase (HDAC) [78].

### *4.1. SCFAs and Host Energy Metabolism*

#### *4.1.1. Energy Supply*

*Bacteroides thetaiotaomicron* can ferment cellulose polysaccharides to produce SCFAs, which provides nutrients for mice. Mice without *Bacteroides thetaiotaomicron* need to eat 30% more food to reach the same weight [11]. Bacteria and their hosts obtain heat from indigestible polysaccharides. Chickens can obtain about 8% of their required energy from SCFAs, while ostriches have well-developed saccular ceca and obtain up to 76% of metabolizable energy from SCFAs [79, 80].

Acetate is the main way for the body to obtain energy from dietary fiber and it is the most important substrate for cholesterol synthesis. About 0.876 MJ/mol energy is supplied by acetate oxidation, and the total amount of energy supplied to the human body can reach 10% every day. Lowland gorillas get ~57% of their metabolizable energy from SCFAs [81]. Propionate is a classic gluconeogenic substrate [82]. It is mainly absorbed by the liver and generates glycogen through gluconeogenesis, with an energy value of 1.536 MJ/mol. Butyrate can be rapidly converted to acetate or oxidated to produce 2.194 MJ/mol of energy. It is the preferred raw material for colon cells [83]. About 95% of butyrate is absorbed into epithelial cells and rapidly oxidized into ketones for ATP synthesis, providing ~70% of energy required for normal colon epithelial cells [84] and promoting epithelial cell proliferation [85].

#### *4.1.2. Energy Consumption*

SCFAs can also increase the oxygen consumption rate, and improve adaptive heat production and lipid oxidation. FFAR2 and FFAR3 may play key roles in this process. FFAR2 increases energy consumption and lipid oxidation by inhibiting fat accumulation and insulin signaling in adipose tissue. FFAR3 controls energy consumption by stimulating sympathetic nervous system activity [86].

### *4.2. SCFAs Regulate Host Appetite*

#### *4.2.1. SCFAs Regulate Appetite via GLP-1 and PYY*

At first, it was thought that the anorexic activity of dietary fiber was mainly due to the swelling effect. Finally, researchers proved that this appetite suppressive effect is the result of SCFAs produced by the microbial fermentation of dietary fiber. SCFAs increase in the level of intestinal peptides involved in regulating food intake and energy balance, such as glucagon like peptide-1 (GLP-1) and peptide tyrosine-tyrosine (PYY), thus reducing the energy intake of the host [87, 88].

GLP-1 is an incretin hormone secreted by intestinal L cells, which is stimulated by food intake (especially carbohydrate and fat) and bile acid, acting on its receptor TGR5. Its main function is to enhance glucose-stimulated insulin secretion, reduce food intake, inhibit gastric emptying, and glucagon secretion [89]. PYY is also secreted by intestinal endocrine L cells. It is stimulated by food intake (mainly fats), and its action sites are in the gastrointestinal tract, pancreas, and central nervous system [90]. Its main function is to improve the body's sense of satiety, reduce food intake, and inhibit gastric emptying and intestinal movement.

SCFAs are recognized by GPR41 and GPR43 receptors on intestinal endocrine L cells [90]. They stimulate the release of gastrointestinal hormones GLP-1 and PYY secreted by L cells [91, 92]. GLP-1 and PYY, in turn, regulate the activity of brain feeding centers of gut hormone receptors expressed in the arcuate nucleus (ARC), the nucleus of solitary tract (NTS), or vagus nerve endings [93], resulting in increased satiety and reduced energy intake [94].

Hypothalamic neurons, which regulate energy homeostasis, are the most deeply studied group [95]. They are located in the ARC of the hypothalamus and include neurons such as agouti-related protein (AGRP), neuropeptide Y (NPY), and proopiomelanocortin (POMC). These neurons contain the PYY receptor [96, 97], but only some POMC neurons have the GLP-1 receptor. GLP-1 [98] and PYY were injected into ARC, resulting in the amount of diet intake reduced. In contrast, direct injection of PYY into ARC inhibited food intake, decreased NPY expression, and increased the electrical activity of POMC neurons [99]. These data indicate that exogenous administration of GLP-1 and PYY can regulate food intake through POMC and/or AgRP/NPY neurons.

#### *4.2.2. SCFAs Regulate Host Appetite Through a Central Mechanism*

SCFAs also regulate appetite through a central mechanism independent of hormones such as GLP-1. Studies have revealed that the fermentation of soluble inulin can produce more acetate in the colons of mice than non-fermentable cellulose. Acetate passes through the blood–brain barrier and is absorbed by the brain through the blood circulation. It increases the production of lactate and gabaergic by supporting glutamine-glutamic acid transcellular circulation, leading to an anorexia signal in the hypothalamic ARC [100]. However, some studies showed that acetate enters the brain through the blood–brain barrier, activates the parasympathetic nervous system, and then instructs islet β-cells to secrete a large amount of insulin. It promotes the transformation of glucose into fat in adipocytes, causing adipocytes to store more fat. At the same time, it also leads to the release of ghrelin in the stomach, thereby increasing the appetites of mice and making them obese [101].

### *4.3. SCFAs and Host Liver Metabolism*

Most of the propionate and acetate produced in the intestine is absorbed into the portal vein [102]. SCFAs entering the liver affect the metabolism of liver function. In the liver, acetate and butyrate can be directly used as substrates for fat synthesis, while propionate is the main substrate for gluconeogenesis. In addition, acetate and butyrate affect liver glucose and lipid metabolism [103]. Studies have shown that the addition of SCFAs to the diet can reduce the contents of triglycerides and cholesterol and the production of glucose in the livers of rats [104]. SCFAs decrease liver lipid accumulation by increasing the expression of peroxisome proliferator-activated receptor (PPARα) target genes involved in the oxidation, thermogenesis, and lipogenesis of volatile fatty acids. The mechanism by which acetate and butyrate improve glucose tolerance is a direct increase in the phosphorylation and activity of adenylate activated protein kinase (AMPK) in the liver through an increase in the AMP/ATP ratio and up regulation of the PPARα target gene, thus increasing the storage of liver glycogen and the oxygenation of fatty acids. These effects may be partly mediated by GPR41 and GPR43 [105].

### *4.4. SCFAs Affect the Glucose Balance*

Studies have demonstrated that propionate and butyrate produced from dietary fiber activated intestinal gluconeogenesis (IGN) through a complementary mechanism [106]. Butyrate directly activates the expression of the IGN gene in intestinal epithelial cells through a cAMP-dependent mechanism, while propionate activates the expression of the IGN gene through the gut–brain neural circuit and FFAR3, thus regulating the glucose and energy balance. Furthermore, this makes the liver produce less glucose.

## 5. Conclusions

Dietary fiber is important for the host, but monogastric animals only rely on gut fiber-degrading bacteria can digest dietary fiber. Excellent fiber-degrading bacteria including *Bacteroides*, *Prevotella*, *Ruminococcus*, *Fibrobacter* and so on. They degrade fiber into monosaccharides via PUL or gp PULs degrading mechanisms. Some monosaccharides produced by dietary fiber degradation are used as carbon for the gut microbiota, thus increasing the diversity of gut microorganisms. Some monosaccharides are fermented into short-chain fatty acids (SCFAs) by SCFA-producing bacteria including *Bifidobacterium*, *Phascolarctobacterium*, *Faecalibacterium* and so on via SCFA receptors. Metabolites SCFAs further regulate the host's metabolism including energy metabolism, host appetite, liver metabolism and the glucose balance. The deep interactions among dietary fiber, gut microbiota, SCFAs and host metabolism need to be further explored.

## Competing Interest

All the authors do not have any possible conflicts of interest.

## Funding

This research was funded by the the Zunyi Innovative Talent Team Training Project (Zunyi Science and Technology Talents [2021] No. 5) and the Guizhou Science and Technology Planning Project (Qian Science Contract [2020] No. 1Z001).

## Authors' Contributions

Methodology, LH; formal analysis, LH and YY; investigation, LH and YY; resources, YY and YJ; data curation, BS and YJ; writing—original draft preparation, LH and BS; writing—review and editing, LH, BS and YY; visualization, LH; supervision, WD and YJ; project administration, WD and YY; funding acquisition, WD.

## References

[1] Human Microbiome Project (HMP) Consortium. Structure, function and diversity of the healthy human microbiome [J]. Nature, 2012, 486 (7402): 207-214.

[2] Qin J, Li R, Raes J, et al. A human gut microbial gene catalogue established by metagenomic sequencing [J]. Nature, 2010, 464 (7285): 59-65.

[3] Moeller A H, Li Y, Ngole E M, et al. Rapid changes in the gut microbiome during human evolution [J]. PNAS, 2014, 111 (46): 16431-16435.

[4] Erica D S, Samuel A S, Mikhail T, et al. Diet-induced extinctions in the gut microbiota compound over generations [J]. Nature, 2016, 529 (7585): 212-215.

[5] Eric C M. Fibre for the future [J]. Nature, 2016, 529 (7585): 158-159.

[6] Edward C D, Jens W. The fiber gap and the disappearing gut microbiome: implications for human nutrition [J]. Trends in Endocrinology & Metabolism, 2016, 27 (5): 239-242.

[7] Mahesh S D, Anna M S, Nicole M K, et al. A dietary fiber-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility [J]. Cell, 2016, 167 (5): 1339–1353.

[8] Larsen N, Vogensen F K, Vanden Berg F W J, et al. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults [J]. Plos One, 2010, 5 (2): e9085.

[9] Xu J, Bjursell M K, Himrod J, et al. A genomic view of the human-*Bacteroides thetaiotaomicron* symbiosis [J]. Science, 2003, 299 (5615): 2074–2076.

[10] Kui W, Gabriel V P, Janaina J V C, et al. *Bacteroides intestinalis DSM 17393*, a member of the human colonic microbiome, upregulates multiple endoxylanases during growth on xylan [J]. Scientific Reports, 2016, 6 (34360): 1-11.

[11] Backhed F, Ley R E, Sonnenburg J L, et al. Host-bacterial mutualism in the human intestine [J]. Science, 2005, 307 (5717): 1915–1920.

[12] Luis A S, Briggs J, Zhang X A, et al. Dietary pectic glycans are degraded by coordinated enzyme pathways in human colonic Bacteroides [J]. Nature Microbiology, 2017, 3 (2): 210-219.

[13] Koropatkin N M, Cameron E A, Martens E C. How glycan metabolism shapes the human gut microbiota [J]. Nature Reviwes Microbiology, 2012, 10 (5): 323–335.

[14] Wexler, Aaron G, Andrew L. An insider's perspective: *Bacteroides* as a window into the microbiome [J]. Nature Microbiology, 2017, 2 (5): 17026.

[15] Seth R N, Kevin R, Foster L E. Comstock. The evolution of cooperation within the gut microbiota [J]. Nature, 2016, 533 (7602): 255–259.

[16] Justin L S, Fredrik B. Diet–microbiota interactions as moderators of human metabolism [J]. Nature, 2016, 535 (7610): 56-64.

[17] Paul I C, Falk H, Manimozhiyan A, et al. Enterotypes in the landscape of gut microbial community composition [J]. Nature Microbiology, 2018, 3 (1): 8–16.

[18] Gorvitovskaia A, Holmes S. P, Huse S. M. Interpreting *Prevotella* and *Bacteroides* as biomarkers of diet and lifestyle [J]. Microbiome, 2016, 4 (1): 15.

[19] Tingting C, Wenmin L, Chenhong Z, et al. Fiber-utilizing capacity varies in *Prevotella*-versus *Bacteroides*-dominated gut microbiota [J]. Scientific Reports, 2017, 7 (1): 2594.

[20] Carlotta D F, Duccio C, Monica D P, et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa [J]. PNAS, 2010, 107 (33): 14691–14696.

[21] Xiaofan W, Tsungcheng T, Feilong D, et al. Longitudinal investigation of the swine gut microbiome from birth to market reveals stage and growth performance associated bacteria [J]. Microbiome, 2019, 7 (109): 1-1.

[22] De Vuyst L, Moens F, Selak M, et al. Summer Meeting 2013: growth and physiology of bifidobacteria [J]. Journal of Applied Microbiology, 2014, 116 (3): 477–491.

[23] Shinkai T, Kobayashi Y. Localization of ruminal cellulolytic bacteria on plant fibrous material as determined by fluorescence in situ hybridisation and real time PCR [J]. Applied and Environmental Microbiology, 2006, 73 (5): 1646–1652.

[24] Suen G, Weimer P J, Stevenson D M, et al. The complete genome sequence of *Fibrobacter succinogenes s85* reveals a cellulolytic and metabolic specialist [J]. Plos One, 2011, 6 (4): e18814.

[25] Dehority B A. Microbial ecology of cell wall fermentation. In: Jung H. G, Buxton D. R, Hatfield R. D, Ralph, J. (Eds.), Forage cell wall structure and digestibility [J]. Soil Science Society of America Inc, Madison, WI, pp. 1993, 425–453.

[26] Denis O K, Stuart E D, Roderick I M, et al. Opportunities to improve fiber degradation in the rumen: microbiology, ecology and genomics [J]. Fems Microbiology Reviews, 2003, 27 (5): 663-693.

[27] Herbert J, Strobel. Pentose transport by the Butyrivibrio fibrisolvens [J]. Fems Microbiology Letters, 1994, 122 (3): 217-222.

[28] Jude J B, Jonathan C D, Fiona Y S K, et al. Carbohydrate transporting membrane proteins of the rumenbacterium, *Butyrivibrio proteoclasticus* [J]. Journal of Proteomics, 2012, 75 (11): 3138–3144.

[29] Cotta M, Forster R. The family *Lachnospiraceae*, including the genera *Butyrivibrio*, *Lachnospira* and *Roseburia* [J]. Prokaryotes, 2006, 190 (2): 1002–1021.

[30] Akinosho H, Yee K, Close D, et al. The emergence of *Clostridium thermocellum* as a high utility candidate for consolidated bioprocessing applications [J]. Front. Chem, 2014, 2 (66): 1-18.

[31] Taku O, Makiko S, Tetsuya K, et al. Recombinant cellulolytic or xylanolytic complex comprising the full-length scaffolding protein RjCipA and cellulase RjCel5B or xylanase RjXyn10C of *Ruminiclostridium josui* [J]. Enzyme and Microbial Technology, 2017, 97: 63–70.

[32] Martens E C, Chiang H C, Gordon J I. Mucosal glycan foraging enhances fitness and transmission of a saccharolytic human gut bacterial symbiont [J]. Cell Host Microbe, 2008, 4 (5): 447–457.

[33] Kaoutari A E, Armougom F, Gordon J I, et al. The abundance and variety of carbohydrateactive enzymes in the human gut microbiota [J]. Nature Reviwes Microbiology. 2013, 11 (7): 497–504.

[34] Abdessamad El Kaoutari, Fabrice Armougom, Jeffrey I. Gordon, et al. The abundance and variety of carbohydrate-active enzymes in the human gut microbiota [J]. Nature Reviews Microbiology, 2013, 11 (7): 1-9.

[35] Lifeng Z, Qi W, Jiayin D, et al. Evidence of cellulose metabolism by the giant panda gut microbiome [J]. PANS, 2011, 108 (43): 17714–17719.

[36] Harry J F, Edward A B, Marco T R, et al. Polysaccharide utilization by gut bacteria: potential for new insights from genomic analysis [J]. Nature Reviews Microbiology, 2008, 6 (2): 121-131.

[37] Yanping Z, Michael d L suits, rew J thompson, et al. Mechanistic insights into a $Ca^{2+}$-dependent family of α-mannosidases in a human gut symbiont [J]. Nature Chemicalbiology, 2010, 6 (2): 125-132.

[38] Cantarel B L, Coutinho P M, Rancurel C, et al. The carbohydrate-active enzymes database (CAZy): an expert resource for glycogenomics [J]. Nucleic Acids Research, 2009, 37 (Database): D233-D238.

[39] Martens E C, Lowe E C, Chiang H, et al. Recognition and degradation of plant cell wall polysaccharides by two human gut symbionts [J]. PLoS Biology, 2011, 9 (12): e1001221.

[40] Terrapon N, Lombard V, Gilbert H J, et al. Automatic prediction of polysaccharide utilization loci in Bacteroidetes species [J]. Bioinformatics, 2015, 31 (5): 647-655.

[41] Anderson K L, Salyers A A. Genetic evidence thatouter membrane binding of starch is required for starch utilization by *Bacteroides thetaiotaomicron* [J]. Journal of Bacteriology, 1989, 171 (6): 3199-3204.

[42] Nathan D, Schwalm, Eduardo A G. Navigating the gut buffet: control of polysaccharide utilization in *Bacteroides spp* [J]. Trends in Microbiology, 2011, 25 (12): 1005-1015.

[43] Tauzin A S, Kwiatkowski K J, Orlovsky N I, et al. Molecular dissection of xyloglucan recognition in a prominent human gut symbiont [J]. Microbiology, 2016, 7 (2): e02134-15.

[44] Sonnenburg E D, Zheng H, Joglekar P, et al. Specificity of polysaccharide use in intestinal *Bacteroides* species determines diet-induced microbiota alterations [J]. Cell, 2010, 141 (7): 1241–1252.

[45] Johan L, Theresa E R, Glyn R H, et al. A discrete genetic locus confers xyloglucan metabolism in select human gut Bacteroidetes [J]. Nature, 2014, 506 (27): 498-502.

[46] Glenwright A J, Pothula K R, Bhamidimarri S P, et al. Structural basis for nutrient acquisition by dominant members of the human gut microbiota [J]. Nature, 2017, 541 (7637): 407-411.

[47] Goh Y J, Klaenhammer T R. Genetic mechanisms of prebiotic oligosaccharide metabolism in probiotic microbes [J]. Annual Review of Food Science and Technology, 2015, 6 (1): 137–156.

[48] Maria L L, Morten E, Christopher W, et al. Differential bacterial capture and transport preferences facilitate co-growth on dietary xylan in the human gut [J]. Nature Microbiology, 2018, 3 (5): 570-580.

[49] Barrangou R, Altermann E, Hutkins R, et al. Functional and comparative genomic analyses of an operon involved in fructooligosaccharide utilization by Lactobacillus acidophilus [J]. Proceedings of the National Academy of Sciences, 2003, 100 (15): 8957–8962.

[50] Cockburn D W, Koropatkin N M. Polysaccharide degradation by the intestinal microbiota and its influence on human health and disease [J]. Journal of Molecular Biology, 2016, 428 (16): 3230–3252.

[51] Saier M H. Families of transmembrane sugar transport proteins [J]. molecular microbiology, 2000, 35 (4): 699–710.

[52] Lior A, Edward A. Bayer and Sarah Moraïs. Cellulosomes: bacterial nanomachines for dismantling plant polysaccharides [J]. Nature Reviews Microbiology, 2016, 15 (2): 1-13.

[53] Ragsdale S W, Pierce E. Acetogenesis and the Wood-Ljungdahl pathway of $CO_2$ fixation [J]. Biochim. Biophys. Acta, 2008, 1784 (12): 1873–1898.

[54] Rey F E, Faith J J, Bain J, et al. Dissecting the in vivo metabolic potential of two human gut acetogens [J]. Journal of Biological Chemistry, 2010, 285 (29): 22082-22090.

[55] Xiaojing L, Daniel E C, Ahmad A C, et al. Acetate production from glucose and coupling to mitochondrial metabolism in mammals [J]. Cell, 2018, 175 (2): 502-513.

[56] Muriel D, Johan E T, Van H V. Fate, activity, and impact of ingested bacteria within the human gut microbiota [J]. Trends in Microbiology, 2015, 23 (6): 354-366.

[57] Hetzel M, Brock M, Selmer T, et al. Acryloyl-CoA reductase from *Clostridium propionicum*. An enzyme complex of propionyl-CoA dehydrogenase and electron-transferring flavoprotein [J]. European. Journal. Biochemistry, 2003, 270 (5): 902–910.

[58] Louis P, Scott K P, Duncan S H, et al. Understanding the effects of diet on bacterial metabolism in the large intestine [J]. Journal of Applied. Microbiology, 2007, 102 (5): 1197–1208.

[59] Hilpert W, Dimroth P. Conversion of the chemical energy of methylmalonyl-CoA decarboxylation into a Na+ gradient [J]. Nature, 1984, 296 (5857): 584-585.

[60] Thierry A, Deutsch S M, Falentin H, et al. New insights into physiology and metabolism of *Propionibacterium freudenreichii* [J]. International journal of food microbiology, 2011, 149 (1): 19-27.

[61] Louis P, Duncan S H, McCrae S I, et al. Restricted distribution of the butyrate kinase pathway among butyrate-producing bacteria from the human colon [J]. Journal of Bacteriology, 2004, 186 (7): 2099–2106.

[62] Louis P, Young P, Holtrop G, et al. Diversity of human colonic butyrate-producing bacteria revealed by analysis of the butyryl-CoA: acetate CoA-transferase gene [J]. Environ Microbiol, 2010, 12, 304–314.

[63] Ara K, Filipe D V, Petia K D, et al. From dietary fiber to host physiology: short-chain fatty acids as key bacterial metabolites [J]. Cell, 2016, 165 (6): 1332-1345

[64] Rajesh J, Julio F D, Berrocoso. Dietary fiber and protein fermentation in the intestine of swine and their interactive effects on gut health and on the environment: a review [J]. Animal Feed Science and Technology, 2016, 212 (): 18–26.

[65] Susan E P, Sylvia H D, Georgina L H, et al. The microbiology of butyrate formation in the human colon [J]. Fems Microbiology Letters, 2002, 217 (2): 133-139.

[66] Munoz-Tamayo R, Laroche B, Walter E, et al. Kinetic modeling of lactate utilization and butyrate production by key human colonic bacterial species [J]. Fems Microbiology Ecology, 2011, 76 (3): 615–624.

[67] Duncan S H, Hold G L, Harmsen H J, et al. Growth requirements and fermentation products of *Fusobacterium prausnitzii*, and a pro-posal to reclassify it as *Faecalibacterium prausnitzii* gen. nov., comb. Nov [J]. INT J SYST EVOL MICR, 2002, 52 (6): 2141-2146.

[68] Duncan S H, Hold G L, Barcenilla A, et al. Roseburia intestinalis sp. Nov a novel saccharolytic, butyrate-producing bacterium from human faeces [J]. INT J SYST EVOL MICR, 2002, 52 (5): 1615-1620.

[69] Hong P S, Sang I L, Ricke S C, et al. Microbial populations in naked neck chicken ceca raised on pasture flock fed with commercial yeast cell wall prebiotics via an Illumina MiSeq Platform [J]. Plos One, 2016, 11 (3): e0151944.

[70] Turroni F, Milani C, Duranti S A, et al. Bifidobacteria and the infant gut: an example of co-evolution and natural selection [J]. Celularl and Molecular Life Sciences, 2018, 75 (1): 103-18.

[71] Macfarlane G T, Gibson G R, Beatty E, et al. Estimation of short-chain fatty acid production from protein by human intestinal bacteria based on branched-chain fatty acid measurements [J]. Fems Microbiology Letters, 1992, 101 (2): 81–88.

[72] Wu G D, Chen J, Hoffmann C, et al. Linking long-term dietary patterns with gut microbial enterotypes [J]. Science, 2011, 334 (602): 105-108.

[73] Allison M J, Bryant M P. Metabolic function of branched-chain volatile fatty acids, growth factors for rumino-coocci [J]. Journal of Dairy Science, 1962, 83 (5): 1084-1093.

[74] Julie A K M, Benjamin H M, Alexandros P, et al. Inhibiting growth of *Clostridioides difficile* by restoring valerate, produced by the intestinal microbiota [J]. Gastroenterology, 2018, 155 (5): 1495-1507.

[75] Gerhart D Z, Leino R L, Drewes L R. Distribution of monocarboxylate transporters MCT1 and MCT2 in rat retina [J]. Neuroscience, 1999, 92 (1): 1-388.

[76] Le P E, Loison C, Struyf S, et al. Functional characterization of human receptors for short chain fatty acids and their role in polymorphonuclear cell activation [J]. Journal of Biological Chemistry, 2003, 278 (28): 25481–25489.

[77] Macia L, Tan J, Vieira A T, et al. Metabolite-sensing receptors GPR43 and GPR109A facilitate dietary fibre-induced gut homeostasis through regulation of the inflammasome [J]. Nature Communications, 2015, 6: 6734.

[78] Valentina T, Fredrik B. Functional interactions between the gut microbiota and host metabolism [J]. Nature, 2012, 489 (7415): 242-249.

[79] Józefiak, A. Rutkowski, S. A. Martin. Carbohydrate fermentation in the avian ceca: a review [J]. Animal Feed Science and Technology, 2004, 113 (1-4): 1–15

[80] Swart D, Mackie R I, Hayes J P. Influence of live mass, rate of passage and site of digestion on energy-metabolism and fiber digestion in the ostrich (struthio-camelus var domesticus) [J]. South African Journal of Animal Science, 1993, 23 (5): 119-126.

[81] Frost G S, Walton G E, Swann J R, et al. Impacts of plant-based foods in ancestral hominin diets on the metabolism and function of gut microbiota in vitro [J]. MBio, 2014, 5 (3): e00853–14

[82] Anderson J W, Bridges S R. Short-chain fatty acid fermentation products of plant fiber affect glucose metabolism of isolated rat hepatocytes [J]. Proceeding of Society Experimental Biology Medicine, 1984, 177 (1): 372–376.

[83] Roediger W E. Utilization of nutrients by isolated epithelial cells of the rat colon [J]. Gastroenterology, 1982, 83 (2): 424–429.

[84] Donohoe D. R, Garge N, Zhang X, et al. The microbiome and butyrate regulate energy metabolism and autophagy in the mammalian colon [J]. Cell Metabolism, 2011, 13 (5): 517–526.

[85] Roediger W E. Role of anaerobic bacteria in the metabolic welfare of the colonic mucosa in man [J]. Gut, 1980, 21 (9): 793–798.

[86] Herd R M, Dawson T J. Fiber digestion in the emu, Dramaius novaehollandiae, a large ratite bird with a simple gut and high rates of passage [J]. Physiological Zoology, 1984, 57 (1): 70–84.

[87] Kimura I, Inoue D, Maeda T, et al. Short-chain fatty acids and ketones directly regulate sympathetic nervous system via G protein coupled receptor 41 (GPR41) [J]. PNAS, 2011, 108 (19): 8030–8035.

[88] Cani P D, Dewever C, Delzenne N M. Inulin-type fructans modulate gastrointestinal peptides involved in appetite regulation (glucagon-like peptide-1 and ghrelin) in rats [J]. British Journal of Nutrition, 2004, 92, 521–526.

[89] Delzenne N M, Cani P D, Daubioul C, et al. Impact of inulin and oligofructose on gastrointestinal peptides J]. British Journal of Nutrition, 2005, 93 (Suppl 1): S157–S161.

[90] Katie C C, Steven A K, David J. Mangelsdorf. Snapshot: hormones of the gastrointestinal tract [J]. Cell, 2014, 159 (6): 1478-1478e1.

[91] Tazoe H. Expression of short-chain fatty acid receptor GPR41 in the human colon [J]. Biomed Research international, 2009, 30 (3): 149–156.

[92] Tolhurst G. Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2 [J]. Diabetes, 2012, 61 (2): 364–371.

[93] Psichas A. The short chain fatty acid propionate stimulates GLP-1 and PYY secretion via free fatty acid receptor 2 in rodents [J]. International Journal of Obesity (Lond.), 2015, 39 (3), 424–429.

[94] Cani, Patrice D, Van Hul, et al. Microbial regulation of organismal energy homeostasis [J]. Nature Metabolism, 2019, 1 (1): 34-46.

[95] Kim, Ki-Suk, Seeley, et al. Signalling from the periphery to the brain that regulates energy homeostasis [J]. Nature Reviews Neuroence, 2018, 19 (4): 185-196.

[96] Lucy B, Alexander V, Anastasia T, et al. Fermentable carbohydrate stimulates FFAR2-dependent colonic PYY cell expansion to increase satiety [J]. Molecular Metabolism, 2017, 6 (1): 48-60.

[97] Myers M G, Olson D P. SnapShot: neural pathways that control feeding [J]. Cell Metabolism. 2014, 19, 732–732. e1.

[98] Marston O J, Garfield A S, Heisler L K. Role of central serotonin and melanocortin systems in the control of energy balance [J]. European Journal of Pharmacology, 2011, 660 (1): 70–79.

[99] Burmeister M A. The hypothalamic glucagon-like peptide 1 receptor is sufficient but not necessary for the regulation of energy balance and glucose homeostasis in mice [J]. Diabetes, 2017, 66 (2): 372–384.

[100] Gary F, Michelle L S, Sahuri-Arisoylu M, et al. The short-chain fatty acid acetate reduces appetite via a central homeostatic mechanism [J]. Nature communications, 2014, 5 (3611): 1-11.

[101] Rachel J P, Peng L, Natasha A B, et al. Acetate mediates a microbiome–brain–β-cell axis to promote metabolic syndrome [J]. Nature, 2016, 534 (7606): 213-217.

[102] Al-Lahham S, Peppelenbosch M P, Roelofsen H, et al. Biological effects of propionate in humans; metabolism, potential applications and underlying mechanisms [J]. Biochimica et Biophysica Acta-Biomembranes, 2010, 1801 (11): 1175–1183.

[103] Todesco T, Rao A V, Bosello O, et al. Propionate lowers blood glucose and alters lipid metabolism in healthy subjects [J]. American Journal of Clinical Nutrition, 54 (5): 860-865.

[104] Jakobsdottir G, Xu J, Molin G, et al. High-fat diet reduces the formation of butyrate, but increases succinate, inflammation, liver fat and cholesterol in rats, while dietary fibre counteracts these effects [J]. Plos One, 2013, 8 (11): e80476.

[105] Emanuel E C, Johan W J, Ellen E B. Short-chain fatty acids in control of body weight and insulin sensitivity [J]. Nature Reviews Endocrinology, 2015, 11 (10): 577-591.

[106] De V F, Kovatcheva-Datchary P, Goncalves D, et al. Microbiota-generated metabolites promote metabolic benefits via gut-brain neural circuits [J]. Cell, 2014, 156 (1-2): 84-96.