

# Commensal Bacteria

The most current, literature-based information on human studies related to increased or decreased levels of the commensal bacteria is summarized in the following chart. Note that the findings in the literature may not be consistent with Genova's findings due to different methodologies, thus treatment efficacy may vary. Most therapeutic interventions do not work in isolation, meaning they do not exclusively only target that one organism. Genova has not conducted outcome studies on the impact of certain therapeutics on the microbiome markers. Clinician discretion is advised for appropriateness of therapeutics.

Under certain conditions, environmental factors may influence specific commensals to become pathobionts. Pathobionts are distinguished from true infectious agents; they are potential pathogens under certain conditions. It is unknown whether these organisms play a causative role in disease or are a consequence of a disease state. Literature is evolving regarding the definition of a pathobiont and the role of commensal bacteria.<sup>1-3</sup>

Organism	Description	Increased Levels	Decreased Levels
<i>Bacteroides uniformis</i>	<p><i>Bacteroides uniformis</i> is a fiber-degrading bacteria. It colonizes the gut in early infancy and is promoted by breast feeding.<sup>4</sup></p> <p>Thought to enhance the gut barrier through the production of butyrate and GABA.<sup>5,6</sup> Also produces beta glucuronidase, degrades mucin, and produces folate.<sup>4,7,8</sup></p> <p>Studied in preclinical trials as a potential probiotic for use in inflammatory and metabolic disorders.<sup>9-11</sup> <i>B. uniformis</i> was found to be decreased in obese patients as compared to healthy or lean groups.<sup>12,13</sup> It was higher in healthy controls as compared to patients with ulcerative colitis.<sup>14</sup></p> <p>Enriched in healthy individuals versus colorectal cancer patients.<sup>15</sup></p> <p>Associated with degradation of the isoflavone genistein, which then becomes less bioavailable to the human.<sup>16</sup></p>	<p>In ten healthy males, the consumption of red wine polyphenols for 4 weeks significantly increased the amount of <i>Bacteroides uniformis</i> as well as other commensal bacteria species.<sup>17</sup></p> <p>Higher levels of insoluble fiber are associated with higher levels of <i>B. uniformis</i>.<sup>18</sup></p> <p>A more favorable metabolic risk profile in men on a healthy plant-based diet was seen with a certain microbial profile featuring increased <i>B. uniformis</i> and decreased <i>Prevotella copri</i>. The healthy diet was characterized by a higher intake of fiber, plant proteins, whole grains, fruits, vegetables, nuts, and legumes, and a lower intake of energy, animal proteins, refined grains, potatoes, sweets, animal fat, egg, dairy, and meats.<sup>19</sup></p> <p>A small study (n=13) showed the presence of <i>B. uniformis</i> and other <i>Bacteroides</i> species in non-vegetarians, versus vegetarians.<sup>20</sup></p>	<p>Higher fiber intake from beans is associated with lower abundance of <i>B. uniformis</i>.<sup>21</sup></p>
<i>Phocaeicola vulgatus</i>	<p>Generally considered a beneficial gut commensal, although is capable of attaching to and invading colonic epithelial cells and inducing pro-inflammatory cytokines.<sup>22</sup></p> <p>Produces beta-glucuronidase, succinate, lactate, acetate, formate, and propionate.<sup>23,24</sup></p>	<p>A high beef diet was associated with increases in <i>Bacteroides fragilis</i>, <i>B. vulgatus</i> and <i>Clostridium</i> spp. in 10 volunteers.<sup>27</sup></p>	<p>Decreased levels were found in 7-12-year olds who consumed oligofructose-enriched inulin (<i>BENEO's</i> prebiotic fiber <i>Synergy1</i>) for 16 weeks in a double-blind-controlled trial.<sup>28</sup></p>

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	<p>Associated with insulin resistance.<sup>25</sup></p> <p>Contains bile salt hydrolases to metabolize bile.<sup>26</sup></p> <p>Formerly named <i>Bacteroides vulgatus</i></p>		Dietary inulin-type fructan prebiotics decreased <i>Bacteroides vulgatus</i> in obese women which positively correlated with changes in body composition and glucose homeostasis. <sup>29</sup>
<i>Barnesiella</i> spp.	<p><i>Barnesiella</i> spp. is a small group made up of two species with <i>B. intestinhominis</i> isolated in humans.<sup>30,31</sup></p> <p><i>B. intestinhominis</i> is found in individuals in industrialized populations versus hunter-gatherer societies and generally correlates with beneficial effects on the human gut.<sup>32,33</sup></p> <p><i>Barnesiella</i> colonization correlates with reduced antibiotic-resistant <i>Enterococcus</i> species,<sup>34</sup> eradication of <i>Klebsiella pneumoniae</i>,<sup>35</sup> and has other beneficial immunoregulatory effects including potential applications in cancer treatment.<sup>36,37</sup> Positively correlates with plasma cholesterol in mice.<sup>38</sup></p>	<p>4 bacteria are enriched with aspirin use versus no medication and includes <i>Bacteroides</i> spp., <i>Prevotella</i> spp., <i>Barnesiella</i> spp. and the family Ruminococaceae.<sup>39</sup></p>	<i>Lactobacillus kefir</i> was given to 20 healthy volunteers for one month and after the probiotic was discontinued for a month, <i>Bacteroides</i> , <i>Barnesiella</i> , <i>Clostridium</i> , <i>Veillonella</i> and other species were significantly reduced compared to baseline samples. <sup>40</sup>
<i>Odoribacter</i> spp.	<p>This genus includes three species: <i>O. denticanis</i>, <i>O. laneus</i>, <i>O. splanchnicus</i>.<sup>41</sup></p> <p>Produces butyrate, acetate, propionate, indole from tryptophan, products of protein breakdown, hydrogen and H<sub>2</sub>S.<sup>41</sup></p>	<p>Animal based diets have been found to increase <i>Odoribacter</i> spp.<sup>42</sup></p> <p>Levels of <i>Bacteroides</i>, <i>Faecalibacterium</i>, <i>Odoribacter</i>, and others enriched after pomegranate extract consumption in overweight-obese subjects. Serum endotoxemia marker LBP was reduced.<sup>43</sup></p>	Higher fiber intake is associated with lower abundance of <i>Odoribacter</i> . <sup>21</sup>
<i>Prevotella</i> spp.	<p>The <i>Prevotella</i> genus is comprised of more than 40 species, and three predominate in the gut with <i>P. copri</i> being most abundant. The majority of <i>Prevotella</i> spp. are found in the oral cavity.<sup>44</sup></p> <p><i>Prevotella</i> has been linked with chronic inflammatory conditions and insulin resistance,<sup>44</sup> however others have linked <i>P. copri</i> with improved glucose tolerance in diets rich in fiber. <i>Prevotella</i> effects may be diet-dependent. For example, <i>P. copri</i> strains associated with an omnivorous diet may result in higher BCAA synthesis, a risk factor for</p>	<p>A <i>Prevotella</i>-dominated microbiome is richer in response to plant-based, complex carb, high-fiber diet.<sup>51</sup></p> <p>Individuals with a high <i>Prevotella</i>-to-<i>Bacteroides</i> ratio lost more body weight and body fat compared to individuals with low P/B, confirming that individuals with a high P/B are more susceptible to weight loss on a diet rich in dietary fiber (30+grams).<sup>50</sup></p> <p>4 bacteria are enriched with aspirin use versus no medication and includes <i>Bacteroides</i> spp., <i>Prevotella</i> spp., <i>Barnesiella</i> spp. and the family Ruminococaceae.<sup>39</sup></p> <p>Cigarette smoking is associated with increased levels.<sup>52</sup></p>	<p><i>Lactobacillus kefir</i> was given to 20 healthy volunteers and at the end of one month, <i>Prevotella</i> and other species were reduced compared to baseline samples.<sup>40</sup></p> <p>A Standard American Diet (low-fiber/high-animal based) has been associated with reduced levels and less diversity of <i>Prevotella</i>.<sup>53</sup></p>

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	<p>glucose intolerance and DM2, whereas fiber-rich diets were linked to <i>P. copri</i> types with enhanced potential for carbohydrate metabolism.<sup>45,46</sup></p> <p>Acetate, propionate, and succinate producer;<sup>47,48</sup> mucin degrader.<sup>49</sup></p> <p>Generally associated with traditional, agrarian diets across Africa, Asia, and South America.<sup>50</sup></p>	<p>Red wine polyphenol intake for 4 weeks in 10 healthy males was associated with increased <i>Prevotella</i>.<sup>17</sup></p>	
<i>Anaerotruncus colihominis/massiliensis</i>	<p>The genus <i>Anaerotruncus</i> includes species <i>Anaerotruncus colihominis</i> and <i>Anaerotruncus massiliensis</i>.</p> <p><i>A. colihominis</i> is a butyrate and acetate producer.<sup>54</sup> Abundance is associated with higher bacterial gene richness in the gut.<sup>55</sup></p> <p><i>A. colihominis</i> is increased in healthy individuals and presumed to be anti-inflammatory.<sup>56</sup> There is an inverse correlation with high BMI and elevated serum triglycerides in older Amish adults.<sup>57</sup></p> <p>There is an inverse relationship with <i>A. colihominis</i> abundance and cognitive function scores in patients with Alzheimer's disease.<sup>58</sup></p> <p><i>A. massiliensis</i> is a newly identified strain similar to <i>A. colihominis</i>.<sup>59,60</sup> They both ferment amino acids and carbohydrates and are mucin degraders.<sup>61</sup></p>	<p><i>Anaerotruncus</i> abundance is associated with high saturated fat consumption in a study on healthy individuals.<sup>62</sup></p> <p>In a study on older men, adherence to a Western diet is associated with higher relative abundance of several bacteria including the genus <i>Anaerotruncus</i>.<sup>63</sup></p>	
<i>Butyrivibrio crossotus</i>	<p>Butyrate producer.<sup>55</sup></p> <p>Abundance may help protect against weight gain.<sup>55</sup></p> <p>Abundance associated with higher bacterial gene richness in the gut.<sup>55</sup></p>	<p><i>B. crossotus</i> correlated with xylanase/xylosidase enzymes that break down complex carbohydrates, mainly from grains.<sup>64</sup></p> <p>Higher counts of <i>Butyrivibrio</i> spp. appear to be associated with a diet richer in complex carbohydrates than animal protein.<sup>65</sup></p>	
<i>Clostridium</i> spp.	<p><i>Clostridium</i> spp. is a genus belonging to the phylum Firmicutes. While interpreting the literature, careful attention should be paid to the phylogenetic classification of this group due to minor spelling differences between the</p>	<p>Cigarette smoking is associated with increased levels.<sup>52</sup></p> <p>Coffee was positively associated with the relative abundance of <i>Clostridium</i>, <i>Lactobacillus</i>, and <i>Lactococcus</i> in 23 allergic patients.<sup>71</sup></p>	<p><i>Lactobacillus kefir</i> was given to 20 healthy volunteers for one month and after the probiotic was discontinued for a month, <i>Bacteroides</i>, <i>Barnesiella</i>, <i>Clostridium</i>, <i>Veillonella</i> and other</p>

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	<p>taxonomic levels. Beyond the phylum level, it is broken down as follows: Class: Clostridia, Order: Clostridiales, Family: Clostridiaceae, and finally, Genus: <i>Clostridium</i>. The <i>Clostridium</i> genus contains more than 100 species, most of which are commensal, however it does include pathogens. The literature discusses Clostridial clusters, which may include other species belonging to <i>Eubacterium</i>, <i>Ruminococcus</i>, <i>Roseburia</i>, <i>Butyrivibrio</i>, <i>Faecalibacterium</i> and other genera. These clusters exist due to historic issues with classification, where unclassified species would be moved into the <i>Clostridium</i> category.<sup>66,67</sup></p> <p>The <i>Clostridium</i> spp. probe is not meant to diagnose pathogenic <i>Clostridium</i> infections. An add-on <i>Clostridium difficile</i> EIA stool test is available if patient symptoms warrant testing.</p> <p>Produces butyrate, acetate, hydrogen, secondary bile acids, beta-glucuronidase.<sup>23,68,69</sup></p> <p>Along with <i>Methanobrevibacter smithii</i>, certain <i>Clostridium</i> and <i>Bacteroides</i> spp. can produce methane gas.<sup>70</sup></p> <p>Necessary for immune homeostasis.<sup>66</sup></p> <p>Many of its species are associated with lower bacterial gene richness.<sup>25</sup></p>	<p>A high beef diet was associated with increases in <i>Bacteroides</i> and <i>Clostridium</i> spp. in 10 volunteers.<sup>27</sup></p>	<p>species were significantly reduced compared to baseline samples.<sup>40</sup></p> <p>After 12 weeks, a significant increase in <i>Bifidobacteria</i>, and decrease in pathogenic <i>Clostridium</i> spp. (<i>C. histolyticum</i> and <i>C. coccooides</i> clusters) were observed in 57 HIV positive adults supplemented with a prebiotic oligosaccharide powder (15 or 30 g short chain galactooligosaccharides/long chain fructooligosaccharides/pectin hydrolysate-derived acidic oligosaccharides (scGOS/lcFOS/pAOS)).<sup>72</sup></p>
<i>Coprococcus eutactus</i>	<p>Butyrate producer.<sup>47,73</sup></p> <p>Abundance associated with greater bacterial gene richness in the gut.<sup>55</sup></p>	<p>Higher abundance was seen on a very low protein diet supplemented with select amino acids in patients with chronic kidney disease. <i>C. eutactus</i> correlated with fiber, vegetable proteins, potassium, and ketoanalogs.<sup>74</sup></p>	
<i>Faecalibacterium prausnitzii</i>	<p><i>Faecalibacterium prausnitzii</i> belongs to the <i>Clostridium</i> cluster IV, also known as the <i>Clostridium leptum</i> group.<sup>67,75</sup></p> <p>Predominant butyrate-producer contributing to a healthy mucosa and barrier function. Controls inflammation through inflammatory cytokine inhibition. <i>F. prausnitzii</i> produces an anti-inflammatory protein called Microbial Anti-</p>	<p>There are many studies on the beneficial effects of fiber and prebiotics on increasing <i>F. prausnitzii</i> levels, however some studies show mixed results in various populations. This may be due to the many strains of <i>F. prausnitzii</i> responding to different substrates.<sup>75,76</sup></p> <p>Higher fiber intake is associated with higher abundance of <i>Faecalibacterium</i>.<sup>21,77</sup></p>	<p>A small study of 10 healthy subjects showed reduced <i>F. prausnitzii</i> after 1 month on a gluten-free diet (GFD).<sup>88</sup> Another study did not find a change in <i>F. prausnitzii</i> levels on a GFD in healthy individuals, but did observe a decrease in abundance of other butyrate-producing bacteria in the Firmicutes phylum.<sup>89</sup></p>

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	<p>inflammatory Molecule (MAM) which inhibits the activation of NF-κB.<sup>76,77</sup></p> <p>There are many strains of <i>F. prausnitzii</i> that respond to different substrates including simple carbohydrates, amino acids, pectin, non-digestive polysaccharides, and host-derived mucosal substrates.<sup>76</sup> It ferments glucose and acetate to produce formate, D-lactate, and butyrate.<sup>77</sup></p> <p><i>F. prausnitzii</i> is an extremely oxygen-sensitive anaerobe. Therefore, the development of a therapeutic supplement proves challenging.<sup>77</sup></p> <p><i>F. prausnitzii</i> growth and butyrate production is favored at a lower pH in culture, around 5.7 to 6.7.<sup>76,78</sup></p>	<p>Long-term consumption of a low-fat, high complex carbohydrate diet was associated with increased abundance of <i>F. prausnitzii</i>, in an obese population.<sup>79</sup></p> <p>Levels of <i>Bacteroides</i>, <i>Faecalibacterium</i>, <i>Odoribacter</i>, and others enriched after pomegranate extract consumption in overweight-obese subjects. Serum endotoxemia marker LBP was reduced.<sup>43</sup></p> <p>Levels increased after polydextrose and soluble corn fiber intake.<sup>80</sup></p> <p><i>F. prausnitzii</i> was more abundant in a raffinose and chick pea diet compared to controls.<sup>75</sup></p> <p>Inulin and inulin-type fructans increased <i>Bifidobacterium</i> and <i>F. prausnitzii</i>.<sup>29,77,81</sup> A systematic review of inulin supplementation in humans showed an increase in <i>Bifidobacterium</i>, and a relative increase in <i>Faecalibacterium</i> and <i>Lactobacillus</i>, and decrease in relative abundance of <i>Bacteroides</i>.<sup>82</sup></p> <p>Red wine consumption was associated with an increased abundance of <i>F. prausnitzii</i>.<sup>83</sup> In ten metabolic syndrome patients, red wine polyphenols significantly increased the number of fecal <i>Bifidobacteria</i> and <i>Lactobacillus</i> (intestinal barrier protectors) and butyrate-producing bacteria (<i>Faecalibacterium prausnitzii</i> and <i>Roseburia</i>) at the expense of less desirable groups of bacteria such as LPS producers (<i>Escherichia coli</i> and <i>Enterobacter cloacae</i>).<sup>84</sup></p> <p>Most strains can grow on apple pectin.<sup>76</sup></p> <p>A decline in <i>F. prausnitzii</i> in 20 patients with IBS on a low FODMAP diet can be recovered with supplementation of prebiotic fructo-oligosaccharides (FOS).<sup>85</sup></p> <p>Physical activity at doses as low as the minimum recommended by the WHO may increase health-promoting species including <i>Bifidobacterium</i> spp., <i>Roseburia hominis</i>, <i>Akkermansia muciniphila</i> and <i>Faecalibacterium prausnitzii</i>. However, in a study</p>	<p>A low FODMAP diet in 52 IBD patients resulted in lower <i>Bifidobacterium adolescentis</i>, <i>Bifidobacterium longum</i>, and <i>Faecalibacterium prausnitzii</i> than patients on a control diet. However, microbiome diversity and markers of inflammation did not differ between the IBD and control groups.<sup>90</sup> Lower <i>F. prausnitzii</i> and <i>Bifidobacterium</i> was observed in 20 patients with IBS-D or IBS-M on a low FODMAP diet. Additionally, total SCFAs and n-butyrate were lower.<sup>85</sup></p> <p>Excess bile salt.<sup>76</sup></p> <p>A ketogenic, low-carbohydrate, high-fat diet was associated with a reduction of <i>Faecalibacterium</i> and abundance of <i>Bacteroides</i> and <i>Dorea</i> spp. in competitive race walkers.<sup>91</sup> However another study on a ketogenic diet in 6 patients with GLUT1 Deficiency Syndrome did not have an effect on <i>F. prausnitzii</i>.<sup>92</sup></p> <p>Oral versus IV iron supplementation in iron-deficient IBD patients resulted in decreased abundances of <i>Faecalibacterium prausnitzii</i>, <i>Ruminococcus bromii</i>, <i>Dorea</i> spp., and <i>Collinsella aerofaciens</i>.<sup>93</sup></p>

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		<p>comparing sedentary to active women, dietary differences were noted, which may account for the bacterial differences. The active group consumed more fiber, fruits and vegetables, and the sedentary group consumed more processed meats.<sup>86</sup></p> <p>The poorly absorbed antibiotic rifaximin was associated with increases in beneficial bacteria <i>F. prausnitzii</i>, <i>Bifidobacterium</i>, and <i>Lactobacillus</i> in human studies.<sup>87</sup></p>	
<i>Lactobacillus</i> spp.	<p>There are over 170 species of <i>Lactobacillus</i>.<sup>94</sup> Many species and strains are found in probiotic supplements and fermented foods. There are numerous studies on the therapeutic benefits of probiotics.<sup>95</sup></p> <p>Ferments carbohydrates to produce lactic acid, inhibits the colonization of pathogens, enhances barrier integrity, and beneficially modulates the immune system.<sup>95</sup></p> <p>Both <i>Lactobacillus</i> and <i>Bifidobacterium</i> (probiotic bacteria) are involved in the process of converting polyphenols to phytoestrogens, converting glucosinolates from cruciferous vegetables to isothiocyanates which are cytoprotective and antioxidative, B vitamin production, and SCFA production.<sup>96</sup> Along with <i>Oxalobacter formigenes</i>, <i>Lactobacillus</i> and <i>Bifidobacterium</i> are also capable of consuming oxalate.<sup>97</sup></p>	<p>Whey and pea protein, a Mediterranean diet, polyphenols (catechins, flavonols, flavones, anthocyanins, proanthocyanidins, phenolic acids found in fruits, seeds, vegetables, tea, cocoa, wine) increase beneficial bacteria <i>Lactobacillus</i> and <i>Bifidobacterium</i>.<sup>98</sup></p> <p>A study using a partially hydrolyzed guar gum preparation was administered to 15 constipated women for 3 weeks. <i>Lactobacillus</i> spp. increased and constipation improved.<sup>99</sup></p> <p>In ten metabolic syndrome patients, red wine polyphenols significantly increased the number of fecal <i>Bifidobacteria</i> and <i>Lactobacillus</i> (intestinal barrier protectors) and butyrate-producing bacteria (<i>Faecalibacterium prausnitzii</i> and <i>Roseburia</i>) at the expense of less desirable groups of bacteria such as LPS producers (<i>Escherichia coli</i> and <i>Enterobacter cloacae</i>).<sup>84</sup></p> <p>A systematic review of inulin supplementation in humans showed an increase in <i>Bifidobacterium</i>, and a relative increase in <i>Faecalibacterium</i> and <i>Lactobacillus</i>, and decrease in relative abundance of <i>Bacteroides</i>.<sup>82</sup></p> <p>Coffee was positively associated with the relative abundance of <i>Clostridium</i>, <i>Lactobacillus</i>, and <i>Lactococcus</i> in 23 allergic patients.<sup>71</sup></p> <p>The poorly absorbed antibiotic rifaximin was associated with increases in beneficial bacteria <i>F. prausnitzii</i>, <i>Bifidobacterium</i>, and <i>Lactobacillus</i> in human studies.<sup>87</sup></p>	<p>A small study of 10 healthy subjects showed reduced <i>Lactobacillus</i>, <i>Bifidobacterium</i> and <i>Bifidobacterium longum</i> after 1 month on a gluten-free diet (GFD).<sup>88</sup></p> <p>High saturated and trans-fat, found in a Western diet, increases the risk of cardiovascular disease and reduces <i>Lactobacillus</i>.<sup>96</sup></p> <p>A Western diet is associated with decreased <i>Lactobacilli</i> and <i>Bifidobacteria</i>.<sup>98</sup></p>
<i>Pseudoflavonifractor</i> spp.	<p>Small group made up of two species: <i>Pseudoflavonifractor capillosus</i> and <i>Pseudoflavonifractor phocaeensis</i>.<sup>100</sup></p>		<p>Decreased in long-term users of proton pump inhibitors.<sup>102</sup></p>

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	Study participants who succeeded in losing weight consistently had a microbiota enriched in <i>Pseudoflavonifractor</i> at baseline. <sup>101</sup>		
<i>Roseburia</i> spp.	<p>The genus <i>Roseburia</i> includes 5 species: <i>Roseburia intestinalis</i>, <i>R. hominis</i>, <i>R. inulinivorans</i>, <i>R. faecis</i> and <i>R. cecicola</i>.<sup>77,103</sup></p> <p>The <i>Roseburia</i> genus, along with <i>Faecalibacterium</i> are the predominant butyrate producers in the human GI tract.<sup>104</sup> <i>Roseburia</i> is involved in immune maintenance and is anti-inflammatory.<sup>103</sup></p>	<p>Higher <i>Roseburia</i> is associated with consuming a plant-based diet, Mediterranean diet and fiber-rich foods.<sup>79,105,106</sup></p> <p><i>Roseburia</i> increased on resistant starch diet.<sup>107</sup></p> <p>In ten metabolic syndrome patients, red wine polyphenols significantly increased the number of fecal <i>Bifidobacteria</i> and <i>Lactobacillus</i> (intestinal barrier protectors) and butyrate-producing bacteria (<i>Faecalibacterium prausnitzii</i> and <i>Roseburia</i>) at the expense of less desirable groups of bacteria such as LPS producers (<i>Escherichia coli</i> and <i>Enterobacter cloacae</i>).<sup>84</sup></p> <p>Physical activity at doses as low as the minimum recommended by the WHO may increase health-promoting species including <i>Bifidobacterium</i> spp., <i>Roseburia hominis</i>, <i>Akkermansia muciniphila</i> and <i>Faecalibacterium prausnitzii</i>. However, in a study comparing sedentary to active women, dietary differences were noted, which may account for the bacterial differences. The active group consumed more fiber, fruits and vegetables, and the sedentary group consumed more processed meats.<sup>86</sup></p>	<p><i>R. faecis</i> decreased on a gluten-free diet in 21 healthy volunteers.<sup>89</sup></p> <p>A small study on 11 healthy volunteers showed that an animal-based diet increased the abundance of bile-tolerant microorganisms (<i>Alistipes</i>, <i>Bilophila</i> and <i>Bacteroides</i>) and decreased the levels of Firmicutes that metabolize dietary plant polysaccharides (<i>Roseburia</i>, <i>Eubacterium rectale</i> and <i>Ruminococcus bromii</i>).<sup>108</sup></p> <p><i>Roseburia</i> decreased on a high-protein, low-carbohydrate weight loss diet in 14 overweight men.<sup>107</sup></p>
<i>Ruminococcus bromii</i>	<p><i>R. bromii</i> ferments resistant starch which is correlated with increased butyrate production downstream.<sup>109,110</sup> The major fermentation products include acetate, H<sub>2</sub>, and CO<sub>2</sub>.<sup>110</sup></p> <p>The byproducts of the degradation of resistant starch are used by bacterial species. Therefore, <i>R. bromii</i> supports microbiome diversity through cross-feeding.<sup>111</sup></p> <p>One study showed that five species, including <i>R. bromii</i>, were significantly more abundant in stool samples from obese individuals versus non-obese individuals.<sup>112</sup></p> <p><i>R. bromii</i> is enriched in healthy twins versus those with food allergies.<sup>113</sup> An infant study</p>	<p><i>R. bromii</i> increased on a resistant starch diet.<sup>89,107</sup></p> <p>In a study on 360 Spanish adults with different levels of adherence to a Mediterranean diet, legume consumption was shown to enhance <i>R. bromii</i>.<sup>115</sup></p> <p>In a population study on 156 asymptomatic Mexican adults, <i>Blastocystis</i> colonization was strongly correlated with an increase in <i>R. bromii</i>.<sup>116</sup></p>	<p><i>R. bromii</i> decreased on a gluten-free diet in 21 healthy volunteers.<sup>89</sup></p> <p>A small study on 11 healthy volunteers showed that an animal-based diet increased the abundance of bile-tolerant microorganisms (<i>Alistipes</i>, <i>Bilophila</i> and <i>Bacteroides</i>) and decreased the levels of Firmicutes that metabolize dietary plant polysaccharides (<i>Roseburia</i>, <i>Eubacterium rectale</i> and <i>Ruminococcus bromii</i>).<sup>108</sup></p> <p>Oral versus IV iron supplementation in iron deficient IBD patients resulted in decreased abundances of</p>

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	showed that depletion of <i>R. bromii</i> and <i>Akkermansia muciniphila</i> was associated with reduced butyrate and the development of atopic dermatitis. <sup>114</sup>		<i>Faecalibacterium prausnitzii</i> , <i>Ruminococcus bromii</i> , <i>Dorea</i> spp., and <i>Collinsella aerofaciens</i> . <sup>93</sup>  A study on 409 type 2 diabetes Chinese patients demonstrated the reduction of <i>R. bromii</i> with berberine. It is thought that the hypoglycemic effect of berberine is mediated by the inhibition of secondary bile acid biotransformation by <i>R. bromii</i> . <sup>117</sup>
<i>Veillonella</i> spp.	The genera <i>Veillonella</i> contains 12 Gram-negative species. This phylogenetic grouping is unusual as the larger Firmicutes phylum is comprised of Gram-positive bacteria. <sup>118</sup> <i>V. parvula</i> is often isolated from the human oral cavity and has also been found in the intestinal tract. Like other gram-negative bacteria, it produces LPS and in the oral cavity it is known to produce biofilm. <sup>119,120</sup>  Utilizes lactate to produce SCFAs acetate and propionate; <sup>68,121</sup> H <sub>2</sub> producer. <sup>122</sup>	Postprandial levels of lactose after milk intake in 14 healthy men were positively correlated with the abundance of <i>Veillonella</i> . <sup>123</sup>  The family <i>Veillonellaceae</i> increased with supplemental polydextrose and soluble corn fiber in 20 healthy adult males. <sup>124</sup> This family includes genera other than <i>Veillonella</i> , although <i>Veillonella</i> represents the majority of this family. <sup>118</sup>  <i>Veillonella</i> spp. increased following Roux-en-Y gastric bypass RYGB within the first 3 months and remained elevated for the first year. <sup>125</sup>	<i>Lactobacillus kefir</i> was given to 20 healthy volunteers for one month and after the probiotic was discontinued for a month, <i>Bacteroides</i> , <i>Barnesiella</i> , <i>Clostridium</i> , <i>Veillonella</i> and other species were significantly reduced compared to baseline samples. <sup>40</sup>  The family <i>Veillonellaceae</i> was decreased on a gluten-free diet in 21 healthy volunteers. <sup>89</sup> This family includes genera other than <i>Veillonella</i> , although <i>Veillonella</i> represents the majority of this family. <sup>118</sup>
<i>Bifidobacterium</i> spp.	Many species and strains are found in probiotic supplements and there are extensive studies on the therapeutic benefits of probiotics. Probiotics can beneficially modulate the microbiome and immune system. <sup>126</sup>  Both <i>Lactobacillus</i> and <i>Bifidobacterium</i> (probiotic bacteria) are involved in the process of converting polyphenols to phytoestrogens, converting glucosinolates from cruciferous vegetables to isothiocyanates which are cytoprotective and antioxidative, B vitamin production, and SCFA production. <sup>96</sup> Along with <i>Oxalobacter formigenes</i> , <i>Lactobacillus</i> and <i>Bifidobacterium</i> are also capable of consuming oxalate. <sup>97</sup> <i>Bifidobacteria</i> can prevent GI infections by competitive exclusion of pathogens. <sup>126</sup> They are equipped with genes related to carbohydrate metabolism from	Whey and pea protein increase beneficial bacteria <i>Lactobacillus</i> and <i>Bifidobacterium</i> . <sup>98</sup>  Human studies on individuals consuming partially hydrolyzed guar gum show an increase in <i>Bifidobacterium</i> and butyrate-producing bacteria. <sup>129-131</sup>  Daily walnut consumption (43 g) in 194 healthy individuals was associated with increased abundance of <i>Ruminococcus</i> and <i>Bifidobacterium</i> . <sup>132</sup>  Red wine polyphenol intake for 4 weeks in 10 healthy males was associated with increased <i>Bifidobacterium</i> . <sup>17</sup> In ten metabolic syndrome patients, red wine polyphenols significantly increased the number of fecal <i>Bifidobacteria</i> and <i>Lactobacillus</i> (intestinal barrier protectors) and butyrate-producing bacteria ( <i>Faecalibacterium prausnitzii</i> and <i>Roseburia</i> ) at the expense of less desirable groups of	Cigarette smoking is associated with decreased levels. <sup>52</sup>  A high beef diet was associated with a decrease in <i>B. adolescentis</i> in 10 volunteers. <sup>27</sup>  A low FODMAP diet in 52 IBD patients resulted in lower <i>Bifidobacterium adolescentis</i> , <i>Bifidobacterium longum</i> , and <i>Faecalibacterium prausnitzii</i> than in patients on a control diet. However, microbiome diversity and markers of inflammation did not differ between the IBD and control groups. <sup>90</sup> Lower <i>F. prausnitzii</i> and <i>Bifidobacterium</i> was observed in 20 patients with IBS-D or IBS-M on a low FODMAP diet. Additionally, total SCFAs and n-butyrate



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Organism	Description	Increased Levels	Decreased Levels
	<p>plants in the diet, milk oligosaccharides, and host-derived glycans. They produce acetate that facilitates the cross-feeding of other bacteria, including butyrate-producers.<sup>77</sup> They also produce lactic acid.<sup>127</sup></p> <p>Along with <i>Collinsella</i>, can modify bile acids to modulate the virulence and pathogenicity of enteric pathogens.<sup>128</sup></p>	<p>bacteria such as LPS producers (<i>Escherichia coli</i> and <i>Enterobacter cloacae</i>).<sup>84</sup></p> <p>The prebiotic effects of FOS, GOS, inulin, and lactulose have been thoroughly assessed in human trials and suggest a beneficial impact on the microbiome by increasing <i>Bifidobacterial</i> levels and decreasing <i>E. coli</i> and enterococci.<sup>126</sup> A systematic review of inulin supplementation in humans showed an increase in <i>Bifidobacterium</i>, and a relative increase in <i>Faecalibacterium</i> and <i>Lactobacillus</i>, and decrease in relative abundance of <i>Bacteroides</i>.<sup>82</sup></p> <p>Physical activity at doses as low as the minimum recommended by the WHO may increase health-promoting species including <i>Bifidobacterium</i> spp., <i>Roseburia hominis</i>, <i>Akkermansia muciniphila</i> and <i>Faecalibacterium prausnitzii</i>. However, in a study comparing sedentary to active women, dietary differences were noted, which may account for the bacterial differences. The active group consumed more fiber, fruits and vegetables, and the sedentary group consumed more processed meats.<sup>86</sup></p> <p>The poorly absorbed antibiotic rifaximin was associated with increases in beneficial bacteria <i>F. prausnitzii</i>, <i>Bifidobacterium</i>, and <i>Lactobacillus</i> in human studies.<sup>87</sup></p>	<p>were lower.<sup>85</sup> Another study in patients with functional GI disorders with flatulence compared a low FODMAP diet with the effects of a prebiotic supplement. <i>Bifidobacterium</i> was reduced in the low FODMAP group and increased in the prebiotic group.<sup>133</sup></p> <p>A small study of 10 healthy subjects showed reduced <i>Lactobacillus</i>, <i>Bifidobacterium</i> and <i>Bifidobacterium longum</i> after 1 month on a gluten-free diet (GFD).<sup>88</sup></p> <p>A study on 250 vegetarian and vegan individuals showed lower counts of <i>Bifidobacterium</i> spp. (vegan), <i>Bacteroides</i> spp. (vegan) and <i>E. coli</i> (vegan and vegetarian).<sup>134</sup></p>
<i>Bifidobacterium longum</i>	<p><i>Bifidobacterium longum</i> is comprised of multiple subspecies the beneficially modulate the immune system.<sup>126,135</sup> It is found in probiotic supplements and fermented foods.</p> <p>Lactate producer; acetate producer. Utilizes diet-derived carbohydrates.<sup>126</sup></p>	<p>Long-term consumption of Mediterranean diet partially restored <i>B. longum</i> in metabolic syndrome patients.<sup>136</sup></p>	<p><i>B. longum</i> and <i>B. adolescentis</i> suppressed by rice in 26 Mongolian individuals who consumed wheat, rice, and oat as the sole carbohydrate staple food for a week each.<sup>64</sup></p> <p>A low FODMAP diet in 52 IBD patients resulted in lower <i>Bifidobacterium adolescentis</i>, <i>Bifidobacterium longum</i>, and <i>Faecalibacterium prausnitzii</i> than patients on a control diet. However, microbiome diversity and markers of inflammation did not differ between the IBD and control groups.<sup>90</sup></p> <p>A small study of 10 healthy subjects showed reduced <i>Lactobacillus</i>,</p>

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Organism	Description	Increased Levels	Decreased Levels
			<i>Bifidobacterium</i> and <i>Bifidobacterium longum</i> after 1 month on a gluten-free diet (GFD). <sup>88</sup>
<i>Collinsella aerofaciens</i>	<p>Possibly proinflammatory, may play a role in altering intestinal barrier integrity.<sup>137,138</sup></p> <p>Produces H<sub>2</sub>, ethanol, short-chain fatty acids including butyrate, and lactate and is a major utilizer of lactose.<sup>128,139</sup> Contains bile salt hydrolases to metabolize bile,<sup>26</sup> and along with <i>Bifidobacterium</i>, can modify bile acids to modulate the virulence and pathogenicity of enteric pathogens.<sup>128</sup></p> <p>Consumes oligosaccharides and simple sugars.<sup>140</sup></p>	<p><i>C. aerofaciens</i> higher levels in healthy adults consuming a whole grain diet (40 g fiber) compared to a red meat diet.<sup>141</sup> Studies are mixed on the association with fiber and the <i>Collinsella</i> genus,<sup>142</sup> which contains at least 6 species.<sup>143</sup></p> <p>Higher levels found in non-vegetarian versus vegetarian Thai adults that were healthy.<sup>144</sup></p>	<p>Decreased on a high-protein, low-carb weight loss diet in a study in 14 overweight men.<sup>107</sup></p> <p><i>C. aerofaciens</i> reduced in elderly subjects taking NSAIDs compared to elderly subjects not taking NSAIDs, or in young adults.<sup>145</sup></p> <p>Oral versus IV iron supplementation in iron-deficient IBD patients resulted in decreased abundances of <i>Faecalibacterium prausnitzii</i>, <i>Ruminococcus bromii</i>, <i>Dorea</i> spp., and <i>Collinsella aerofaciens</i>.<sup>93</sup></p>
<i>Desulfovibrio piger</i>	<p><i>Desulfovibrio piger</i> is Gram-negative and the most common sulfate-reducing bacteria (SRB) in healthy adults. Although SRB are positively associated with inflammation, both pro- and anti-inflammatory signaling have been attributed to H<sub>2</sub>S.<sup>140</sup></p> <p>Utilizes H<sub>2</sub> and lactate and releases acetate and hydrogen sulfide (H<sub>2</sub>S). H<sub>2</sub>S is highly toxic to colonic mucosa. H<sub>2</sub>S may create colonic cellular energy deficiency by inhibiting the beta-oxidation of butyrate.<sup>146,147</sup> May work together with <i>Collinsella aerofaciens</i>, a hydrogen producer.<sup>140</sup></p> <p>H<sub>2</sub>S can be derived from sulfur compounds in the diet including sulfur-containing amino acids or endogenous mucin.<sup>146</sup> Sulfate and sulfite are used as preservatives, additives and antioxidants in foods such as bread, preserved meat, dried fruit, carrageenan, and wine, and is also present in the supplement chondroitin sulfate.<sup>140</sup></p>	<p>A study on sigmoid biopsies from 9 healthy subjects over 9 months showed correlation with <i>Desulfovibrio</i> spp. and red meat and cholesterol intake.<sup>149</sup> The <i>Desulfovibrio</i> genus contains several species, so it is not clear whether this correlation pertains to <i>D. piger</i>, specifically.</p>	<p><i>D. piger</i> was reduced with supplemental <i>Lactobacillus plantarum</i>.<sup>150</sup></p> <p>A study on 10 healthy individuals showed reduction of H<sub>2</sub>S with bismuth subsalicylate. The study only looked at H<sub>2</sub>S levels, not bacterial composition.<sup>151</sup></p> <p>A diet containing whole grains, traditional Chinese medicinal foods and prebiotics was given to 93 overweight individuals and resulted in a decrease in the family <i>Desulfovibrionaceae</i>.<sup>152</sup> The <i>Desulfovibrionaceae</i> family contains several species, so it is not clear whether this correlation pertains to <i>D. piger</i>, specifically.</p>

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Organism	Description	Increased Levels	Decreased Levels
	Displays resistance to most broad-spectrum antibiotics, as H <sub>2</sub> S is a defense mechanism against antimicrobials. <sup>148</sup>		
<i>Escherichia coli</i>	<p><i>Escherichia coli</i> is a Gram-negative facultative anaerobe.<sup>153</sup> Many strains belong to the species <i>Escherichia coli</i>, and most strains are harmless, normal GI inhabitants. The <i>Escherichia coli</i> probe is not meant to diagnose pathogenic <i>E. coli</i> infections. An add-on shiga-toxin producing <i>E. coli</i> EIA stool test is available if patient symptoms warrant testing.</p> <p>H<sub>2</sub>S producer.<sup>148</sup> Ethanol producer which may promote gut permeability.<sup>154</sup> Both commensal and pathogenic strains capable of biofilm production. The presence of mucin stimulates biofilm formation and <i>E. coli</i> utilizes mono-, disaccharides and other simple glycoprotein degradation molecules to form the biofilm.<sup>155</sup> Produces vitamin K and vitamin B12.<sup>153</sup></p> <p><i>E. coli</i> has been associated with intestinal inflammatory disorders in animal and human studies.<sup>155</sup></p> <p>Consumes oligosaccharides and simple sugars and ferments amino acids.<sup>140</sup> Consumes oxygen, thus maintaining an environment for strictly anaerobic bacteria. Competitively excludes pathogens.<sup>153</sup></p> <p><i>E. coli</i> Nissle is a probiotic that has a protective effect on the intestinal barrier and can ameliorate certain GI disorders.<sup>156,157</sup></p> <p><i>E. coli</i> thrives in higher stool pH environments, as seen in omnivorous diets higher in animal protein.<sup>134</sup></p>	A small study of 10 healthy subjects showed increased <i>E. coli</i> and reduced <i>Lactobacillus</i> , <i>Bifidobacterium</i> and <i>Bifidobacterium longum</i> after 1 month on a gluten-free diet (GFD). <sup>88</sup>	<p>In ten metabolic syndrome patients, red wine polyphenols significantly increased the number of fecal <i>Bifidobacteria</i> and <i>Lactobacillus</i> (intestinal barrier protectors) and butyrate-producing bacteria (<i>Faecalibacterium prausnitzii</i> and <i>Roseburia</i>) at the expense of less desirable groups of bacteria such as LPS producers (<i>Escherichia coli</i> and <i>Enterobacter cloacae</i>).<sup>84</sup></p> <p>A study on 250 vegetarian and vegan individuals showed lower counts of <i>Bifidobacterium</i> spp. (vegan), <i>Bacteroides</i> spp. (vegan) and <i>E. coli</i> (vegan and vegetarian). <i>E. coli</i> was lower in groups with lower stool pH, as seen in higher carbohydrate and fiber diets.<sup>134</sup></p> <p>The prebiotic effects of FOS, GOS, inulin, and lactulose have been thoroughly assessed in human trials and suggest a beneficial impact on the microbiome by increasing <i>Bifidobacterial</i> levels and decreasing <i>E. coli</i> and enterococci.<sup>126</sup></p>
<i>Oxalobacter formigenes</i>	Gram negative anaerobic bacteria that depends on oxalate metabolism for energy. Key bacterium responsible for the degradation of oxalate, therefore reducing oxalate absorption, oxalate excretion in urine, and the risk of calcium oxalate kidney stones developing. <sup>97,158</sup>		Sensitive to and reduced with commonly used antibiotics. <sup>97</sup>

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Organism	Description	Increased Levels	Decreased Levels
	Lactobacillus and Bifidobacterium are also capable of consuming oxalate. <sup>97</sup>		
<i>Methanobrevibacter smithii</i>	<p><i>Methanobrevibacter smithii</i> is not a bacteria, but rather an archaea, and is the most common methanogen in humans.<sup>159</sup> It uses CO<sub>2</sub> and H<sub>2</sub> to produce methane gas.<sup>160</sup> <i>M. smithii</i> levels correlate with breath methane levels.<sup>159</sup> (This correlation was also observed in an internal Genova data analysis.)</p> <p>Certain <i>Clostridium</i> and <i>Bacteroides</i> spp. can produce methane gas.<sup>70</sup></p> <p>Methane has been associated with constipation, possibly due to the gasotransmitter effect on intestinal transit.<sup>70</sup></p> <p>It is suggested that since methanogens consume hydrogen, flatulence is reduced through a 4:1 conversion of hydrogen gas to methane gas.<sup>161</sup></p> <p><i>M. smithii</i> is strongly associated with the presence of the parasite <i>Blastocystis</i>.<sup>162</sup> (This correlation was also observed in an internal Genova data analysis.)</p>	<p><i>M. smithii</i> is present in milk products and their consumption may determine archaeal gut colonization in children.<sup>163</sup></p> <p>Methanobrevibacter levels were positively associated with diets high in carbohydrates.<sup>164</sup></p>	<p>A smaller study on 11 prediabetic, obese patients who were treated with Rifaximin and Neomycin eradicated <i>M. smithii</i> and lowered breath methane levels. Additionally, LDL, total cholesterol, and insulin levels improved.<sup>165</sup></p> <p>Statins are being studied for their ability to lower methanogen and thus, methane levels.<sup>160</sup></p> <p>Twenty-one healthy adults received a probiotic containing <i>Lactobacillus</i> and <i>Bifidobacterium</i> strains for 60 days and abundance of <i>Methanobrevibacter</i> was reduced.<sup>166</sup></p>
<i>Fusobacterium</i> spp.	<p>The genus <i>Fusobacterium</i> has approximately 20 species.<sup>167</sup> Though most of the members of the <i>Fusobacterium</i> genus are normal commensals, the genus also comprises some questionably pathogenic species – (<i>F. nucleatum</i> has some association with colorectal cancer). Although the prevalence of <i>Fusobacterium</i> is higher in fecal samples in patients with CRC, <i>Fusobacterium</i> is a passenger that multiplies in the more favorable conditions caused by malignancy rather than a causal factor in cancer development. Commensal <i>Fusobacterium</i> are also found in the oral cavity and have been implicated in periodontal disease.<sup>168</sup></p> <p>May be proinflammatory; some species produce butyrate and H<sub>2</sub>S.<sup>148,169</sup></p>	<p>Low fiber, high fat diet in Africans was associated with an increase of <i>F. nucleatum</i>.<sup>170</sup></p>	<p>The green and black tea extracts (EGCG) and theaflavins decreased the adherence of <i>F. nucleatum</i> to oral epithelial cells and attenuated <i>F. nucleatum</i>-mediated hemolysis and H<sub>2</sub>S production.<sup>171</sup></p> <p>Levels of Fusobacteria decreased after ingestion of barley β-glucans (whole grain barley pasta and durum wheat flour).<sup>172</sup></p> <p>No statistically significant associations were found between dietary and lifestyle exposures except for a positive association between higher BMI and inverse association between vegetable</p>

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Organism	Description	Increased Levels	Decreased Levels
<i>Akkermansia muciniphila</i>	<p>Mucin degrading bacteria.<sup>173</sup> Low levels associated with obesity, diabetes, inflammation, and gut permeability.<sup>77</sup></p> <p>Produces acetate and propionate – supports the growth of butyrate producers by degrading mucin and providing acetate. Can use pseudovitamin B12 produced by other bacteria for its propionate production.<sup>173</sup></p> <p>May limit toxicity of sulfate-reducing bacteria – there is a release of sulfate during mucin degradation. This sulfate might be used by sulfate-reducing bacteria, producing hydrogen sulfide. In turn, <i>A. muciniphila</i> predictively harbors genes in L-cysteine biosynthesis using hydrogen sulfide, suggesting that it has a role in the detoxification of hydrogen sulfide in the intestines.<sup>174</sup></p> <p>In development as a probiotic supplement for metabolic conditions.<sup>175</sup></p>	<p>Resveratrol supplementation led to increased <i>A. muciniphila</i> in obese, insulin-resistant USA Caucasians, but not other ethnic groups.<sup>176</sup></p> <p>Pomegranate (1000 mg of pomegranate extract daily) increased levels of <i>Akkermansia</i> in 20 healthy participants.<sup>177</sup></p> <p>Significant increase in <i>A. muciniphila</i> after inulin and butyrate supplementation in 60 overweight and obese diabetic patients.<sup>178</sup></p> <p><i>Akkermansia</i> increased with polydextrose – but lowered <i>Ruminococcus</i> and <i>Coprococcus</i>.<sup>80</sup></p> <p>A study on 28 patients with diabetes, those taking metformin had higher <i>Akkermansia</i> compared to those not taking metformin.<sup>179</sup></p> <p>Physical activity at doses as low as the minimum recommended by the WHO may increase health-promoting species including <i>Bifidobacterium</i> spp., <i>Roseburia hominis</i>, <i>Akkermansia muciniphila</i> and <i>Faecalibacterium prausnitzii</i>. However, in a study comparing sedentary to active women, dietary differences were noted, which may account for the bacterial differences. The active group consumed more fiber, fruits and vegetables, and the sedentary group consumed more processed meats.<sup>86</sup> A study on a group of 40 rugby players showed higher proportions of <i>Akkermansia</i> compared with higher BMI controls. Athletes consumed more protein in the form of meat and protein supplements, as well as more vegetables, fiber, and mono/polyunsaturated fats.<sup>180</sup></p>	<p>consumption and <i>Fusobacterium</i> in advanced adenoma patients.<sup>168</sup></p> <p>Lower abundance on low FODMAP diet.<sup>67,181</sup></p>

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