

1 **TITLE**

2 **A comprehensive review on the impact of β -glucan metabolism by *Bacteroides* and**
3 ***Bifidobacterium* species as members of the gut microbiota.**

4 **Running title: β -glucan metabolism by *Bacteroides* and *Bifidobacterium* species.**

5

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15

16 **ABSTRACT**

17 β -glucans are polysaccharides which can be obtained from different sources, and which
18 have been described as potential prebiotics. The beneficial effects associated with β -
19 glucan intake are that they reduce energy intake, lower cholesterol levels and support
20 the immune system. Nevertheless, the mechanism(s) of action underpinning these health
21 effects related to β -glucans are still unclear, and the precise impact of β -glucans on the
22 gut microbiota has been subject to debate and revision. In this review, we summarize
23 the most recent advances involving structurally different types of β -glucans as
24 fermentable substrates for Bacteroidetes (mainly *Bacteroides*) and *Bifidobacterium*
25 species as glycan degraders. *Bacteroides* is one of the most abundant bacterial
26 components of the human gut microbiota, while bifidobacteria are widely employed as a
27 probiotic ingredient. Both are generalist glycan degraders capable of using a wide range
28 of substrates: *Bacteroides spp.* are specialized as primary degraders in the metabolism
29 of complex carbohydrates, whereas *Bifidobacterium spp.* more commonly metabolize
30 smaller glycans, in particular oligosaccharides, sometimes through syntrophic
31 interactions with *Bacteroides spp.*, in which they act as secondary degraders.

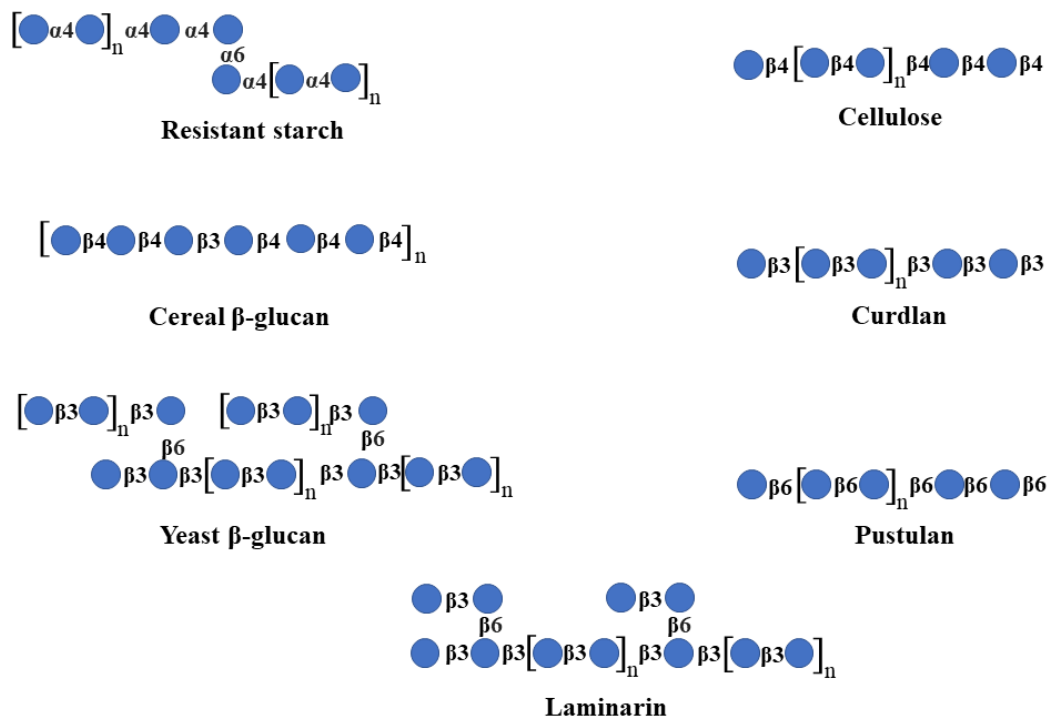
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33 **Keywords:** β -glucans; *Bacteroides*; *Bifidobacterium*; Syntrophic interactions;
34 metabolism; Carbohydrate active enzymes.

35

36 **1. Introduction**

37 β -Glucans are complex polysaccharides composed of D-glucopyranosyl residues that
 38 are linked through β -bonds. These ubiquitous polymers are present in cells walls of
 39 yeast, fungi, seaweed, bacteria and cereals, such as wheat, oat and barley [1, 2]. The
 40 macromolecular structure of β -glucans is different according to the extraction source.
 41 For instance, cereal β -glucans have a backbone of single $\beta(1,3)$ -bonds separating short
 42 sections of $\beta(1,4)$ -bonds, while seaweed β -glucans typically consist of a $\beta(1,3)$ -linkage
 43 backbone with single $\beta(1,6)$ branching points, in which the resulting side chain contains
 44 $\beta(1,3)$ -linkages (Fig. 1). Additionally, mushroom-derived β -glucans typically represent
 45 polymers composed of $\beta(1,6)$ -linked branches from a $\beta(1,3)$ backbone, while bacterial
 46 β -glucans simply consist of a linear $\beta(1,3)$ backbone (Fig. 1) [3-6].



47 **Fig. 1.** Structure of different types of alpha- (resistant starch) and β -glucans. The sources of β -
 48 glucans are varied: cereals, brown algae (Laminarin), *Saccharomyces cerevisiae* (yeast), Fungi
 49 *Lasallia pustulata* (Pustulan), bacteria, e.g. *Alcaligenes faecalis* (Curdlan), and plants
 50 (cellulose) [5].

52

53 β -glucans can be modified by physical, chemical and biological methods, which affect
54 their primary structure, spatial conformations and bioactivity. In fact, modification and
55 transformation of β -glucans may not only improve their biological functionalities in the
56 human gut, but also their applications as a prebiotic [7-9]). Such processed β -glucans
57 have been reported to (i) reduce glucose and cholesterol blood levels, (ii) promote
58 production of short chain fatty acids (SCFAs), which may act as important modulators
59 of host immune function, (iii) decrease energy intake, and (iv) lower obesity, diabetes
60 and cardiovascular risk [10-16]. Moreover, several studies have underlined a wide range
61 of interesting properties of β -glucans, such as anticancer effects [17-20],
62 immunomodulatory abilities [21], anti-inflammatory activities [22], or their role as
63 potential adjuvants for vaccine delivery and efficacy [23] or as delivery vehicles for
64 probiotics [24].

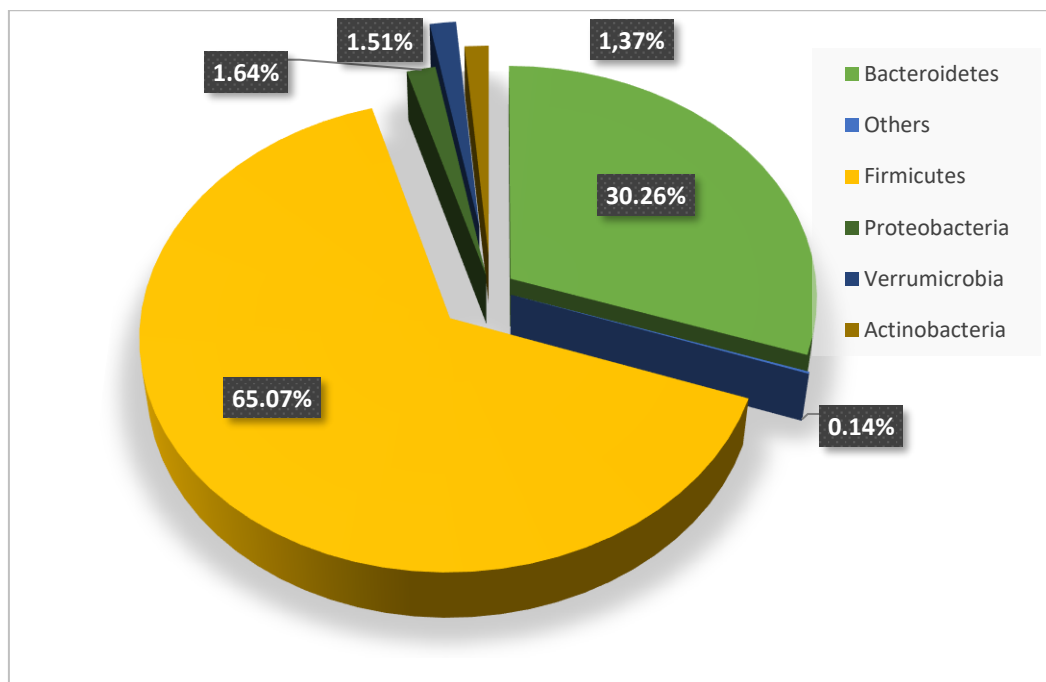
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66 The focus of this review is on outlining various metabolic routes described for
67 structurally different dietary β -glucans by human gut *Bacteroides* and *Bifidobacterium*
68 *spp.* in order to clarify the various effects these polysaccharides may have on the
69 abundance and metabolic activity of mentioned gut commensals. Understanding glycan
70 metabolism is fundamental to determine how polysaccharides shape the microbial gut
71 communities, as well as its associated health effects. In addition, this understanding will
72 facilitate the development of nutraceutical-based strategies to increase the content of
73 specific beneficial bacteria.

74

75 The gut and its associated Human Gut Microbiota (HGM) together form a recently
76 considered novel organ of the human body that impacts on human health in a variety of
77 ways [25, 26]. The HGM in Western populations represents a complex microcosm of

78 trillions of microorganisms, with Bacteroidetes and Firmicutes being the most dominant
79 phyla, and Actinobacteria, Proteobacteria and Verrucomicrobia being less abundant
80 components (Fig. 2) [27, 28]. Nonetheless, such minor components may still represent
81 important ecological players in the complexity of HGM, especially for the metabolic
82 interactions they offer to members of the Bacteroidetes and Firmicutes phyla. For
83 example, *Akkermansia muciniphila* (which belongs to the Verrucomicrobia phylum) has
84 recently been shown to represent a human gut commensal that supports host health [29,
85 30]. The relative abundance of *Akkermansia muciniphila* has been inversely correlated
86 with obesity, diabetes, cardiometabolic diseases and low-grade inflammation,
87 highlighting its potential as a probiotic to support human health and well-being [29, 30].



88
89 **Fig. 2.** Distribution of major bacterial phyla population according to their relative abundance in
90 the human gut [28].

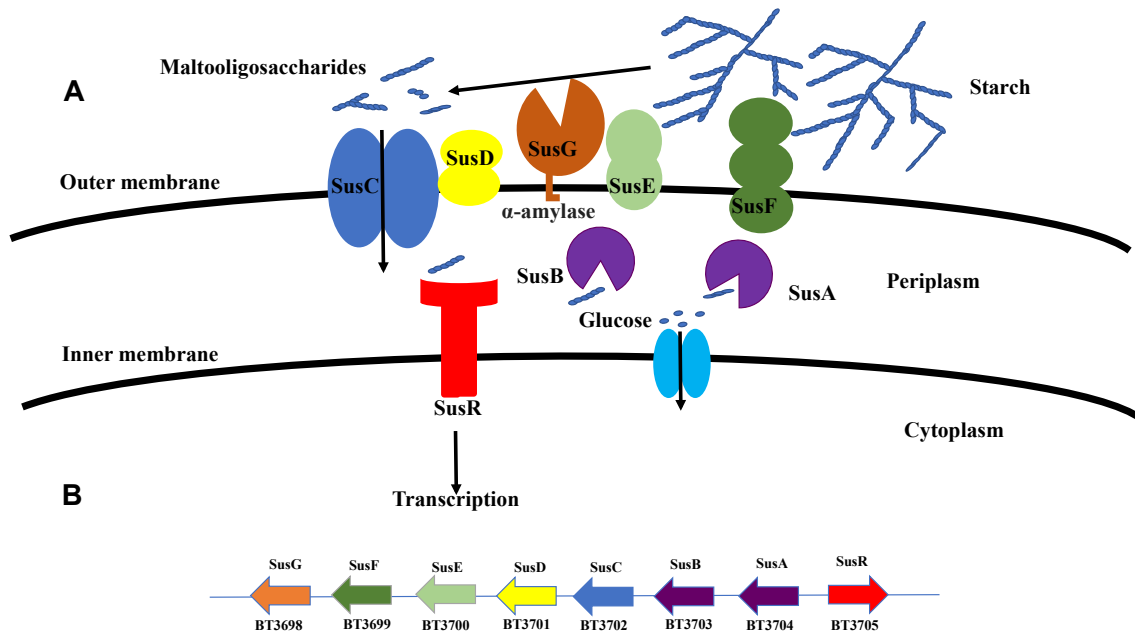
91
92 *Bacteroides* is the main genus within the Bacteroidetes phylum, though recent
93 metagenome studies have indicated that four distinct *Prevotella* clades in this phylum
94 have been underrepresented in Western populations [31]. Most *Bacteroides* members

95 are common gut commensals, though they can act as opportunistic pathogens under
96 certain conditions, an example of this being *Bacteroides fragilis* [32, 33]. *Bacteroides*
97 are widespread in different natural niches and human populations and possess a wide
98 range of mechanisms to adapt to and persist in various competitive environments [31,
99 34-37]. *Bacteroides* species are widely known for their role as primary glycan degraders
100 since their genomes contain a relatively high number of genes (when compared to other
101 members of the gut microbiota) encoding carbohydrate active enzymes, such as
102 glycoside hydrolases (GHs) and polysaccharide lyases (PLs) [38, 39]. For this reason,
103 they are able to access a broad range of complex carbohydrate substrates [40]. Some
104 members, such as *Bacteroides thetaiotaomicron* (289 GHs and 23 PLs) or *Bacteroides*
105 *cellulosilyticus* (431 GHs and 30 PLs), dedicate around 18% of their genome content to
106 carbohydrate metabolism, thereby reflecting their huge metabolic capacity and
107 versatility to use this type of carbon and energy source [41, 42]. Carbohydrate active
108 enzymes or CAZYmes are classified into different families according to protein
109 sequence similarities, which means that they commonly elicit related activities.
110 Therefore, enzymes belonging to the same family have a similar protein sequence, a
111 conserved catalytic apparatus and similar quaternary structure [42-44].

112

113 *Bacteroides* genomes harbour polysaccharide utilization loci (PULs), which are clusters
114 of genes involved in the detection and digestion of a specific polysaccharide. To date,
115 all sequenced *Bacteroides* genomes contain PULs, which typically encode surface
116 glycan binding proteins (SGBPs), enzymes for carbohydrate degradation (GHs and
117 PLs), TonB-dependent transporters (TBDT) and sensors/regulators [43]. Polysaccharide
118 breakdown usually begins at the cell surface by a GH or PL, which degrades the
119 complex intact polysaccharide into oligosaccharides. These released oligosaccharides

120 are then transported by the *Bacteroides* species into the periplasm by SusC-like TBDT
121 proteins [45], although they may also be utilized by other bacteria as substrates through
122 *cross-feeding*, a common phenomenon observed for complex polysaccharides or
123 cofactors [38, 39, 46-48]. In the periplasm, several exo- and endo-glycosidases are
124 responsible for further hydrolysis of the internalized oligosaccharides, and this
125 degradation commonly releases a signal molecule (typically a di-/tri-/tetrasaccharide),
126 which binds to the sensor/regulator, thereby triggering transcriptional induction of the
127 corresponding PUL. The final step of this degradative process involves the
128 incorporation of monosaccharides into the cytoplasm where they are channelled into
129 central carbon catabolism. This general PUL model was first described for starch
130 metabolism by *Bacteroides thetaiotaomicron* [49, 50] and was the first to describe how
131 *Bacteroides* species carried out starch degradation [51-53]. The corresponding PUL,
132 designated *sus*, is composed of eight genes, *susRABCDEFG*, whose encoded proteins
133 constitute a complex and cell envelope-associated apparatus highly specialized in starch
134 catabolism [51-53]. The SusC/D complex is predominantly responsible for starch
135 binding with SusE and SusF being involved in increasing the efficiency of the binding
136 process [51-53]. SusG generates internal hydrolytic cuts in the bound starch, releasing
137 oligosaccharides that are transported into the periplasmic compartment by SusC [51-
138 53]. Here, SusA and SusB, both glycoside hydrolases, degrade these malto-
139 oligosaccharides to glucose, which is then transported into the cytosol [51-53].
140 Transcriptional regulation of the whole process is accomplished by SusR in response to
141 starch availability [51-53]. A schematic representation of this starch degradation process
142 is shown in Fig. 3.



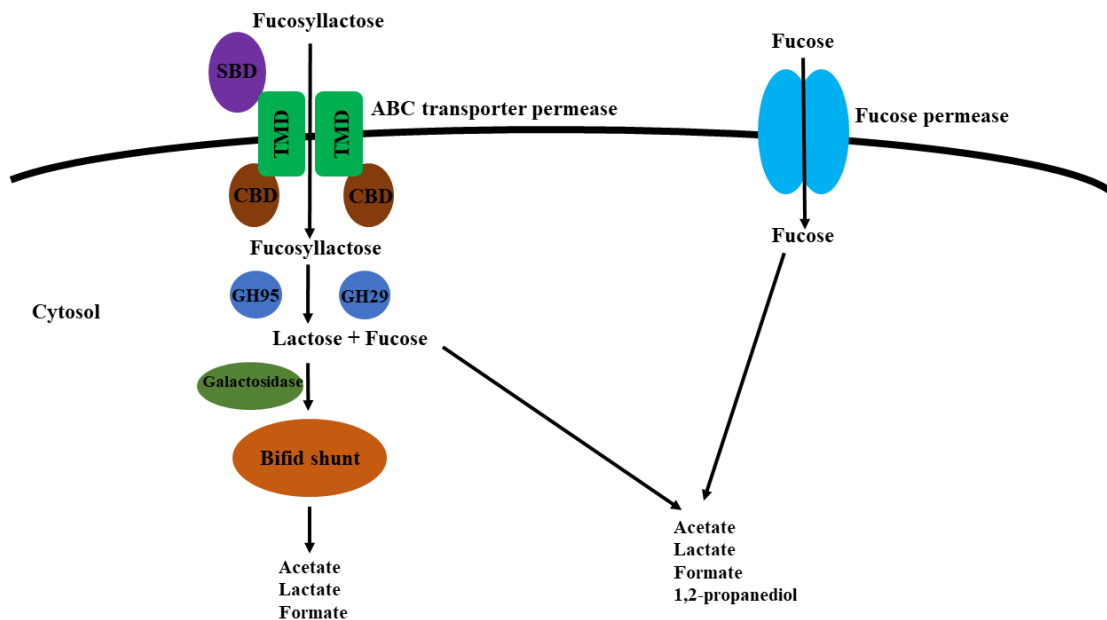
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144 **Fig. 3. A.** Cartoon representation of starch utilization system model in *Bacteroides*
 145 *thetaitaomicron* VPI-5482 [51, 54]. The hydrolytic degradation of complex intact
 146 polysaccharide is initiated at the outside surface of the cell by SusG (alpha-amylase), thereby
 147 generating oligosaccharides. These oligosaccharides are incorporated into the periplasm by
 148 binding and import proteins (facilitated by the SusC/SusD pair), which allows further
 149 degradation to glucose by other glycoside hydrolases (SusA and SusB) and which generates a
 150 signal molecule for the regulator (SusR), causing transcriptional activation of the entire PUL. **B.**
 151 Genomic content of the PUL for starch metabolism in *Bacteroides thetaiotaomicron* VPI-5482
 152 [51, 54].

153

154 *Bifidobacterium* is a genus belonging to the Actinobacteria phylum whose species
 155 occupy several ecological niches, since they may be isolated from waste water, the oral
 156 cavity and the gastrointestinal tract of humans and other mammals [55, 56]. Some
 157 species are commonly identified in adults, such as *Bifidobacterium adolescentis* and
 158 *Bifidobacterium pseudocatenulatum*, while *Bifidobacterium bifidum*, *Bifidobacterium*
 159 *breve*, and *Bifidobacterium longum* subsp. *infantis*, are typically isolated from faecal
 160 samples of breast-fed infants [57, 58]. Various studies have demonstrated the positive

161 health impact or probiotic effect of certain bifidobacterial species/strains, such as those
 162 belonging to *Bifidobacterium breve*, *Bifidobacterium longum* or *Bifidobacterium*
 163 *bifidum* [24, 59]. In the context of this review, it should be noted that certain
 164 bifidobacteria have been reported to ferment laminarin, curdlan or oat β -glucan [60].
 165
 166 Also bifidobacteria contain gene clusters, each of which being dedicated to the
 167 metabolism of a specific poly/oligosaccharide [61]. These clusters encode ABC
 168 transporters (most frequently observed), permeases or proton symporters to facilitate
 169 transport of mono-/oligo-saccharides, such as fucosyllactose, fucose or
 170 galactooligosaccharides, into the cytoplasm. Once internalized, intracellular glycoside
 171 hydrolases degrade these oligosaccharides into monosaccharides and/or channel these
 172 hexoses or pentoses into the central carbohydrate metabolic pathway for energy
 173 generation (Fig. 4) [62].



174
 175 **Fig. 4.** Schematic representation of the fucose and fucosyllactose utilization system in
 176 *Bifidobacterium kashiwanohense* [62]. Fucosyllactose is incorporated into the cytoplasm by an
 177 ABC transporter permease with a sugar binding domain (SBD), transmembrane domain (TMD)

178 and an ATP-hydrolysing cytosolic domain (CBD). Once in the cytoplasm, a fucosidase (GH95
179 or GH29) and a β -galactosidase break the oligosaccharide into fucose, galactose and glucose,
180 which are then further channelled into the central carbohydrate metabolic pathways, i.e. the
181 bifid shunt, or in the case of fucose into a separate metabolic pathway. The monomer fucose is
182 imported into the cytoplasm by means of a fucose permease after which it enters the fucose
183 metabolic pathway [62].

184

185 *Bifidobacterium* is unique in using a specialized central metabolic carbohydrate route,
186 called the “bifid shunt”, which employs a number of key enzymes, such as fructose-6-
187 phosphoketolase, being considered a key taxonomic marker for the Bifidobacteriaceae
188 family [61, 63, 64]. The bifid shunt is used by *Bifidobacterium* for the metabolism of
189 hexoses and pentoses, and theoretically can produce more ATP molecules per molecule
190 of glucose than alternative carbohydrate fermentation strategies used by lactic acid
191 bacteria or *Bacteroides* species [65]. This unique bifidobacterial pathway lacks the
192 enzymes aldolase, which is characteristic of glycolysis, and glucose-6-phosphate
193 dehydrogenase, typical of hexosemonophosphate pathways [61, 63, 64]. However,
194 monosaccharide fermentation in bifidobacteria is characterized by fructose-6-phosphate
195 phosphoketolase, from which the pathway obtained its name as the phosphoketolase
196 route or “bifid shunt” [61, 63, 64].

197

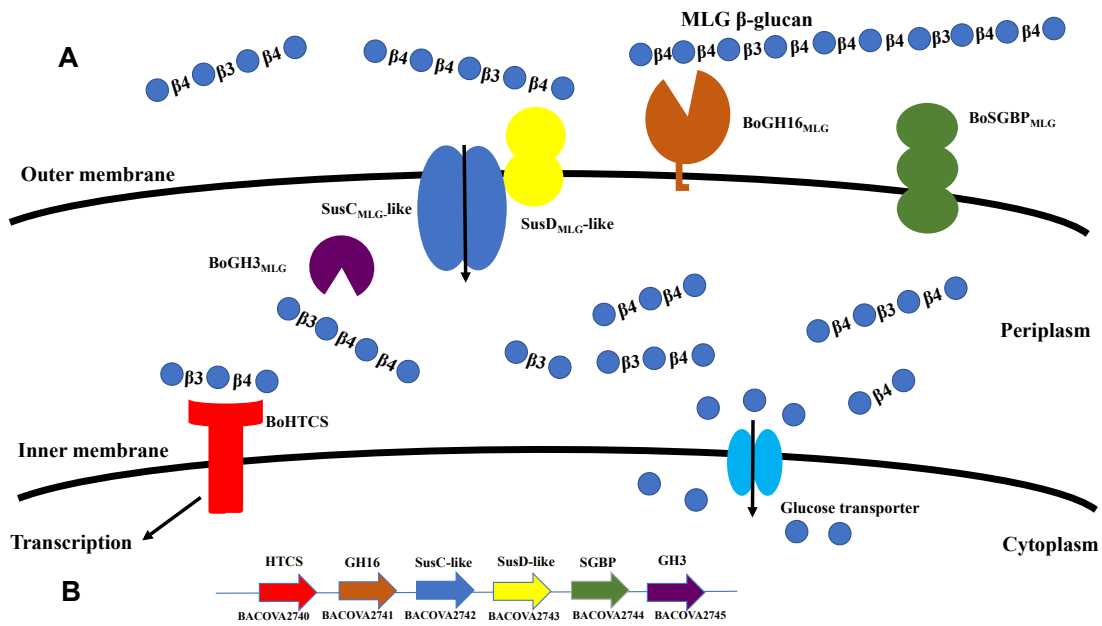
198 **2. Cereal β -glucans**

199 Cereals are the most common and widespread source of β -glucan in the human diet and
200 their chemical structures are usually described as homoglucopepolysaccharides with a
201 backbone of single $\beta(1,3)$ -bonds separating short sections of $\beta(1,4)$ bonds [1, 2]. Due to
202 the large variety of existing cereals, we will focus our review on β -glucans isolated from
203 oat, barley and wheat.

204

205 One particular utilization locus was identified in *Bacteroides ovatus* ATCC 8483
206 (Bovatus_02740-Bovatus_02745) when this strain metabolizes barley-derived, mixed-
207 linkage β -glucans (MLG, Fig. 5) [66, 67]. This locus encodes a GH16 *endo*- β -glucanase
208 (BoGH16_{MLG}) which hydrolyses β (1,4)-linkages that are preceded by a β (1,3)-linked
209 glucosyl residue, and a GH3 *exo*- β -glucosidase that digests the oligosaccharides
210 released by BoGH16_{MLG} to glucose. This PUL also encodes two Surface Glycan
211 Binding Proteins (SGBPs), a SusD_{MLG}-like homolog and BoSGBP_{MLG}. The SusD_{MLG}-
212 like homolog is essential for growth of *Bacteroides ovatus* ATCC8483 on barley β -
213 glucan because it incorporates the oligosaccharides originated by BoGH16_{MLG} into the
214 periplasm. In contrast, BoSGBP_{MLG} is not essential for growth though it may assist in
215 oligosaccharide scavenging. PULs homologous to the Bovatus_02740-Bovatus_02745
216 PUL of *Bacteroides ovatus* are present in the genomes of *Bacteroides xylosolvens*
217 XB1A and *Bacteroides uniformis* ATCC 8492, which highlights the apparent
218 prevalence of PULs dedicated to β -glucan metabolism among *Bacteroides* species [66,
219 67].

220



221

222 **Fig. 5. A.** Example of the mixed-linkage glycan (MLG) utilization locus in *Bacteroides ovatus*
223 ATCC 8483 [67]. In a similar way to starch metabolism, mixed linkage β -glucan is first
224 degraded outside the cell by a cell surface-associated GH16 (BoGH16_{MLG}), which generates
225 oligosaccharides. The SusC/SusD-like pair incorporates these oligosaccharides into the
226 periplasm, where a GH3 (β -glucosidase, BoGH3_{MLG}) degrades these internalized
227 oligosaccharides into glucose monomers, which are then internalized into the cytoplasm. **B.**
228 Genomic content of the MLG PUL in *Bacteroides ovatus* ATCC 8483 [66, 67].

229

230 2.1. Oat β -glucans

231 The effect of oat β -glucan ingestion has been shown to be associated with a modest
232 increase in bacterial richness (yet decreasing the *Bacteroides* population) in both ileal
233 effluent and faecal samples when compared with intake of cellulose or
234 carboxymethylcellulose (Table 1) [68]. Also, the effect was viscosity-dependent, since
235 low-viscosity oat β -glucan reduces the relative abundance of *Bacteroides* to a higher
236 degree when compared to high-viscosity oat β -glucan. Moreover, the same decreasing

237 effect was observed in a similar study where oat β -glucan was compared with pectin,
238 inulin and arabinoxylan (Table 1) [69].

239

240 However, in a subsequent study in BALB/c mice, oat β -glucan ingestion decreased
241 bacterial biodiversity yet caused an increase in the relative abundance of the phylum
242 Bacteroidetes compared with the control and with a mixture oat β -glucan-cellulose. In
243 addition, *Bacteroides* was found as the dominant genus in the colon and it was
244 associated with a higher concentration of beneficial short chain fatty acids (SCFAs),
245 such as propionate and acetate (Table 1) [70]. The increase in *Bacteroides* populations
246 was also reported by Carlson *et al.* using Oatwell (oat-bran containing 28% oat β -
247 glucan, Table 1) [71].

248

249 Additionally, different studies have demonstrated the effect of oat β -glucans in
250 *Bifidobacterium* (Table 2). Wu *et al.* found that *Bifidobacterium* content was decreased
251 by the dietary supplementation with oat β -glucans [72]. Nevertheless, an *in vitro*
252 fermentation study by Ji-lin *et al.* showed *Bifidobacterium longum* BB536 as a good
253 degrader of raw and hydrolysed oat β -glucans hydrolysates, with preference for the
254 hydrolysed fractions (Table 2) [73]. Another study concluded that the addition of β -
255 glucan to yogurt increased survival of *Bifidobacterium longum* R0175 (Table 2) [74].
256 Furthermore, *Bifidobacterium* abundance was demonstrated to increase significantly in
257 rats fed with oat whole meal or oat β -glucan compared with a control group, with rats
258 exhibiting a higher growth rate when fed on pure oat β -glucan (Table 2) [75].

259

260 2.2. Barley β -glucans

261 Supplementation with barley β -glucan in rats with low or high-fat diet increased the
262 production of SCFAs, reduced inflammation and cholesterol levels, and lowered the
263 abundance of *Bacteroides fragilis* NCTC 9343 in the caecum (Table 1) [76].
264 Additionally, in a study with polypectomyed patients (patients having colorectal
265 polyps), no significance difference was observed during a 90-day feeding intervention
266 using 3 g/day of barley β -glucan. Nevertheless, two weeks after cessation of the
267 treatment, the abundance of the genus *Bacteroides* was found to be significantly
268 decreased (Table 1) [77]. A similar negative correlation was observed in
269 hypercholesterolemic rats fed with a medium molecular weight (530 kDa) barley β -
270 glucan diet (Table 1) [78]. However, the application of 3 g/day of this medium
271 molecular weight barley β -glucan in hypercholesterolemic human patients increased the
272 relative abundance of Bacteroidetes, while that of Firmicutes was decreased.
273 Interestingly, no significant differences were observed when patients received 3 g/d or 5
274 g/d of low molecular weight barley β -glucan. These findings therefore suggest that the
275 promoting effect of Bacteroidetes abundance by barley β -glucan is molecular weight-
276 dependent (Table 1) [79]. In addition, *Bacteroides ovatus* ATCC 8483 prioritizes the
277 use of barley β -glucan in a mixture with pectin, xyloglucan and arabinoxylan, being
278 able to use this substrate when it was the only carbon source in the medium, with higher
279 growth rates than *Bifidobacterium longum* subsp. *longum*, *Megasphaera elsdenii*, and
280 *Ruminococcus gnavus*, but lower than *Veillonella parvula* (Table 1) [80].

281

282 In *Bifidobacterium*, the bifidogenic effect of barley β -glucan supplementation in
283 food/feed has been described in various publications. For instance, Arora et al.
284 discovered that C57BL/6 mice, when maintained on a high fat diet containing 10 %
285 barley β -glucan during 8 weeks, showed a lower body weight gain and also an increase

286 in relative abundance of *Bifidobacterium* in both faecal and caecal samples (Table 2)
287 [81]. Similar results were found in rats fed on a low fat diet supplemented with barley β -
288 glucan for 25 days [76] and, in a similar way, in other murine trials (Table 2) [82].

289

290 2.3. Wheat β -glucans

291 In obese subjects with an unhealthy dietary behaviour, wheat β -glucan was correlated
292 with a relative abundance increase in members belonging to the Bacteroidetes phylum
293 and *Bacteroides* genus. It was also suggested that *Bacteroides* reduces the levels of
294 inflammatory markers TNF- α and IL-6, and that it plays a role in reducing pathologies
295 associated with inflammation (Table 1) [83]. In a similar study, *Bacteroides*
296 *cellulosilyticus*, *Bacteroides ovatus* and *Bacteroides stercoris* were described as
297 predominantly wheat-bran β -glucan degraders, while *Bacteroides uniformis*,
298 *Bacteroides dorei* and *Bacteroides eggertii* were enriched in β -glucans derived from
299 wheat-lumen, so apparently not all *Bacteroides* species exhibit the same glycan
300 utilization behaviour (Table 1) [84]. The authors showed differences in the structure and
301 composition of wheat bran and lumen, suggesting that these differences explain the
302 different metabolic capabilities [84]. Nevertheless, the use of whole grains instead of
303 extracted β -glucan requires further studies for wheat.

304

305 2.4. Mix of different cereals

306 A dietary intervention using 3 g/d of durum wheat flour and whole-grain barley pasta
307 for 2 months did not reveal any significant differences in the microbiota composition of
308 the subjects (Table 1) [85]. However, in another trial with wheat bran and barley in
309 Japanese adults, a positive interaction was observed when both cereals were combined,
310 causing an increase in relative abundance of the genus *Bacteroides* and other butyrate-

311 producing species (Table 1) [86]. Differences in the microbiota composition of distinct
312 human populations as a result of varying diets and life styles may explain these
313 apparently conflicting findings [87-89].

314

315 Regarding *Bifidobacterium*, Shen et al. carried out a comparative study of the prebiotic
316 efficacy of oat and barley β -glucan in rats. The study resulted in an increase in
317 *Bifidobacterium* abundance using either of these cereals, with a more pronounced effect
318 for oat β -glucan [90].

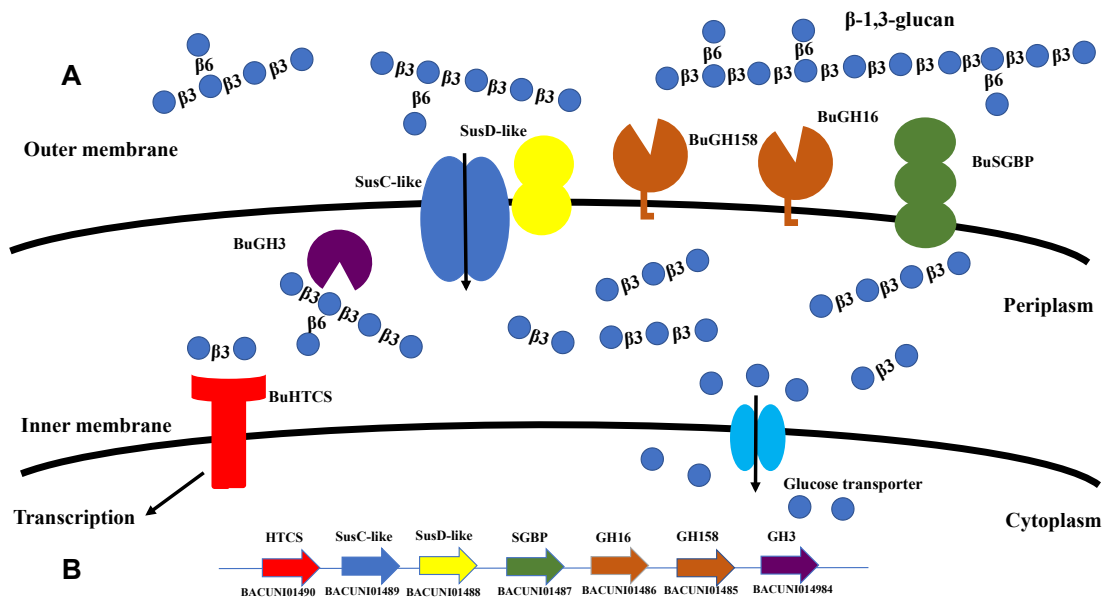
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320 **3. Seaweed β -glucans**

321 Seaweeds are potential prebiotics rich in three polysaccharides depending on the
322 seaweed source, being either brown, green or red algae. In brown algae, fucoidan,
323 alginate and laminarin have been shown to act as antioxidant, cognitive protective, anti-
324 inflammatory, anti-angiogenic, anti-cancer, anti-viral, and anti-hyperglycemic agents,
325 thus having very promising potential as a food additive and prebiotic [91, 92].
326 Laminarin (Fig. 1) is a glucose-based homopolysaccharide with a $\beta(1,3)$ backbone and
327 $\beta(1,6)$ branches at a 3:1 ratio, being isolated from the brown algae species *Laminaria*
328 and *Alaria*, representing almost a 50 % of algal dry matter. Laminarin is a type of β -
329 glucan with special interest because of its proposed anticancer, antioxidant and
330 immunomodulatory activities [93-95]. For instance, in a recent study, both native
331 laminarin and its enzymatic digestion products inhibited cell transformation on SK-
332 MEL-28 human melanoma and DLD-1 human colon cancer cells, where the maximum
333 anticancer effect was shown to be correlated with a high level of branching [95].

334

335 Recently, a paper on $\beta(1,3)$ -glucan metabolism by *Bacteroides* species, showed that
336 *Bacteroides uniformis* ATCC 8492, *Bacteroides thetaiotaomicron* NLAE-zl-H207 and
337 *Bacteroides fluxus* YIT 12057 have the ability to metabolize laminarin as a carbon
338 source because of the defined PUL architecture where a GH158 is key in the release of
339 oligosaccharides [96]. These authors described a putative $\beta(1,3)$ -glucan utilization locus
340 in *Bacteroides uniformis* ATCC 8492 (Fig. 6A and 6B, BACUNI_01484-
341 BACUNI_01490) that encodes a TonB-dependent transporter (TBDT, SusC-like), two
342 cell surface glycan-binding proteins (SusD-like and BuSGBP), three glycoside
343 hydrolases (BuGH16, BuGH158 and BuGH3) and a hybrid two-component regulatory
344 system (BuHTCS) (Fig. 6B). BuGH158 was described as a specific laminarinase, while
345 BuGH16 was shown to be a broad-specificity *endo*- $\beta(1,3)$ -glucanase with activity
346 towards yeast β -glucan and mixed-linkage glucan from cereals. For its part, BuGH3 was
347 described as a specific $\beta(1,3)$ glucosidase which handles the hydrolysis products of
348 BuGH158 and BuGH16. However, only BuSGBP was able to bind $\beta(1,3)$ -glucans (Fig.
349 6A). Despite the fact that homologous PULs active on $\beta(1,3)$ -glucans have been
350 detected in some species of *Bacteroides thetaiotaomicron* NLAE-zl-H207 and
351 *Bacteroides fluxus* YIT 12057, the one described in *Bacteroides uniformis* ATCC 8492
352 was shown to be highly prevalent in the microbiome of humans, and unique with an
353 ability to utilize three different types of $\beta(1,3)$ -glucan, i.e. that from laminarin, curdlan
354 and yeast.



355

356 **Fig. 6. A.** Schematic representation of $\beta(1,3)$ -glucan degradation by *Bacteroides uniformis*
 357 ATCC 8492 based in analogy with the starch utilization system [96]. **B.** Genomic content of the
 358 $\beta(1,3)$ -glucan PUL in *Bacteroides uniformis* ATCC 8492 [96].

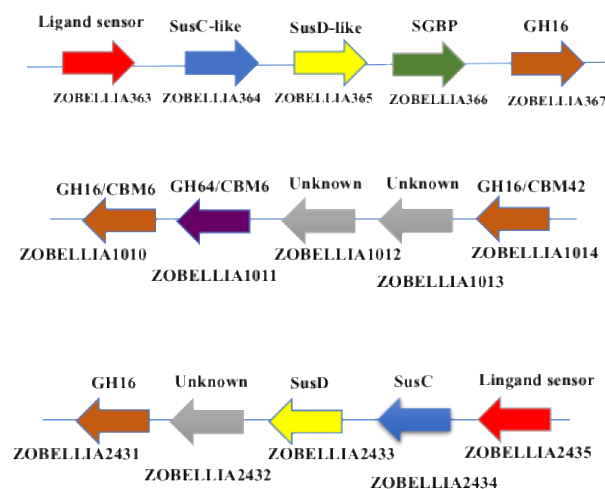
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360 Although the main purpose of this review is the effect of β -glucans on selected elements
 361 of the HGM, laminarin has also been widely studied as a growth substrate for various
 362 marine *Bacteroides* species. An analysis of Bacteroidetes-fosmids from ocean regions
 363 showed that 4 out of 14 identified PULs were laminarin-specific, and were co-located
 364 with predicted β -glucosidase-encoding genes, thereby underscoring the role of
 365 laminarin as a common metabolic substrate for ocean-derived Bacteroidetes species
 366 [97].

367

368 At species level, the degradation of laminarin in the marine bacterium *Zobellia*
 369 *galactanivorans* has been described in different studies. Thomas et al. studied gene
 370 transcription in *Zobellia galactanivorans* Dsij^T when it grows on laminarin as its sole
 371 carbon source (Fig. 7) [98]. The authors determined that this marine polysaccharide
 372 induced the expression of the cluster ZOBELLIA_209 to ZOBELLIA_214, which is

373 predicted to encode two TonB-dependent receptors (ZOBELLIA_212 and ZOBELLIA
 374 _214) and their associated surface glycan-binding proteins (ZOBELLIA_211 and
 375 ZOBELLIA_213), respectively. These gene pairs are characteristic features of PUL
 376 clusters present in Bacteroidetes genomes [43]. In addition, this cluster encodes a
 377 predicted carbohydrate binding module family 4 (CBM4, ZOBELLIA_209), whose
 378 family has been characterized to bind to $\beta(1,3)$ -glucan, $\beta(1,3-1,4)$ -glucan, $\beta(1,6)$ -glucan,
 379 xylan, and amorphous cellulose (CAZY database, <http://www.cazy.org/>; [99-102]).
 380 Therefore, this cluster is involved in the recognition, binding and incorporation of
 381 laminarin at the cellular surface of *Zobellia galactanivorans*, which has been used as a
 382 bacterial model to understand the algal carbon metabolism showing several adaptive
 383 traits to algal-associated life [103], representing a clear example for a genomic cluster
 384 dedicated to laminarin, Fig. 7.



385

386 **Fig. 7.** Genomic composition of the laminarin PUL in *Zobellia galactanivorans* Dsij^T [103].

387

388 Another study showed that the incorporation of 2% of brown algae laminarin in feed for
 389 a rat trial decreased the relative abundance of the Bacteroidetes phylum in caecal

390 microbiota populations. Specifically, the ratio of identified clones, based on 16S rRNA
391 gene sequencing, of *Bacteroides capillosus* fell around 27 % compared to the control
392 (Table 1) [104]. By contrast, in a study with mice fed with a high fat diet as control and
393 comparing with a high fat + laminarin diet, the authors found that the diet without
394 laminarin led to an increase in Actinobacteria, whereas dietary supplementation with
395 laminarin witnessed an increase in the relative abundance of Bacteroidetes, especially
396 the genus *Bacteroides*, and a decrease in Firmicutes. Laminarin ingestion shifted the
397 microbiota at species level towards a higher energy metabolism, increasing the
398 *Bacteroides* species, and therefore increasing the number of carbohydrate active
399 enzymes. Laminarin also slowed weight gain in mice and decreased the bacterial
400 species diversity (Table 1) [105]. The same increase in Bacteroidetes/Firmicutes ratio
401 was observed in a recent study with albino mice (Table 1) [106] in which laminarin was
402 shown to be metabolized by *Bacteroides intestinalis* and *Bacteroides acidifaciens*,
403 producing succinate and acetate as end-products, which are precursors of the beneficial
404 short chain fatty acids (SCFAs) propionate and butyrate, respectively [107-109].

405

406 In contrast, several feeding studies have concluded that laminarin from *Laminaria*
407 *digitata* and *Laminaria hyperborea* does not affect the relative abundance of
408 *Bifidobacterium* in the gut microbiota [110, 111]. Nevertheless, Lynch et al. reported a
409 linear decrease in caecal *Bifidobacterium* in boars as a result of the addition of laminarin
410 from *Laminaria hyperborea* [112]. The above reports do highlight the need for further
411 in depth studies to thoroughly analyse the effect of laminarin on the HGM.

412

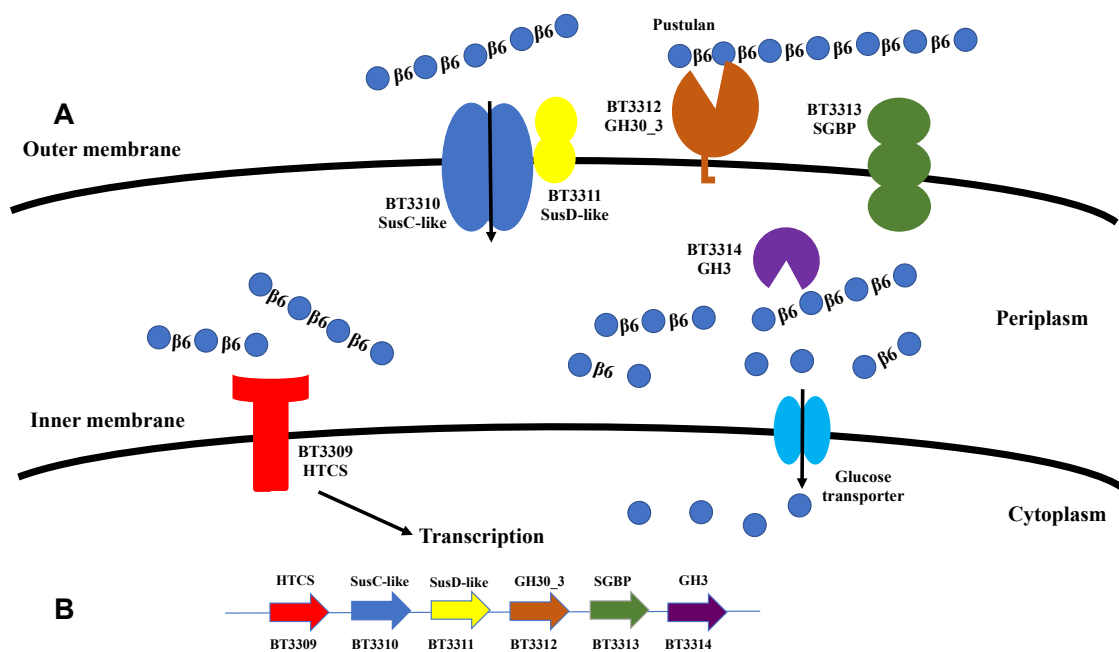
413 **4. Fungal β -glucans**

414 Fungal β -glucans are polymers composed of a $\beta(1,6)$ or $\beta(1,3)$ backbone, with a variable
415 branching degree (Fig. 1). *Bacteroides* species have been reported as degraders of
416 different types of fungal β -glucan. For example, when β -glucan from *Saccharomyces*
417 *cerevisiae* (β -1,3-glucan with β -1,6-linked side chains) was administered to C57BL/6
418 mice, it was shown to cause a reduction in bacterial diversity, yet an increase in relative
419 abundance of the phylum Bacteroidetes. This effect was accompanied with higher levels
420 of SCFAs such as acetic, propionic and butyric acids [113]. Also, the positive
421 correlation between an increase in Bacteroidetes and SCFA production was observed
422 when mice with colorectal polyps were fed with a complex β -glucan-chitin complex
423 (KytoZyme SA) [114].

424

425 As we stated in the seaweed β -glucan section, Dejean et al. showed the ability of certain
426 *Bacteroides* species to metabolize $\beta(1,3)$ -glucan from laminarin, yet also from yeast
427 [96]. They showed that the same PUL was involved in the degradation of both of these
428 β -glucan substrates (Fig. 6). In another study, $\beta(1,3)$ -glucan from *Candida albicans* was
429 shown to increase the relative abundance of the *Bacteroides* genus when mice were
430 administered live or heat killed-*Candida* [115]. In addition, one particular PUL
431 (BT3309-BT3314) from *Bacteroides thetaiotaomicron* VPI-5182 has been associated
432 with the degradation of fungal $\beta(1,6)$ -glucan (pustulan, Fig. 8A and 8B), a common
433 component of fungal cell walls of mushrooms and yeast [116]. BT3312 (GH30_3)
434 represents an endo- $\beta(1,6)$ -glucanase located at the cell surface accompanied by a SGBP
435 (BT3313), a SusC-like (BT3310), a SusD-like (BT3311) and a β -glucosidase (GH3,
436 BT3314). *Bacteroides thetaiotaomicron* employs a very efficient mechanism to fully
437 metabolize pustulan as a carbon and energy source (Fig. 8A). The SGBP BT3313
438 binding protein starts the degradation process by recognising and binding the intact

439 polysaccharide at the cell surface of *Bacteroides thetaiotaomicron*. Following this, the
 440 BT3312 (GH30_3) enzyme cleaves the intact glycan into smaller glucooligosaccharides,
 441 which will then be internalized into the periplasm by the permease pair
 442 BT3310/BT3311 (SusC-like/SusD-like). In the periplasm, a GH3 enzyme (BT3314)
 443 will continue metabolism by degrading the internalized 1,6-glucooligosaccharides (Fig.
 444 8A). BT3314 has been shown to exhibit a 30-fold higher activity for 1,6-glucobiose
 445 than for 1,3- or 1,4-glucobiose, and probably possesses two subsites into the active site,
 446 because of its similar activity on 1,6-glucobiose and 1,6-glucotriose [116]. The latter
 447 report postulated that the observed slow metabolism of 1,6-glucooligosaccharides in the
 448 periplasm of *Bacteroides thetaiotaomicron* may allow the persistence of a higher
 449 concentration of the “induced ligand” for BT3309 (HTCS or regulator of the PUL),
 450 enabling the locus to be up-regulated for an extended period of time for the use of
 451 pustulan as a carbon source by *Bacteroides thetaiotaomicron*. Comparative genome
 452 analysis with other species revealed that homologous PULs are located in the genomes
 453 of *Bacteroides uniformis* ATCC 8492, *Bacteroides ovatus* ATCC 8483 and *Bacteroides*
 454 *xylanosolvans* XB1A [116].



455

456 **Fig. 8. A.** Schematic of β -(1,6)-glucan (pustulan) degradation by *Bacteroides thetaiotaomicron*
457 VPI-5482 [116]. This linear β -glucan is degraded by a GH30_3 in the surface of *Bacteroides*
458 *thetaiotaomicron* and the resulted oligosaccharides are incorporated into the periplasm, where
459 another GH3 (β -glucosidase) hydrolyses the smaller oligosaccharides into single glucose
460 monomers. **B.** Genomic content of the pustulan PUL in *Bacteroides thetaiotaomicron* VPI-5482
461 [116].

462

463 Recent studies have addressed the role of fungal β -glucans in *Bifidobacterium*. For
464 instance, Wang et al. studied the correlation between sulphated β -glucan from
465 *Saccharomyces cerevisiae* and immune response [117]. Using immuno-suppressed
466 chickens as a result of cyclophosphamide treatment, the addition of 0.4 g of yeast β -
467 glucans per kilogram of chicken was shown to alleviate the immuno-suppression,
468 affecting the concentration of cytokines and promoting the proliferation of
469 *Bifidobacterium* [117]. Furthermore, supplementation with yeast β -glucans in
470 Alzheimer-induced mice has been shown to cause an increase in the relative abundance
471 of the genus *Bifidobacterium*, which was similar to that found in control mice [118].
472 Recently, in a macro study by Alessandri et al., the authors evaluated the growth ability
473 of hundred bifidobacterial strains using glucan-chitin complex from *Aspergillus niger* as
474 the only carbon source. All strains were shown to exhibit some, though mostly modest
475 growth with *Bifidobacterium breve* and *Bifidobacterium bifidum* strains eliciting the
476 highest levels of growth [119].

477

478 Zhao and Cheung showed that mushroom β -glucans elicit a prebiotic effect by
479 enhancing growth of *Bifidobacterium longum* subsp. *infantis* [59]. These authors
480 studied the proteomic profile of this catabolic process, showing that this bifidobacterial
481 species expresses 17 proteins that may be linked to mushroom β -glucan degradation.

482 These proteins include ABC transporters of sugars, enolase and a phosphoenol
483 phosphotransferase system. Among the 17 proteins, a predicted intracellular glucanase
484 is highly expressed. The authors proposed a metabolic model for this degradation where
485 (some parts of) the autoclaved polysaccharide (which is likely to cause hydrolysis of
486 this glycan) is incorporated into the cytoplasm by ABC transport system and PTS
487 (phosphotransferase system) proteins. After this incorporation, the intracellular
488 glucanase breaks down the polysaccharide into glucose monomers, which are
489 subsequently incorporated into the central fermentative pathway or “bifid shunt” [59].

490

491 Several papers have addressed the impact and metabolism of dietary plant glucosides,
492 such as flavonoids and gingenosides, on bifidobacterial and *Bacteroides* metabolism
493 [120-123]. However, very few studies have identified bifidobacterial β -glucosidases
494 active on β -glucan. Pokusaeva et al. identified the *cldC* gene in *Bifidobacterium breve*
495 UCC2003 to be involved in the metabolism of cellodextrins, which are β (1,4)-glucose
496 hydrolysis products from cellulose (Fig. 1) [124]. The authors showed the ability of this
497 bacterium to use cellobiose, cellotriose, cellotetraose and cellopentaose through the
498 *cldEFGC* gene cluster with a higher preference for cellobiose. Disruption of the *cldC*
499 gene resulted in the inability of *Bifidobacterium breve* UCC2003 to use these
500 cellodextrins as a carbon source, confirming that this gene cluster is uniquely required
501 for cellodextrin metabolism by this bacterium. It is reasonable to assume that these
502 enzymes would be able to degrade MLG oligosaccharides in a similar way to
503 cellodextrin oligosaccharides, though this hypothesis awaits experimental validation.
504 Indeed, more studies are required to fully understand the impact of β -glucan
505 oligosaccharide metabolism on proliferation of bifidobacterial species in the gut.

506

507 **5. Conclusions**

508 In this review we discussed recent publications that have studied the effect of β -glucans
509 from different sources on microbiota changes pertaining to Bacteroidetes (mainly
510 *Bacteroides* species) and *Bifidobacterium*. As previously reported, *Bacteroides* species
511 possess an extensive ability for glycan degradation, due to the presence of PULs in their
512 genomes [38, 39], allowing them to use different types of substrates and to occupy
513 different niches and environments [31, 35, 36]. We have focussed our review on the
514 most predominant types of β -glucans, clarifying the role of these polysaccharides as
515 potential substrates for Bacteroidetes and *Bifidobacterium*, as important bacterial
516 representatives of the adult gut microbiota [34]. Of a total of 16 studies involving
517 fungal, seaweed and cereal β -glucans, 8 concluded that dietary inclusion of β -glucans
518 causes an increase in the relative abundance of members of the Bacteroidetes phylum or
519 *Bacteroides* genus, where some studies also highlight beneficial effects elicited by
520 specific species (Table 1) [84, 106]. Nevertheless, 7 studies (6 with β -glucans from
521 cereals and 1 from seaweed) revealed the opposite results, a negative effect on the
522 relative abundance of Bacteroidetes or *Bacteroides*, and only one reported a ‘no effect’
523 conclusion (Table 1). The most significant disparity was found for cereal β -glucans
524 [86]. In oat β -glucans, we found a similar number of studies with positive or negative
525 correlations on the Bacteroidetes increase. In addition, for barley β -glucans, the number
526 of studies published showing negative conclusions was higher than the published with
527 positive correlations.

528

529 One would imagine that the same substrate should have equal consequences for a
530 specific bacterial genus, so the variation in the results may be due to the utilization of
531 different models, substrates and/or methodologies (Table 1) [79]. The results may differ

532 in a molecular weight-dependent manner even when using the same substrate.
533 Furthermore, the utilization of different model systems (pigs, rats, mice or humans) is
534 likely to play an important role in this variation, because of the distinct microbiota
535 composition in each of these mammalian species (Table 1) [77-79, 82]. While it seems
536 that the positive effects are very clear for fungal and seaweed β -glucans [88, 101, 102],
537 the differences observed between the three types of β -glucans must be tested in more
538 detail and further studies should be done for the three sources in order to clarify if the
539 observed disparity in the experimental results is caused by the application of non-unique
540 procedures, or, by contrast, if these correlations between the substrates and the
541 degraders remain stable [77-79, 99-102]. Due to the increasing interest in β -glucans as
542 potential prebiotics and their effect on human health, this work provides further avenues
543 to understand the behaviour of β -glucan-fed HGM.

544

545 Very little is currently known about the molecular mechanism how *Bifidobacterium*
546 degrade different β -glucan types. Only a small number of papers have established the
547 prebiotic effect of cereal and fungal β -glucans, both through *in vitro* fermentations and
548 by means of human trials. Strains from *Bifidobacterium breve*, *Bifidobacterium bifidum*
549 and *Bifidobacterium longum* have been shown to be able to at least partially degrade
550 fungal β -glucan-chitin complex [119]. These authors showed the transcriptional profile
551 of *Bifidobacterium breve* 2L when using this complex substrate as a unique carbon
552 source. Due to the complexity of β -glucan-chitin, the authors expect that other bacterial
553 members of the gut microbiota community are involved in the complete metabolism of
554 β -glucan-chitin through syntrophic interactions [119].

555

556 More mechanistic studies are needed to understand the size of oligosaccharides
557 incorporated by bifidobacterial transporters. In addition, detailed structural mechanistic
558 insights and substrate specificity studies of glucosidases and glucanases in
559 *Bifidobacterium* species, when they act on several types of β -glucan, are required to
560 expand our knowledge on the direct or indirect (through cross-feeding) use of these
561 glycans as prebiotics. Finally, there is a clear knowledge gap regarding the cross-
562 feeding process between different members of *Bacteroides* and *Bifidobacterium* and
563 further studies are needed to shed light on the molecular details of such syntrophic
564 interactions, a good example of this being the cross-feeding interactions involving
565 dietary arabinogalactan [46]. Such studies will allow the rational design of nutraceutical
566 strategies with the help of particular β -glucans as functional food ingredients, perhaps in
567 combination with certain bifidobacterial species in so-called synbiotic formulations.

568

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574

575 **Author contributions**

576 P.F.-J.: writing – original draft preparation. D.v.S. and J.M.-M.: writing – review,
577 editing, and conceptualization. All authors contributed to the article and approved the
578 submitted version.

579

580 **Conflict of interest**

581 The authors declare no conflict of interests.

582

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TABLE 1. Carbohydrate intake and intervention parameters for the intervention trials with *Bacteroides* genus influences.

Reference	Type of β -glucan	Duration	Organism	Analyzed parameters	Main Outcomes
[68]	Oat β -glucan	17 days	8 cross-bred Duroc-Landrace pigs	Bacterial populations, SCFAs levels	Oat β -glucan ingestion was associated with a reduction in <i>Bacteroides</i>
[69]	Oat β -glucan	12 hours of incubation	15 healthy humans	Bacterial populations, BCFAs and SCFAs fermentation	Oat β -glucan ingestion was associated with a reduction in <i>Bacteroides</i> and <i>Bifidobacterium</i>
[70]	Oat β -glucan	8 weeks	28 health male BALB/c mice,	Bacterial populations, SCFAs production, feed intake, body weight gain	Oat β -glucan decreased the bacterial biodiversity yet increased the relative abundance of the phylum Bacteroidetes. <i>Bacteroides</i> was found as the predominant genus in the colon and it was associated with a higher concentration of beneficial short chain fatty acids (SCFAs), such as propionate and acetate
[71]	Oatwell (28% oat β -glucan)	24 hours of incubation	3 healthy humans	Bacterial populations, SCFAs production	Oatwell was related to higher <i>Bacteroides</i> abundance and propionate concentration
[76]	Barley β -glucan	25 days	8 groups of 7 male Wistar rats	Bacterial populations, SCFAs production, feed intake, body gain, amino acid production, cholesterol levels	Barley β -glucan increased the production of SCFAs, reduced inflammation and cholesterol levels, and lowered the abundance of <i>Bacteroides fragilis</i> in the caecum
[77]	Barley β -glucan (125 g/day of bread with 3 g of barley β -glucan)	3 months	20 polictemized human patients	Bacterial populations, SCFAs concentration	No significance difference during the intervention. Nevertheless, two weeks after cessation of the treatment, <i>Bacteroides</i> genus was found significantly decreased
[78]	Low and medium molecular weight barley β -glucan	39 days	48 male Wistar rats	Bacterial populations, SCFAs concentration, Feed intake, body gain, plasma lipid	The ratio <i>Bacteroides/Prevotella</i> was reduced by low and medium molecular weight barley β -glucan

				levels	
[79]	Low and high molecular weight barley β -glucan	35 days	30 human subjects	Bacterial populations, CVD risk factors	High molecular weight barley β -glucan can significantly increase <i>Bacteroides</i> and reduce CVD risk
[80]	Barley β -glucan extracted from Glucagel™ and arabinoxylan, xyloglucan, glucan, and pectin.	48 hours of incubation	<i>Bacteroides ovatus</i> ATCC 8483T310 , <i>Bifidobacterium longum</i> subspecies <i>longum</i> ATCC 15707T, <i>Megasphaera elsdenii</i> DSM 20460T311 , <i>Ruminococcus gnavus</i> ATCC 29149T, and <i>Veillonella parvula</i> DSM 2008T	Bacterial growth	<i>Bacteroides ovatus</i> ATCC 8483T310 prioritizes the use of barley β -glucan before the other substrates, with higher growth rates than the other studies species except <i>Veillonella parvula</i> .
[83]	Whole wheat grains	8 weeks	68 human subjects	Bacterial populations, phenolic compounds levels glycaemia, plasma lipids, inflammatory markers and	Wheat β -glucan was correlated with an increase in Bacteroidetes phylum and <i>Bacteroides</i> genus. <i>Bacteroides</i> could reduce inflammatory markers TNF- α and IL-6 and plays a role in reducing pathologies associated with inflammation
[84]	Whole wheat grains	48 hours of incubation	10 health humans	Bacterial populations,	<i>Bacteroides cellulosilyticus</i> , <i>Bacteroides ovatus</i> and <i>Bacteroides stercoris</i> were described as predominantly wheat-bran β -glucan degraders, while <i>Bacteroides uniformis</i> , <i>Bacteroides dorei</i> and <i>Bacteroides eggertii</i> were enriched in the β -glucans from wheat-lumen, so not all <i>Bacteroides</i> present the same feed-responsive behaviour
[85]	durum wheat flour and whole-grain barley pasta	2 months	26 healthy humans	Bacterial populations, blood cholesterol, amino acid concentration, SCFAs levels	No clear change in the microbiota composition. Increase in 2-methyl-propanoic acid, acetic acid, butanoic

					(butyric) acid, and propanoic (propionic) acid
[86]	wheat bran and BarleyMax	4 weeks	60 healthy humans	Dietary Intake, Biochemical Analysis, Microbiota Composition, SCFA levels	Increase in <i>Bacteroides</i> genus, Higher SCFAs concentrations, especially butyric acid
[104]	Laminaran	2 weeks	18 male Wistar rats	Microbiota composition, body weight, carbohydrate levels, organic acids levels	Reduction in Bacteroidetes abundance. Laminaran also can reduce the levels of cecal putrefaction substances levels
[105]	Laminaran	6 weeks	18 female BALB/c mice	Bacterial population, carbohydrate active enzymes activity, body weight	Increase in relative abundance of Bacteroidetes phylum, especially the genus <i>Bacteroides</i> , and a decrease in the Firmicutes phylum. Laminarin ingestion shifted the microbiota at the species level towards a higher energy metabolism, and therefore increasing the number of carbohydrate active enzymes. Laminarin also slowed weight gain in mice and decreased the bacterial species diversity.
[106]	Laminaran	11-13 days	18 male ICR mice	Bacterial populations	<i>Bacteroides intestinalis</i> and <i>Bacteroides acidifaciens</i> , producing succinate and acetate, which are precursors of beneficial propionate and butyrate

TABLE 2. Carbohydrate intake and intervention parameters for the intervention trials with *Bifidobacterium* genus influences.

Reference	Type of β -glucan	Duration	Organism	Analyzed parameters	Main Outcomes
[72]	Oat β -glucan	25 days	32 weaned pigs	Bacterial populations, body weight, serum parameters	Oat β -glucan supplementation decreased <i>Bifidobacterium</i>
[73]	Oat β -glucan and its hydrolysates	1 week	3 male Sprague-Dawley rats	SCFA production, bacterial growth of different faecal microbiota	No significant differences with intact oat β -glucan. However, the oat β -glucan hydrolysates OGH treatment evidently promoted the growth of <i>Bifidobacterium longum</i> BB536. The hydrolysates of oat β -glucan produced greater amounts of SCFA (mainly acetate, propionate and butyrate) with no significant difference in SCFA pattern when compared with oat β -glucan.
[74]	Oat β -glucan	35 days	Pure strains of <i>Bifidobacterium breve</i> R0070, <i>Bifidobacterium longum</i> R0175	Bacterial growth	These data indicate that the addition of beta-glucan to yogurt increased survival of <i>Bifidobacterium longum</i> R0175
[75]	Oat β -glucan	4 weeks	30 male SD rats	Food Intake, body Weight, ATPase activity, bacterial population	Oat β -glucan decreased glycaemia and insulin response while it increased ATPase activity and <i>Bifidobacterium</i> relative abundance
[81]	Glucagel™ (80% barley derived β -glucan)	8 weeks	36 C57BL/6 male mice	Body weight, food intake, tissue weights and adiposity Data, Gut microflora composition and SCFAs	Barley β -glucan attenuate weight gain and increase relative abundance of <i>Bifidobacterium</i> both in faeces and caecal contents over the 8 weeks of dietary intervention
[76]	Barley β -glucan	25 days	56 male Wistar rats	Cecal microbiota, SCFAs levels, cholesterol, TAG and inflammatory levels, feed intake, weight gain, caecal content, pH, tissue weight	Barley β -glucan was related with an increase in the abundance of <i>Bifidobacterium</i> and SCFA levels and a reduction in cholesterol levels and inflammatory markers
[82]	Barley β -glucan	8-12 weeks	male C57BL/6J mice (amount not given)	Bacterial populations, SCFAs production	Barley β -glucan suppressed appetite and improved insulin sensitivity. Furthermore, barley β -glucan increased the relative abundance of the genus <i>Bifidobacterium</i> and SCFA production