Fermentation in the Human Large Intestine

Its Physiologic Consequences and the Potential Contribution of Prebiotics

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Abstract: The human large intestine harbors a complex microbiota containing many hundreds of different bacterial species. Although structure/function relationships between different components of the microbiota are unclear, this complex multicellular entity plays an important role in maintaining homeostasis in the body. Many of the physiologic properties of the microbiota can be attributed to fermentation and the production of short-chain fatty acids (SCFAs), particularly acetate, propionate, and butyrate. In healthy people, fermentation processes are largely controlled by the amounts and different types of substrate, particularly complex carbohydrates that are accessible to bacteria in the colonic ecosystem. However, other factors impact on bacterial metabolism in the large gut, including large bowel transit time, the availability of inorganic terminal electron acceptors, such as nitrate and sulfate, and gut pH. They all affect the types and levels of SCFA that can be formed by the microbiota. This is important because to a large extent, acetate, propionate, and butyrate have varying physiologic effects in different body tissues. Prebiotics such as galactooligosaccharides together with inulins and their fructooligosaccharide derivatives have been shown to modify the species composition of the colonic microbiota, and in various degrees, to manifest several health-promoting properties related to enhanced mineral absorption, laxation, potential anticancer properties, lipid metabolism, and anti-inflammatory and other immune effects, including atopic disease. Many of these phenomena can be linked to their digestion and SCFA production by bacteria in the large gut.

Key Words: large intestine, fermentation, carbohydrate metabolism, short-chain fatty acids, prebiotics

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fungi can sometimes be recovered, although their cell population densities are low. Certain Gram-negative species such as bacteroides exist in high numbers in the large bowel, but Gram-positive anaerobic rods and cocci predominate. Several hundred different bacterial species and strains have been isolated from fecal material and many more have been detected using molecular approaches to community analysis, but surprisingly little is known of the metabolic interactions that occur between different groups of microorganisms in the large gut or of the ecology and multicellular organization of the microbiota. Bacterial species diversity in the gut largely derives from the multiplicity of different carbon and energy sources that are accessible for growth and two of the principal host factors regulating the microbiota in health are substrate availability and colonic transit time. Other important determinants include competition for nutrients and space, whereas cooperative interactions between individual groups of bacteria such as those involved in the breakdown of complex polymeric substances are also significant factors in defining community structure. The microbiota is a stable and immensely complex entity, which like all climax ecosystems is to a large extent self-regulating. Although many microorganisms are able to invade and temporarily colonize the gastrointestinal tract, indigenous species afford a degree of protection to the host by acting as a barrier to invading pathogens. However, the effectiveness of this process is frequently diminished during illness or by antibiotic treatment.

COLONIC MICROBIOTA

In humans, the vast majority of microorganisms inhabiting the large intestine are bacteria. Protozoa are seldom detected in healthy people, but yeasts and other

SUBSTRATE AVAILABILITY

Although large numbers of amino acid fermenting bacteria and syntrophic species are present in the large bowel, the vast majority of bacteria have predominantly saccharolytic metabolisms, and as a consequence, carbohydrate availability is almost certainly the most important nutritional factor that controls the composition and metabolic activities of the microbiota.[1] Many different types of carbohydrate participate in fermentation processes in the large intestine,[2] and modeling studies have shown that changes in the availability of polysaccharide substrates can cause significant shifts in luminal anaerobic populations in gut fermentor systems.[3,4] A variety of nutritional, host, and dietary factors affect the outcome of carbohydrate fermentation reactions in the colon and because the majority of carbohydrate entering the large bowel does so in the form of polysaccharides, the rate at which these substances can be depolymerized controls the rate at which fermentable carbohydrate becomes available for assimilation by the bacteria.[5]

Substantial amounts of starch (8 to 40 g) and nonstarch polysaccharides (8 to 18 g) enter the human colon daily.[6] In European countries, approximately 50% of nonstarch polysaccharides are derived from cereals, 31% comes from vegetables, and 16% is present in fruit, and although derived from only 10 common monosaccharides, the carbohydrate polymers found in plant cell walls are structurally diverse.[7,8] The physical properties of plant cell wall polysaccharides are affected by the presence of lignin, which provides hydrophobic surfaces and charged groups that modify their ionic properties.[9] This can prevent access of bacterial hydrolytic enzymes that are involved in substrate depolymerization reactions. Although starches and nonstarch polysaccharides are the principal sources of carbohydrate in the large bowel,[10] nondigestible oligosaccharides are increasingly being introduced into the western diet,[11] many of which are claimed to have prebiotic properties. A wide range of mucins from the upper gastrointestinal tract also enter the colon in ileal effluent, whereas more mucus is formed by goblet cells in the colonic mucosa. In small intestinal effluent, particulate substances such as partly digested plant cell materials are entrapped in a viscoelastic mucus gel, which must be broken down by bacteria in the colon to facilitate access to the food residues.
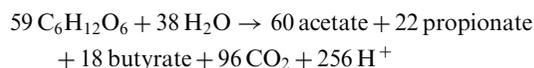
PREBIOTICS

The definition of a prebiotic has gone through several iterations over the last few years; however, the definition by Pineiro et al[11] that a prebiotic is a nonviable food component that confers a health benefit on the host associated with modulation of the microbiota, is as good as any that have been put up so far. To this, the following qualifiers can be added: (1) a prebiotic is not an organism or drug but a substance that can be characterized chemically, in most cases it will be a food grade material. (2) With respect to health benefits, these should be measurable and not accrue from simple absorption of the food component into the bloodstream or result from the prebiotic acting alone. (3) It should be shown that the sole presence of the prebiotic, and the formulation in which it is being delivered, changes the composition or activities of the microbiota in the host. The majority of studies involving prebiotic oligosaccharides have been made with inulins, their fructooligosaccharide (FOS) derivatives, and various types of galactooligosaccharides (GOS). Although a number of intestinal bacteria seem to be able to ferment these substances to a certain degree, most investigations have shown that the growth of beneficial species such as bifidobacteria and, to a lesser degree, lactobacilli, is particularly favored. Owing to their safety, general stability, organoleptic properties, resistance to digestion in the upper gut, and fermentability in the colon, these prebiotics are being increasingly incorporated into the western diet. Inulin-derived oligosaccharides and GOS are mildly laxative and can result in flatulence if consumed in large amounts, but any deleterious effects on bowel habit are relatively minor. Although the literature dealing with the health significance of prebiotics is not as extensive as that on probiotics, considerable evidence has accrued showing that prebiotic consumption can have significant health benefits, particularly in relation to their influence on laxation, mineral absorption, potential anticancer properties, lipid metabolism, and anti-inflammatory, and other immune effects, including atopic disease (for review, see

Ref. 12). Many of these phenomena can be attributed to prebiotic digestion by bacteria, and short-chain fatty acid (SCFA) production in the large intestine.

FERMENTATION PROCESSES

Anaerobic chemoheterotrophic communities in the colon include species that carry out anaerobic respiration, but the majority of organisms are fermentative species that generate energy through substrate-level phosphorylation reactions. In fermentation, the electron acceptors are metabolic products derived from the original substrate. As a result of this, fermentation reactions are self-balancing with the redox differential between substrates and products determining the amount of energy that can be produced. Compared with oxidative metabolism, fermentations are energetically inefficient processes that give low ATP yields. Substantial amounts of substrate are therefore required for growth in fermentative bacteria, which results in large quantities of metabolic end-products being formed. Fermentations are governed by the need to maintain redox balance, mainly by the reduction and oxidation of ferredoxins, flavins, and pyridine nucleotides. This affects the flow of carbon through bacteria, the energy yield obtained from the substrate, and the types of fermentation products that can be formed. In quantitative terms, SCFAs are the principal end-products generated by the colonic microbiota, whereas the formation of reduced substances (electron sink products) such as hydrogen gas, lactate, succinate, butyrate, and ethanol is used to effect redox balance.[13,14] An equation describing overall carbohydrate fermentation in the large gut has been outlined by Cummings.[15]

$$59\,C_6H_{12}O_6 + 38\,H_2O \rightarrow 60\,\text{acetate} + 22\,\text{propionate}$$
$$+ 18\,\text{butyrate} + 96\,CO_2 + 256\,H^+$$

In Vitro Modeling Studies

As >95% of SCFAs are absorbed from the gut, measurements of these metabolites in stools does not really tell us very much about the fermentability of different carbohydrates. However, in vitro studies, particularly those involving fecal microbiotas, can provide useful models for studying fermentation processes. The chemical composition of the growth substrate markedly influences the fermentation products that can be formed by bacteria. This was demonstrated by Englyst et al,[5] who originally showed that acetate and butyrate were the principal SCFAs produced from starch by fecal bacteria, whereas acetate was the main fermentation product from both pectin and xylan. Qualitative and quantitative differences in biofilm metabolism were seen in SCFA production rates, in in vitro fermentation studies, particularly when oligosaccharides served as substrates.[16] These results showed clearly that nonadherent bacteria fermented oligosaccharides considerably more rapidly than the biofilm communities, whereas this was only true with highly soluble polymers such as starch and, to a lesser degree, mucin. The relatively insoluble polysaccharide arabinogalactan associated with cell wall material was digested more rapidly by bacteria desorbed from the biofilms, reflecting their adaptation to this substrate. It interesting to note that butyrate was primarily formed by nonadherent fecal communities, irrespective of the fermentation substrate, indicating that these bacteria are of physiological importance to the host. Fermentation of oligosaccharides was in some cases slower than the

breakdown of their more complex polysaccharide counterparts. Indeed, in biofilm bacteria, SCFA generation from xylan and arabinogalactan was faster than with the corresponding oligosaccharides. However, the molar ratios of acetate, propionate, and butyrate produced from polysaccharides and chemically similar oligosaccharides were not sufficiently distinct to suggest that different groups of bacteria were involved in their fermentation. This indicates that substrate uptake was a significant factor affecting fermentation rate.

Inorganic electron acceptors such as nitrate and sulfate can dramatically affect fermentation reactions in colonic microorganisms.[17,18] This can be seen in Table 1, in which the addition of either nitrate or sulfate to fecal bacterial incubations resulted in marked reductions in the production of chemically reduced fermentation metabolites such as lactate and butyrate, with concomitant increases in acetate, which is a more oxidized metabolic end-product. Acetate is associated with increased ATP formation and increased fermentation efficiency.[14]

As stated previously, large bowel transit time is one of the most important factors affecting the structure and function of the colonic microbiota. This can be seen in results from experiments using a 3-stage continuous culture model of the colon.[4] Vessel 1 was designed to simulate environmental and nutritional conditions in the proximal colon, whereas V2 and V3 modeled the transverse and distal colons, respectively. System retention time is analogs to colonic transit time, and the model was operated under fast ($R = 27$ h) and typical western ($R = 66.7$ h) parameters. Table 2 shows that short-retention times were associated with higher specific rates of carbohydrate utilization and a lower percentage of substrate utilization in vessel 1. This enabled more carbohydrate to become available for bacterial growth in vessel 2. In terms of bacterial metabolic processes, this resulted in increased SCFA production rates and greatly enhanced fermentation efficiencies in every part of the model system (Table 3). When placed in an in vivo context, these data indicate that faster colonic times are linked to higher energy recoveries by the host due to increased breakdown of digestive residues by colonic microorganisms.

Studies on FOS and GOS fermentation by fecal bacteria show that both prebiotics are butyrigenic. At concentrations of 10 g/l, FOS, GOS, and inulin were shown to increase acetate and butyrate formation in pH-controlled fermentors, with transient accumulation of lactate.[19] This can also be seen in Table 4. Interestingly, acetate and lactate formation are consistent with bifidobacterial and lactobacillus metabolism, but butyrate is not produced by these organisms, showing that other species are involved in

TABLE 1. Effects of Inorganic Electron Donors on Fermentation Product Formation by Human Fecal Bacteria Incubated In Vitro

	Acetate	Propionate	Butyrate	Lactate
Nitrate				
Control	55	14	21	10
+ 5 mM NO_3^-	76	12	10	Not detected
Sulfate				
Control	40	31	19	10
+ 5 mM SO_4^{2-}	54	38	8	Not detected

Values show relative molar ratios.

TABLE 2. Modeling the Effects of Retention Time (R) and Substrate Availability on Carbohydrate (CHO) Utilization by Fecal Bacteria Using a 3-stage Continuous Culture Model of the Colon

	$R = 27$ h		$R = 66.7$ h	
Vessel	Specific Rate of CHO Utilization (q_s)	Percentage Utilized	Specific Rate of CHO Utilization (q_s)	Percentage Utilized
1	16.55	56.0	10.92	78.7
2	7.67	92.3	1.51	95.7
3	0.73	95.9	0.25	97.9

q_s [nmol sugar utilized min^{-1} (mg. dry weight bacteria)$^{-1}$]. Polymerized CHO comprised starch, mucin, pectin, guar gum, arabinogalactan, xylan, and inulin.

prebiotic digestion. Potential mechanisms whereby FOS and GOS can act as butyrate sources were provided by Belenguer et al,[20] who showed how butyrate-producing species such as *Anaerostipes caccae* and *Eubacterium halli* could cross-feed on lactate produced by *Bifidobacterium adolescentis* growing on FOS, while a nonlactate utilizing, butyrate-forming *Roseburia* sp. could assimilate carbohydrate fragments formed from the hydrolysis of complex polymeric substances by the bifidobacterium.

PHYSIOLOGIC SIGNIFICANCE OF CARBOHYDRATE FERMENTATION

Although the most obvious metabolic effects of carbohydrate breakdown by intestinal bacteria are associated with the biochemical effects of SCFA in human body tissues, the significance of saccharolytic metabolism is more widespread. For example, laxative effects resulting from increased bacterial cell mass increase colonic transit times. Thus, digestive materials move through the large bowel faster, giving less time for significant levels of protein breakdown and amino acid fermentation to occur. This means that less putrefactive substances, such as ammonia, phenols, indoles, amines, and hydrogen sulfide, accumulate in gut contents. The inhibitory effects on toxin accretion in the large bowel are also due to low pH conditions resulting from carbohydrate fermentation and increased biosynthetic requirements for nitrogen-containing precursors during saccharolytic bacterial growth.[21,22]

PHYSIOLOGIC EFFECTS OF SCFA

Acetate

Acetate has a multiplicity of effects on mammalian physiology. In colonic tissues, it has been shown that there is a concentration-dependent reduction in the frequency of spontaneous longitudinal muscle contractions in rat colonic smooth muscle,[23] whereas this SCFA stimulates proliferation of normal crypt cells.[24] Acetate also enhances ileal motility and increases colonic blood flow,[24] and it may have a role in adipogenesis, through interacting with the G protein-coupled receptor GPCR43 on adipose tissue.[25]

With respect to the host immune system, acetate has been shown to interact with GTP-binding proteins (GPCR43 and GPCR41) in immune cells,[26,27] whereas it activates the free fatty acid receptor FFA2R on leucocytes.[28] Acetate has also been reported to reduce lipopolysaccharide-stimulated tumor necrosis factor (TNF) α release from human neutrophils and to

TABLE 3. Modeling the Effects of System Retention Time (R) and Substrate Availability on Carbohydrate (CHO) Utilization and SCFA Formation by Fecal Bacteria Using a 3-stage Continuous Culture Model of the Colon

	$R = 27\,h$			$R = 66.7\,h$		
Vessel	CHO Utilized	SCFA Produced	Apparent Conversion (%)	CHO Utilized	SCFA Produced	Apparent Conversion (%)
1	8.53	5.68	66.6	12.00	5.36	44.7
2	14.06	8.84	62.9	14.59	5.92	40.6
3	14.62	9.24	63.2	14.92	6.68	44.8

Experimental values are grams per liter.
SCFA indicates short-chain fatty acid.

inhibit nuclear factor (NF)-κB reporter activity in human colon carcinoma colo320DM cells,[26] it also suppresses interleukin (IL)-6 release from mouse colon organ cultures.[26] Intravenous administration of acetate increases peripheral blood antibody production and natural killer cell activity in cancer patients.[29]

Propionate

Similar to acetate, this SCFA has been shown to exert a concentration-dependent increase in the frequency of spontaneous contractions in longitudinal and circular rat colonic smooth muscle.[23] Propionate reduces food intake and increases satiety in animal-feeding studies,[30,31] whereas dietary supplementation of a dairy beverage fermented with propionic acid bacteria has been reported to increase satiety in humans.[32] It increases production of leptin, a satiety hormone in human and murine tissues,[33,34] stimulating its formation through the G protein-coupled receptor GPR41.[34,35] Propionate increases adipogenesis through GPCR43 in mouse adipose tissue and upregulates peroxisomal proliferator-activated receptor PPAR-γ2.[25] It also activates the G protein-coupled receptor 43 in adipocytes and inhibits lipolysis.[36] Propionate may be protective against carcinogenesis, as it has been found to play a role in growth arrest and differentiation of human colon cancer cells, which is associated with hyperacetylation of histone proteins.[37] It also induces colorectal cancer apoptosis through the mitochondrial adenine nucleotide transporter.[38]

TABLE 4. SCFA Production by Fecal Bacteria During In Vitro Prebiotic Fermentations in Batch Culture

	Concentration (mM)			
Time (h)	Acetate	Propionate	Butyrate	Lactate
Control				
0	10.2	3.3	3.2	1.1
3	11.0	3.2	3.8	Not detected
12	16.4	4.7	3.9	Not detected
FOS				
0	10.2	3.3	3.2	1.1
3	19.7	5.8	12.6	30.1
12	140	32.4	50.5	Not detected
GOS				
0	10.2	3.3	3.2	1.1
3	23.5	7.8	11.0	14.7
12	148	34.9	42.3	1.8
Inulin				
0	10.2	3.3	3.2	1.1
3	15.2	5.0	7.6	15.2
12	97.6	19.0	28.2	Not detected

FOS indicates fructooligosaccharides; GOS, galactooligosaccharides.

Propionate derivatives inhibit bovine cycloxygenase activity,[39] which is involved in the production of proinflammatory eicosanoids.[40] It interacts with GTP-binding proteins (GPCR43 and GPCR41) in immune cells,[27,28] and inhibits NF-κB, as well as reducing the expression of cytokine-induced adhesion molecules such as VCAM-1 and ICAM-1 in human endothelial cells.[41] Propionate inhibits lipopolysaccharide-stimulated TNFα production in human neutrophils[26] and the formation of proinflammatory cytokines produced by human adipose tissue[42] as well as regulating and inhibiting the proliferation of human and animal-activated lymphocytes.[33,43]

Other physiologic effects are associated with this fatty acid, for example, diets supplemented with propionate lower blood cholesterol levels in rats and pigs.[44,45] While it inhibits cholesterol synthesis in isolated rat hepatocytes,[46] lowers blood glucose, and alters lipid metabolism in healthy human individuals.[47] More problematically, intraventricular infusions can impair social behavior and cause brain abnormalities in rats, similar to those detected in human autism.[48–50] Propionate infusion also results in alterations of brain phospholipid and acylcarnitine profiles in rats,[51] while inducing neuroinflammation and oxidative stress in the brain in intraventricular infused rats.[52]

Butyrate

This SCFA is probably the most interesting bacterial fermentation product in the human colon. It is the principal fuel for intestinal epithelial cells and plays an important role in maintaining colonic health. Acetate, propionate, and butyrate are all metabolized to some extent by the epithelium to provide energy, but butyrate is especially important as a fuel for these cells and may also play a critical role in moderating cell growth and differentiation. The colonic epithelium derives 60% to 70% of its energy from bacterial fermentation products.[53–55] Experiments on CO_2 formation using mixtures of SCFA indicate that cellular activation is in the order of butyrate > propionate > acetate. SCFA are metabolized to CO_2 and ketone bodies and are precursors for mucosal lipid synthesis. More than 70% of oxygen consumption in isolated colonocytes is due to butyrate oxidation, although there are regional differences in enterocyte energy metabolism in the large bowel.[56] The uptake and utilization of butyrate by the colonic epithelium have been demonstrated from the study of levels of SCFA in portal and arterial blood and in colonic contents. SCFA measurements in body tissues shows that the molar proportion of butyrate falls from 21% in the gut lumen to 8% in portal blood, indicating a 65% clearance by the mucosa.[57]

Butyrate exhibits a range of anti-inflammatory properties and has been shown to restore intestinal permeability by

enhanced activation of peroxisomal proliferator-activated receptor and reduced expression of *IL-8* genes in HT-29 cell lines.[58] Butyrate represses inflammatory responses by inhibition of NF-κB activation.[59,60] It also mediates in vitro modulation of the immune system by proliferation-related induction of apoptosis.[61] Butyrate suppresses production of TNFα in macrophage-like synoviocytes in rheumatoid arthritis patients, and in human peripheral monocytes by regulating mRNA degradation.[62] Butyrate enemas have been shown to reduce infiltrating neutrophils and lymphocytes, and to decrease disease activity indices in active distal ulcerative colitis.[60] Moreover, this SCFA directly interacts with the immune system through specific G-coupled receptors GR41 and GR43.[27] It reduces the expression of IL-12 and increases IL-10 production in activated human monocytes,[63] and it transcriptionally activates and enhances the peptide transporter PepT1, which is induced in the large gut during chronic inflammation in colonic epithelial cells.[64] Butyrate also increases apoptosis of activated and nonactivated neutrophils.[65]

Butyrate manifests diverse properties in a wide range of mammalian cell types.[56] These include the arrest of cell growth early in G_1, induction of differentiation, stimulation of cytoskeletal organization, and alterations in gene expression. The effect of this fatty acid on cellular differentiation is related to the control of gene expression. This affects many cellular processes, including the induction of hemoglobin synthesis in murine erythroleukemia cells, EGF receptors in hepatocytes, plasminogen activator synthesis in endothelial cells, thyroid hormone receptors in the pituitary gland, metallothionein in hepatoma cells, estrogen, prolactin, and EGF receptors in breast tissue cells. In colorectal cancer cells, a number of changes in gene expression can be seen such as the induction of c-fos, PLAP, and carcinoembryonic antigen; inhibition of urokinase and release of plasminogen activator inhibitor; and the expression of brush border glycoprotein and P-glycoprotein. The induction of differentiation in tumor cell lines is associated with changes in cytoskeletal architecture and their adhesion properties; butyrate induces apoptosis in human colonic carcinoma cells and may be protective in colorectal cancer.[66–71] It inhibits tumor cell progression by inhibiting decay-accelerating expression[72] and prometastatic metalloproteinase activation[73] and protects against chromosome-induced damage in human colon carcinoma cells.[74] The migration and invasion potential of Ht1080 tumor cells is also inhibited.[75] Butyrate modulates vascular endothelial growth factor and hypoxia-inducible factor-1α angiogenesis-related proteins, which leads to inhibition of tumor-induced angiogenesis.[76,77] It hyperinduces Wnt transcriptional activity in colorectal cancer cell lines, induces apoptosis, and may protect against colorectal cancer.[78] Butyrate reduces in vitro lymphocyte proliferation in mice and rats.[79,80] This SCFA therefore modulates the expression of a wide range of genes associated with cell proliferation, differentiation, and apoptosis.[81]

Butyrate has been found to exert a number of protective effects against oxidative H_2O_2-induced DNA damage in isolated human colonocytes and HT29 tumor cells.[82] It was shown to increase levels of the antioxidant glutathione in mucosal biopsies from the sigmoid colon of healthy volunteers given daily butyrate enemas,[83] whereas butyrate enemas resulted in increased transcriptional regulation of fatty acid metabolism as well as electron transport and oxidative stress pathways in the colonic

mucosa of healthy volunteers.[84] In vitro studies have supported these findings and have shown that it is able to modulate the expression of genes associated with oxidative and metabolic stress in human colonic cells.[85]

Barrier function in the gut is enhanced by butyrate, in which it upregulates the expression of mucin-associated genes (*MUC1-4*) in intestinal epithelial goblet cells.[86] Administration of rectal enemas to mice increases colonic expression of secreted Muc2 and membrane linked (*Muc1*, *Muc3*, *Muc4*) genes, but effects a reduction in adherent mucus layer thickness.[87] Butyrate affects the expression of tight junction proteins such as zonulin and occludin,[88] and even low concentrations promote intestinal barrier function and reduce epithelial permeability.[89] Interestingly, it has been shown to reduce translocation of *Escherichia coli* across metabolically stressed dinitrophenol-treated epithelial human colonic T84 and HT29 cell lines.[90]

A range of other physiologic attributes have been linked to butyrate. Similar to propionate, butyrate promotes satiety and has been found to increase the expression of peptides involved in the regulation of appetite such as peptide YY and proglucagon in rat epithelial cells[91] and to downregulate the expression of the neuroendocrine factor leptin in rat anterior pituitary cells.[92] Oligofructose consumption has been reported to promote satiety in humans, which is suggested to be due to increased production of SCFA such as butyrate,[93] which also reverses and prevents diet-induced insulin resistance in mice.[94] Rectal enemas are known to reduce visceral sensitivity in healthy volunteers,[95] and butyrate has been shown to regulate enteric neuronal function and to control intestinal motility in rats,[96] whereas increased butyrate concentrations in the large bowel of rats effectuated by feeding butyrylated starch have been reported to reduce colonic smooth muscle contractility.[97]

CONCLUSIONS

The breakdown of complex carbohydrates is one of the most important processes carried out by bacteria growing in the human large intestine. Through fermentation and SCFA formation, the colonic microbiota plays a central role in biochemical and physiologic processes in the large bowel and in remote body sites. Fermentation is regulated, in large part, through substrate availability in the colon. This ultimately affects the way in which different fatty acids, such as acetate, propionate, and butyrate, are produced. The metabolic significance of this to the host is that in many respects, individual SCFA are handled in different ways by the body. For example, butyrate, in particular, has been linked with energy generation by the colonic epithelium, and has a variety of anticancer properties, whereas propionate is most often associated with lipid metabolism. Work over the last 2 decades has shown consistently that prebiotic oligosaccharides such as FOS and GOS escape digestion in the upper gut but are fermented by bacteria inhabiting the large intestine. There is a growing body of evidence that shows that prebiotics have a diverse range of health benefits, particularly in relation to their influence on microbial ecology in the gut, mineral absorption, laxation, potential anticancer properties, and lipid metabolism, together with anti-inflammatory and other immune effects, including atopic disease. Many of these phenomena can be attributed to fermentation processes and SCFA production in the large bowel.

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