

2

3 **Host-associated probiotics, a key factor in sustainable aquaculture?**

4

5 **Hien Van Doan¹, Seyed Hossein Hoseinifar², Einar Ringø^{3, *}, Maria Ángeles Esteban⁴,**
6 **Maryam Dadar⁵, Mahmoud A.O. Dawood⁶ and Caterina Faggio⁷**

7

8 ¹Department of Animal and Aquatic Sciences, Faculty of Agriculture, Chiang Mai University,
9 Chiang Mai 50200, Thailand

10 ²Department of Fisheries, Faculty of Fisheries and Environmental Sciences, Gorgan University
11 of Agricultural Sciences and Natural Resources, Gorgan, Iran

12 ³Norwegian College of Fisheries Science, Faculty of Bioscience, Fisheries and Economics,
13 UiT The Arctic University of Norway, Tromsø, Norway

14 ⁴Fish Innate Immune System Group, Department of Cell Biology & Histology, Faculty of
15 Biology, Regional Campus of International Excellence "Campus Mare Nostrum", University
16 of Murcia, Spain

17 ⁵Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension
18 Organization (AREEO), Karaj, Iran

19 ⁶Department of Animal Production, Faculty of Agriculture, Kafrelsheikh University, 33516,
20 Kafrelsheikh, Egypt

21 ⁷Department of Chemical, Biological, Pharmaceutical and Environmental Sciences, University
22 of Messina Viale Ferdinando Stagno d'Alcontres, 31 98166, S. Agata–Messina, Italy

23

24 * To whom correspondence should be addressed:

25 Einar Ringø, Norwegian College of Fisheries Science, Faculty of Bioscience, Fisheries and
26 Economics, UiT The Arctic University of Norway, Tromsø, Norway. E-mail address:
27 Einar.Ringo@uit.no

28

29 **Abstract**

30 The aquaculture industry has dramatically developed during the last two decades. However,
31 this development has, in some cases, resulted in environmental degradation, emergence of
32 diseases and low productivity. The need for improving disease resistance, growth performance,
33 feed efficiency, and safe aquatic production for human consumption has stimulated
34 development and applications of probiotics in aquaculture. Probiotics used in aquaculture
35 include genera of *Bacillus*, *Lactobacillus*, *Enterococcus*, and *Carnobacterium*, and yeast.
36 However, most of these probiotics are derived from terrestrial sources and not from the
37 environment in which the aquatic animals live or the host animal. The use of “host-associated
38 probiotics” has recently gained attention, as they offer an alternative strategy within
39 aquaculture, which *per se* is dependent on the use of terrestrial microorganisms. The benefits
40 of host-associated probiotics include improved growth performance, feed value, enzymatic
41 contribution to digestion, inhibit adherence and colonization of pathogenic microorganisms in
42 the gastrointestinal tract, increase hematological parameters, and immune response.
43 The present review addressed insight into the application of host-associated probiotics within
44 aquaculture, with special focus on their immunomodulatory and growth enhancing effects.
45 Furthermore, the current review discusses research gaps and issues that merit further
46 investigations.

47

48 **Keywords:** Host-associated probiotics, Sustainable aquaculture, Immunomodulation, Growth
49 promoter, Terrestrial microorganisms; Disease resistance

50

51

52

53

54 **1. Introduction**

55 Aquaculture is the fastest growing animal protein sectors to meet the demands of today's
56 growing worldwide population. For the satisfaction of the increased human consumption,
57 intensive aquaculture systems at high densities have been developed (Tal et al., 2009). This
58 intensification has however, resulted in significant damage to the aquaculture environment, due
59 to organic wastes production which consume dissolved oxygen in ponds, and increase toxic
60 metabolites; responsible for high mortality (Martinez Cruz et al., 2012). For long time,
61 chemotherapies and antibiotics were applied as an effective remedy for disease outbreaks in
62 aquatic animals (Serrano, 2005). However, due to their excessive use, aquatic pathogens have
63 become resistant to such treatments, along with the suppression of the host's immune system
64 (Capkin et al., 2015, 2017; Dawood & Koshio, 2016). Furthermore, the application of
65 antibiotics may extend to human consumption, which could adversely affect human health and
66 weaken the immune systems (Cheng et al., 2014; Hoseinifar et al., 2015; Langdon et al., 2016).
67 As a result, strict regulations against antibiotic administration in livestock-, poultry-, and the
68 aquaculture sector have been established in several countries. Alternative strategies such as;
69 vaccines, pro -, pre -, synbiotics, and medicinal herbs must further be investigated to improve
70 health of aquatic animals (Martínez Cruz et al., 2012; Altinok et al., 2015; Adel et al., 2016;
71 Abdelkhalek et al., 2017; Van Doan et al., 2017; Dawood et al., 2018).

72 Host aquatic microorganisms play a crucial role in the health maintenance by boosting the
73 immune system, and increasing the resistance against opportunistic pathogens via the
74 production of antimicrobial substances (e.g. Llewellyn et al., 2014; Ibrahem, 2015; Yan et al.,
75 2017). When discussing the functionality of gut microbiota, it depends on the ability of
76 microorganisms to interact within the gastrointestinal (GI) tract, which benefit the host through
77 influence upon its biological functions (Ramírez & Romero, 2017).

78 For nearly half a century the word probiotic has been used in several different ways, since [Lilly](#)
79 [& Stillwell \(1965\)](#) first used it. [Gatesoupe \(1999\)](#) defined probiotics as “*live microbial feed*
80 *supplements that improve the health of both humans and terrestrial livestock*”, and according
81 to [Dawood et al. \(2016\)](#), probiotics is required to maintain a healthy environment for aquatic
82 animals and to increase their performance, without any negative impacts upon the consumers.
83 Supplementation of aquatic animal diets with probiotics positively influences growth
84 performance, feed utilization, physiological conditions, optimize cell proliferation under
85 stressful conditions, promote immune cell stimulation, modulate the gut microbiota and
86 improve disease resistance (e.g. [Irianto & Austin, 2003](#); [Merrifield et al., 2010](#); [De et al., 2014](#);
87 [Ringø et al., 2014](#); [Hai, 2015a](#)).

88 When discussing disease resistance, the importance of a stable microbiota is worth to mention.
89 The best evidence for this protective effect of the gut microbiota stems from an early study
90 revealing that germfree animals are more susceptible to diseases compared to corresponding
91 conventional animals with a “complete gut microbiota” ([Collins & Carter, 1978](#)). Germfree
92 mouse can be killed with 10 cells of *Salmonella enteritidis* whereas 10⁶ cells are needed to kill
93 conventional mouse with a conventional gut microbiota. Therefore, it is crucial to increase our
94 knowledge on probiotics adhering and colonising the GI tract of endothermic animals as well
95 as aquatic animals, in the context of improved growth performance and health.

96 When discussing the importance of probiotics in aquaculture, the mode of action and their
97 effects on the intestinal microbiota, immunological, physiological responses, as well as growth
98 performance must be continually investigated. Recently, there has been increasing attention
99 towards administration of host-associated probiotics in aquaculture ([Lazado et al., 2015](#); [Li et](#)
100 [al., 2018](#)). However, as no clear definition *per se* exist, we defined host-associated probiotics
101 as; bacteria originally isolated from the rearing water or the GI tract of the host to improve
102 growth and health of the host. In aquaculture, *per se* it is not clear, whether host-associated

103 probiotics are more effective than probiotics from other origins, even though there is some
104 evidence demonstrating beneficial effects of host-associated probiotics vs. probiotics isolated
105 from other sources (Lazado et al., 2015). One possible reason for their superior function may
106 be because they perform better within their own original environment. Therefore, the present
107 review addressed on the health benefits of host-associated probiotics in aquaculture, and their
108 potential immunomodulatory and growth promoting effects.

109

110 **2. Sustainable aquaculture: the role of probiotics**

111 Outbreaks of infectious diseases are a major obstacle for the development of aquaculture, which
112 adversely affect the sustainability of this industry (Mardones et al., 2018). Throughout the last
113 decades, the aquaculture industry was heavily dependent on the use of antibiotics and
114 chemotherapeutics for diseases control and prevention (Romero et al., 2012; Fečkaninová et
115 al., 2017). However, the abusive use of these substances caused many adverse effects upon the
116 host and its environment (e.g. Romero et al., 2012; Miller et al., 2016; Capkin et al., 2017;
117 Suzuki et al., 2017), and therefore development of alternative strategies to antibiotics and
118 chemotherapeutics are needed (e.g. Defoirdt et al., 2011; Altinok et al., 2016; Founou et al.,
119 2016).

120 Sustainable aquaculture has been created to preserve and develop the industry (Bostock et al.,
121 2010). In this context, several criteria have been put forward and include; vaccines,
122 immunostimulants, pro -, pre - and synbiotics (e.g. Ringø et al., 2014; Lazado et al., 2015;
123 Hoseinifar et al., 2016). Several types of vaccines have been developed for aquaculture, in
124 which the most successful effects are reported in salmonids and cyprinids (e.g. Dhar et al.,
125 2014; Ringø et al., 2014; Lazado et al., 2015; Hoare et al., 2017). Recent findings have revealed
126 that vaccines are effective for disease control in aquaculture (e.g. Johnson et al., 2008;
127 Brudeseth et al., 2013; Assefa & Abunna, 2018). However, individual vaccines are known to
128 be effective against only one type of pathogen; which limiting their use in aquaculture (Ardó et

129 al., 2008; Feodorova et al., 2014). Immunostimulants with a wide range of applications and
130 functions have therefore, been considered as an alternative strategy to overcome the
131 “drawback” of vaccines (Barman et al., 2013; Hoseinifar et al., 2017). These bioactive
132 compounds boost the immune system of the host, and protect the host against wide range of
133 pathogens (e.g. Bricknell & Dalmo 2005; Ringø et al., 2012; Hoseinifar et al., 2015; Nawaz et
134 al., 2018).

135 Probiotics have many beneficial properties to the host and its environment, and they are now
136 widely used in aquaculture as growth promoters, immunostimulants, and for disease protection
137 (Pérez-Sánchez et al., 2014; Hai, 2015b). The word *probiotic* stems from the Greek
138 roots *pro* and *bios*, or “*profile*” (Schrezenmeir & de Vrese, 2001). As a concept, the use of
139 probiotics to control disease is referred to as “the use microorganisms against microorganisms”
140 (Lazado et al., 2015). During the last two decades, numerous comprehensive reviews have
141 addressed on probiotics and their impacts in aquaculture (e.g. Gatesoupe 1999; Verschuere et
142 al., 2000; Irianto & Austin, 2003; Balcázar et al., 2006; Merrifield et al., 2010; Pérez-Sánchez
143 et al., 2014; Ringø et al., 2014; Hai, 2015a,b; Hoseinifar et al., 2016) with multidimensional
144 actions. Probiotics offer numerous beneficial effects, including immunomodulatory, nutritional,
145 and environmental capacity, and therefore have a great competitive advantage as prophylactic
146 against disease (Ohashi & Ushida, 2009; Lazado et al., 2015). While there is no concrete
147 evidence to conclude that probiotics are better than immunostimulants or vaccines, the
148 beneficial effects upon the host and their environment ensure that probiotics will remain one of
149 the most promising approaches used to control diseases and the subsequent environmental
150 modifiers (Newaj-Fyzul & Austin, 2015). Several probiotics species are used in aquaculture;
151 e.g. *Bacillus* sp., *Lactobacillus* sp., *Enterococcus* sp., *Streptomyces*, *Carnobacterium* sp., and
152 yeast (e.g. Gatesoupe, 2007; Martínez Cruz et al., 2012; Tan et al., 2016; Elshagabee et al.,

153 2017). Table 1, 2 and 3 summarize the results of studies from 2005 to 2018, focusing on the
154 effects of host-associated probiotics as growth promoters and immunostimulants in aquaculture.

155

156 **3. Host-associated vs. terrestrial probiotics**

157 To our knowledge, commercial probiotics have been used in aquaculture since the early 80ties
158 (Boyed et al., 1984) and until today (e.g. Zheng et al., 2017; Zhou et al., 2017; Interaminense
159 et al., 2018; Pereira et al., 2018). However, recently, attention has focused on using host-
160 microbiota as a probiotics source (e.g. Lazado et al., 2015; Interaminense et al., 2018; Li et al.,
161 2018; Wang et al., 2018). They are naturally established within the host defense system (Gomez
162 et al., 2013; Llewellyn et al., 2014), and revealed a large number of beneficial characteristics;
163 such as intestinal enzymes and novel bioactive lipid sebastenoic acid (Lazado et al., 2012;
164 Sanchez et al., 2012). This is important for fish farming, as fish are a rich source of probiotic
165 strains that provide additional mechanisms against numerous infectious diseases (e.g.
166 Spanggaard et al., 2000; Pandiyan et al., 2013; Carnevali et al., 2017). Host-related microbiota
167 can be an alternative probiotic source within aquaculture, as terrestrial sources *per se* are mostly
168 used (Lakshmi et al., 2013; Lazado et al., 2015). Today, most probiotic candidates are derived
169 from the mucosal layers, the autochthonous bacteria, of aquatic animals (Balcázar et al., 2007;
170 Newaj-Fyzul et al., 2007; Caipang et al., 2010; Lazado et al., 2010; Maeda et al., 2014; Lazado
171 & Caipang 2014a; Tzuc et al., 2014). For example, probiotics isolated from the GI tract of
172 channel catfish (*Ictalurus punctatus*) (Larsen et al., 2014), rainbow trout (*Oncorhynchus*
173 *mykiss*) (Spanggaard et al., 2000; Araújo et al., 2015), Atlantic cod (*Gadus morhua*) (Dhanasiri
174 et al., 2011; Fjellheim et al., 2007), and Atlantic salmon (*Salmo salar*) (Jöborn et al., 1999).

175 Two basic principles are generally applied as a guide for the use of host-associated bacteria as
176 a probiotic (Lazado & Caipang, 2014a). The differences in physiological peculiarities and
177 discrepancies of each host, as well as the considerable influences of various environmental
178 factors make it hard to establish a probiotic candidate for global application (Lazado et al.,

179 2015). For example, growth and bacteriocin production of *Leuconostoc mesenteroides* and
180 *Lactobacillus curvatus* are affected by pH, temperature, and aquatic animal species (Mataragas
181 et al., 2003). These parameters were reported to affect the adhesion ability of lactic acid bacteria
182 (LAB) (Tuomola et al., 2001). Physiological variances between marine and terrestrial
183 microorganisms exist, and impose differential responses to diverse environment (Morgan-Kiss
184 et al., 2006; Lazado et al., 2015). Furthermore, a discrepancy exists in acquisition mechanism
185 between marine and terrestrial microorganisms involved in inhibition of pathogen growth
186 (Sandy & Butler, 2009), which is controlled by siderophore production; a mechanism of
187 probiotics (Lazado et al., 2010; Ahmed & Holmström, 2014). The mode of action of bacterial
188 iron acquisition includes siderophore-mediated transport, direct import through divalent metal
189 transporters, or direct piracy from ironbound host proteins (Caza & Kronstad, 2013;
190 Pokorzynski et al., 2017). Siderophores are low molecular weight substances with a high
191 affinity for ferric iron, which are synthesized and secreted by bacteria in order to scavenge iron
192 when the availability is limited. In Gram-negative bacteria, siderophore-bound iron is
193 transported through cognate outer membrane receptors that require energy transduction via the
194 TonB-ExbB-ExbD protein complex (Andrews et al., 2003; Ellermann & Arthur, 2017). The
195 second mechanism depends on specific enzymatic hydrolysis of the siderophore, which serves
196 to weaken its interactions with iron, and enable its liberation. In both Gram-negative and Gram-
197 positive bacteria, ferrous iron is directly transported through cytoplasmic membrane permeases
198 or ABC transporters (Kammler et al., 1993; Sabri et al., 2006; Shapiro & Wencewicz, 2016).
199 Some bacterial pathogens belonging to family Neisseriaceae, Pasteurellaceae and
200 Moraxellaceae are also capable of utilizing host sources of iron by expressing outer membrane
201 receptors that directly bind to host iron-binding proteins such as transferrin (Cornelissen, 2003;
202 Parrow et al., 2013). The bottlenecks caused by the physio-chemical parameters on probiotic
203 properties may be eliminated by using host-associated microorganisms as probiotics if these

204 microorganisms are originally isolated from the environment where they were applied
205 ([Verschuere et al., 2000](#); [Vadstein et al., 2013](#)). Because the highest physiological activities of
206 microorganisms are obtained in their natural habitats, we may presume that the ultimate benefits
207 are achieved when they are applied in those conditions ([Ibrahim, 2015](#)).

208 Because existing knowledge is fragmentary, it is difficult to draw a solid scientific conclusion
209 to whether host-associated microbiota are superior to terrestrial sources ([Lazado et al., 2015](#)).

210 However, it is believed that the survival rate and function of host-associated probiotics are
211 optimal when they are applied in the “natural” environment ([Murall et al., 2017](#)). The
212 application of both host and non-host candidate probiotics in aquaculture represent promising
213 future alternatives ([Lazado et al., 2015](#)). Additional beneficial effects are obtained when
214 combining two or more microorganisms, providing that they do not inhibit each other. Previous
215 findings have indicated that the functionality and efficacy of their administration are improved
216 with the use of multi-strain probiotics ([Timmerman et al., 2004](#); [Mohapatra et al., 2014](#)). In
217 probiotics-mediated disease prevention, the best level of protection for a broad spectrum of fish
218 pathogens can only be achieved through the use of multiple strains in dietary preparations
219 ([Merrifield et al., 2010](#)). Interestingly, the use of host-associated probiotics addresses the above
220 concerns, but also shows that host-microbiota have functions other than being a part of natural
221 defense system, such as immunomodulation and nutrient conversion ([Lazado et al., 2015](#);
222 [Montalban-Arques et al., 2015](#)). This is bioprospecting in a lesser scale, with a sustainable core
223 concept of improving the health and welfare of aquaculture animals, through the utilization of
224 their own commensal microbes ([Llewellyn et al., 2014](#); [Lazado et al., 2015](#)). Recent findings
225 have revealed that the microbial community of fish intestines are a new source of probiotics,
226 and offer a biosynthetic diversity for natural products discovery ([Sanchez et al., 2012](#)).

227

228

229 **4. Host specificity**

230 When discussing host-associated vs. terrestrial probiotics, host specificity is an important
231 subject to mention. Adhesion of probiotic LAB was previously reported to be host specific, and
232 Fuller (1989) stated, “*The attachment to epithelial cells is very host specific which means in*
233 *practical terms that a strain which is suitable as pig probiotic may not be active in chick and*
234 *other animals*”. However, later studies have indicated that LAB originated from one host adhere
235 to mucus of other species (e.g. Tuomola et al., 1999; Rinkinen et al., 2000, 2003; Nikoskelainen
236 et al., 2001a,b). In a recent review by Li et al. (2018), adherence and colonization of
237 microorganisms in the GI tract of fish was discussed. As *in vitro* and *ex vivo* studies suggested
238 host specificity of LAB colonization in sturgeon (Askarian et al., 2011; Salma et al., 2011), Li
239 et al. (2018) put forward the controversial hypothesis that host specificity of LAB does not
240 occur in “*younger*” fish species, e.g. Atlantic cod, Atlantic salmon and turbot, while it occurs
241 in older species, sturgeons; “*living fossil*”. However, adhesion ability of LAB may be related
242 to; adhesive and non-adhesive ability (Zhou et al., 2012), variation of mucin adhesion and cell
243 surface characteristics depending on their isolation habitats indicated by Buntin et al. (2017),
244 and hydrophobic properties (Grajek et al., 2016).

245

246 **5. Mode of actions of probiotics**

247 Probiotic microorganisms influence the immune responses of the host, as well as the interaction
248 between these responses and their intestinal bacterial communities (Derrien & van Hylckama
249 Vlieg, 2015; Fischbach & Segre, 2016). During the last decades, intensive studies on probiotics
250 have shed new light on the importance of probiotics and their modes of action (Papadimitriou
251 et al., 2015), and several modes of action have been proposed.

252 (I) Probiotics enhance feed utilization and weight gain promoters of aquatic animals
253 (Hai, 2015b; Zorriehzahra et al., 2016). Probiotics improve the host’s appetite and feed

254 digestion by breaking down indigestible components, increase production of vitamins, and
255 detoxify compounds in the diet (Giraffa et al., 2010; Zorriehzahra et al., 2016).

256 (II) Competitive exclusion of pathogens in the GI tract (Ringø et al., 2010a), by
257 production of peroxide, bacteriocin, siderophore, and lysozyme enzymes (Yan et al., 2002). The
258 physiological and immunological effects (Mohapatra et al., 2014; De et al., 2014) are
259 considered to be two of the most important beneficial mechanisms of probiotic bacteria
260 (Collado et al., 2010; Zorriehzahra et al., 2016).

261 (III) Improve the resistance of farmed aquatic animals against stress caused by several
262 environmental hazards throughout the aquaculture activity (Nimrat et al., 2012; Zorriehzahra et
263 al., 2016).

264 These modes of actions present the beneficial effects of probiotics in cultured aquatic animals.
265 Nonetheless, future researches on the interaction between probiotics and the host, involving
266 transcriptomic and proteomic analyses, are needed to understand of probiotic activity.

267

268 **6. Host-associated probiotics and their applications in aquaculture**

269 **6.1 *Bacillus* sp.**

270 Bacteria belonging to genus *Bacillus* has simple nutritional requirements, fast metabolic rate,
271 ease to isolate and preserve, and secrete multiple bacteriocins make them good probiotic
272 candidates (Moriarty, 1998; Ziaei-Nejad et al., 2006). Genus *Bacillus* is the most studied host-
273 associated probiotic, among a wide variety of aquatic animals. To our knowledge, Yanbo and
274 Zirong (2006) conducted the first study using host-associated probiotics in aquaculture. Their
275 findings showed that *Bacillus* sp. supplementation diets significantly improved growth
276 performance, survival rate, and feed conversion ratio; as well as protease and lipase activities
277 in common carp (*Cyprinus carpio*) (Yanbo & Zirong, 2006). The authors suggested that these
278 improvements were due to enhanced enzyme activities, resulting in improved diet digestibility;
279 including proteins, starches, and lipid.

280 In channel catfish, dietary inclusion of *Bacillus* spp. isolated from oil or intestine, significantly
281 increased channel catfish resistance towards *Edwardsiella ictaluri* and *Aeromonas hydrophila*
282 (Ran et al., 2012). The improved diseases resistance was suggested to be attributable to a
283 biologically meaningful discrepancy in the interactions between *Bacillus* strains and their
284 respective host. Additionally, interactions may exist between host, pathogen, and probiotic
285 bacteria that are influenced by environmental factors. Ran et al. (2012) suggested that more
286 research is needed to clarify the complex interactions between the host, pathogen and the
287 probiotic *Bacillus* strains, as well as how to improve the environment in order to obtain optimal
288 biological control of disease.

289 A study with *Bacillus* sp. isolated from shrimp intestine, Cha et al. (2013) reported significant
290 increase in growth performance, innate immune response, and disease resistance in olive
291 flounder (*Paralichthys olivaceus*), to *Streptococcus iniae*. The authors speculated that the
292 increase in growth performance of fish fed dietary *Bacillus* sp. was a result of improved diet
293 utilization. The GI tract of fish are known to be very sensitive to nutrients, presenting immediate
294 changes in digestive enzyme activity, leading to enhanced growth and well-being (Bolasina et
295 al., 2006; Shan et al., 2008). Zhang et al. (2010) indicated that the growth improvement in sea
296 cucumber (*Apostichopus japonicus*) fed a *Bacillus subtilis* supplemented diet was due to the
297 increase in digestive activity via enhanced enzymatic activity. Previous probiotic studies
298 suggested that supplementation increases the favorable microorganism in the host's gut, which
299 in turn release exoenzymes that can improve feed utilization and health conditions (Vine et al.,
300 2006; Yanbo & Zirong, 2006). These beneficial organisms secrete numerous proteases, which
301 may play an important role in breakdown of peptide bonds of proteins, into monomers and free
302 amino acids, which positively affect host's nutritional status (Macfarlane & Macfarlane, 2012).
303 Similarly, a significant increase in growth performance, immune response, and disease
304 resistance were observed in orange-spotted grouper (*Epinephelus coioides*) larvae (Sun et al.,

305 2013), rohu (*Labeo rohita*) (Ramesh et al., 2015), and striped catfish (*Pangasianodon*
306 *hypophthalmus*) (Truong Thy et al., 2017) fed host-associated *Bacillus* sp. The authors
307 suggested that further investigations are needed to evaluate the effect of probiotics on the
308 immune function in fish larvae, and to estimate the duration of persistence of the *Bacillus* after
309 discontinuation of probiotic supplementation.

310 There is limited information available regarding the effects of host-associated probiotics on the
311 health and well-being of crustacean and mollusk. Nimrat et al. (2011) reported that giant tiger
312 prawn (*Penaeus monodon*) fed *Bacillus* spp. isolated from shrimp intestines and pond sediment,
313 presented significantly improved growth performance, and survival rate; as well as increasing
314 the number of additional beneficial microbial probiotics. In mud crab (*Scylla paramamosain*),
315 dietary administration of *Bacillus* spp. isolated from the crab's intestine significantly enhanced
316 survival rate, respiratory burst activity, immune related genes expression, and resistance to
317 *Vibrio parahaemolyticus* (Wu et al., 2014). A significant decrease in hemocytes mortality and
318 increase resistance toward *Vibrio harveyi* were observed in Pacific oyster (*Crassostrea gigas*)
319 fed *Bacillus* sp. isolated from Tunisian hypersaline (Fdhila et al., 2017). The significant
320 improvement in growth performance within these findings may be due to the ability
321 of *Bacillus* spp. to adhere to the intestinal mucosa of the host, allowing them to secrete a wide
322 range of digestive enzymes; such as amylase, lipase, and protease; all of which facilitate feed
323 utilization (Marzouk et al., 2008; Latorre et al., 2016). Moreover, *Bacillus* spp. has been
324 reported to detoxify potentially harmful food components, and produce many essential vitamins
325 in the B-complex group (particular vitamin B₁₂ and biotin), which results in higher feed
326 utilization and digestibility of feed components (Blain Kennedy et al., 1998; El-Haroun et al.,
327 2006). Regarding the immunomodulatory effects of probiotics, it should be noted that adhesion
328 and colonization of probiotics in the intestines of the host are necessary to enhance the immune
329 response (Ausubel, 2005; Govender et al., 2014; Nishiyama et al., 2016; Li et al., 2018).

330 Probiotics interact with immune system via microbe associated molecular patterns (MAMPs),
331 consisting of cell wall polysaccharides, peptidoglycans, lipoprotein anchors, and lipoteichoic
332 acids (Hosoi et al., 2003). Cells or components within the immune system are then able to
333 interact with MAMPs through pattern recognition receptor; such as Toll like receptors, C-type
334 receptor, and nucleotide oligomerization domain like receptors (Kleerebezem et al., 2010;
335 Lebeer et al., 2010; Bron et al., 2012). Another critical feature of probiotics is their presence
336 inside the host, in which they are potentially colonizing and replicating, which further serves to
337 improve the host's health (Pandiyan et al., 2013). The colonization ability of probiotics within
338 the GI tract of animals provides a necessary competition to indigenous microbiota (Hill, 1993).
339 The ability to attach the gut surface is an important aspect of probiotics, which in turn is
340 associated with mucous formation of the bacteria. These abilities are useful for protection
341 against pathogen (Olsson et al., 1992), or immune stimulation (Salminen et al., 2007).

342 Other species within genus *Bacillus*; *Bacillus* OJ, *Bacillus amyloliquifaciens*, and *Bacillus*
343 *aerophilus*, isolated from GI tracts of Pacific white shrimp (*Litopenaeus vannamei*), yellow fin
344 bream (*Acanthopagrus latus*), and rohu significantly enhanced growth performance, immune
345 response, and disease resistance of Pacific white shrimp (Li et al., 2009), Nile tilapia
346 (*Oreochromis niloticus*) (Ridha & Azad, 2012), and rohu (Ramesh et al., 2017). More recently,
347 Meidong et al. (2018) reported that *B. aerius* isolated from pla-mong (*Pangasius bocourti*)
348 improved growth performance, immune responses, as well as resistance against *A. hydrophila*.

349 **6.2 *Bacillus subtilis***

350 *B. subtilis* is one of the most studied species within genus *Bacillus*. Dietary administration of
351 *B. subtilis* isolated from mrigal (*Cirrhinus mrigala*) significantly improved total serum protein,
352 globulin content, antibody level, hematology and immune response, as well as disease
353 resistance against *E. tarda* and *A. hydrophila* in rohu (Nayak et al., 2007; Kumar et al., 2008).
354 In a study with grass carp (*Ctenopharyngodon idella*), Wu et al. (2012) revealed that dietary

355 administration of *B. subtilis* isolated from grass carp significantly improved specific growth
356 rate, feed conversion ratio, enzyme activity, and total bacteria counts in the GI tract of the fish.
357 In a study using rainbow trout, reported [Newaj-Fyzul et al. \(2007\)](#) that dietary supplementation
358 of *B. subtilis* isolated from rainbow trout intestines significantly enhanced respiratory burst,
359 serum and gut lysozyme, peroxidase, phagocytic killing, and all α 1-antiprotease activities.
360 Furthermore, the study revealed a significant increase in lymphocyte population, as well as the
361 resistance towards *A. hydrophila*. Likewise, the supplementation of *B. subtilis* isolated from
362 intestines of sea cucumber, Japanese eel (*Anguilla japonica*), and pond water significantly
363 enhanced the growth performance, immune response, enzyme activity, and disease resistance
364 of sea cucumber, Japanese eel and Nile tilapia ([Zhao et al., 2012](#); [Lee et al., 2017](#); [Liu et al.,](#)
365 [2017](#)). In Pacific white shrimp dietary inclusion of *B. subtilis* significantly increased survival
366 rate, immune response, and resistance to *V. harveyi* ([Liu et al., 2014](#)). However, body crude
367 lipid content significantly decreased in the shrimp fed *B. subtilis*, vs. the control diet. More
368 recently, a *Bacillus* spp. revealing exoenzymes activities improved the host's growth
369 performance, including weight gain and feed efficiency ([Liu et al., 2017](#)). *Bacillus* exoenzymes
370 are very efficient at metabolizing a large variety of carbohydrates, lipids, and proteins ([Liu et](#)
371 [al., 2009](#)), and dietary supplementation of bacilli may improve digestive enzyme activities ([Han](#)
372 [et al., 2015](#)). It is widely accepted, that the level of digestive enzyme activity is a useful
373 comparative indicator of the host's food utilization rate, digestive capacity, and growth
374 performance ([Ueberschär, 1995](#); [Suzer et al., 2008](#)).

375 Regarding immunomodulation and disease improvement, several mechanisms have been
376 suggested, antimicrobial synthesis, pathogen competition, prevention of intestinal
377 inflammation, and improvement of the GI tract microbiota ([Suva et al., 2016](#)). *B. subtilis* spores
378 trigger specific humoral and cell-mediated immune responses ([Amuguni & Tzipori, 2012](#)). The
379 interaction between *B. subtilis* spores and macrophages plays an important role in the

380 development of both innate and adaptive immune responses of the host (Guo et al., 2016). Two
381 studies have demonstrated that the inclusion of *B. subtilis* leads to successful macrophage
382 activation. Suva et al. (2016) revealed that *B. subtilis* B10, *B. subtilis* BS02, and *B. subtilis*
383 (*natto*) B4 spores might possess immunomodulatory activities, obtained through the induction
384 of pro-inflammatory cytokines, which exert probiotic activities through activated macrophage
385 functions. Commensal bacteria play an important role in the development of the gut-associated
386 lymphoid tissue (GALT), and are important for both innate and adaptive immunity. *B. subtilis*
387 promotes active lymphocyte proliferation within GI tract, due to their high metabolic activity.
388 *Bacillus* activity is determined mainly by their ability to produce antibiotics; of which, *B.*
389 *subtilis* is the most productive species. *Bacillus subtilis* devotes 4%–5% of its genome to
390 antibiotic synthesis, and produces as many as 66 antibiotics. Each *Bacillus* antibiotic contains
391 a different structure and spectrum of antimicrobial activity (Sorokulova, 2013).

392 **6.3 *Bacillus cereus***

393 Few studies have used *B. cereus* as potential probiotic in fish and shrimp. Navin et al. (2014)
394 indicated that the giant tiger prawn (*Penaeus monodon*) fed dietary inclusion of *B. cereus*
395 isolated from shrimp's intestines; significantly increase growth performance, feed conversion
396 ratio, and immune response. Rengpipat et al. (2000) reported a similar improvement in immune
397 response in shrimp, which they attributed to the presence of the surface antigens of *Bacillus* S11
398 and their metabolites, which serve as immunogens in the shrimp's immune defense
399 mechanisms. They also noted that the additional of *Bacillus* S11 cell wall peptidoglycan may
400 trigger immune functions in shrimp. In a study using sea cucumber, Zhao et al. (2016) observed
401 significant increases in phagocytosis, respiratory burst, and total nitric oxide synthase activities;
402 as well as disease resistance to *Vibrio splendidus*. The dietary *B. cereus* isolated from the mud
403 of sea cucumber culturing water bodies, while effective in the above ways, showed no changes
404 in growth performance, total coelomocytes counts, acid phosphatase, or superoxide dismutase

405 activities. This difference could be attributed to the specific *Bacillus* strains, the size and source
406 of sea cucumbers, as well as experimental period and conditions (Zhao et al., 2016).

407 **6.4 *Bacillus pumilus***

408 *Bacillus pumilus* is a *host-associated probiotic* of recently interest in the field of aquaculture.
409 Dietary administration of *B. pumilus* or *B. pumilus* in combination with *B. clausii* isolated from
410 fish hosts significant improved growth performance, immune response, and disease resistance
411 of Nile tilapia and orange-spotted grouper (Sun et al., 2010; Srisapoom & Areechon, 2017).
412 They concluded that the significant improvement in growth performance via *B. pumilus* diet
413 was attributed to the absence of an antigenic stimulus provided by the pathogenic bacteria could
414 reduce a number of immune cells. This condition may create the efficient absorption and
415 utilization of nutrients in the intestines (Sun et al., 2010). Significant enhancement of fish health
416 and disease resistance may be credited to the increase in non-specific immunity by enhancing
417 phagocytic activity, the number of vital leukocytes, and superoxide anion production. In
418 theory, *B. pumilus* provides high anti-spore IgG titers, pro-inflammatory tumor necrosis factor,
419 and a bacteriocin-like activity against other *Bacillus* (Duc et al., 2004); as well as complement
420 activity (Sun et al., 2010). These abilities may effectively elevate the survival rate of
421 experimental fish fed *B. pumilus* (Aly et al., 2008).

422 **6.5 *Bacillus licheniformis***

423 *B. licheniformis* is another efficient *host-associated probiotic* in aquaculture. Grass carp fed
424 dietary *B. licheniformis* and *B. subtilis* isolated from the grass carp pond, significantly increased
425 globulin level, IgM, lysozyme, and complement activities; as well as myeloperoxidase content,
426 superoxide anion production, total antioxidant activity, glutathione, and anti-superoxide anion
427 free radical (Weifen et al., 2012). The improvement in fish immunity may be due to
428 supplementation of *Bacillus*, which improves water quality, resulting in better living
429 condition for fish (Lalloo et al., 2007; Borges et al., 2008; Wang et al., 2008). The addition of

430 probiotic bacteria to the water environment can decrease harmful microorganisms, act as a
431 food source for zooplanktons, and stimulate remineralization of macronutrients and
432 micronutrients that boost phytoplankton growth, and thereby enhance the oxygen level
433 (Verschuere et al., 2000). *Bacillus* species reduces the abundance of pathogenic *Vibrio*
434 bacteria in *in vitro* test and improves water quality through the reduction of toxic NH_4^+ and
435 NO_2^- , maintaining a neutral pH (Nimrat et al., 2012). Additionally, *Bacillus* produce
436 antimicrobial compounds (Rengpipat et al., 1998; Ringø et al., 2007; Nayak, 2010; Nandi et
437 al., 2018). *Bacillus* preparations, added to the water, 10^8 CFU m^3 , increased serum
438 immunoglobulin levels, non-specific immune parameters and the antioxidant ability of grass
439 carp, but by adding *Bacillus* preparations into the water and feed, 10^8 CFU g^{-1} , significantly
440 improved immune effects were revealed (Weifen et al., 2012). Adding probiotics in both water
441 and feed may provide better opportunities for the colonization of probiotics in the fish
442 intestine, thereby enabling them to compete with pathogens for nutrients, and/or to inhibit the
443 growth of pathogens; thus altering the prophylactic use of chemicals, antibiotics, and biocides
444 (Decamp et al., 2008; Ma et al., 2009). The approach by adding probiotics to water and feed
445 is better to use in saltwater as the environment is saltier, the fish loses water passively, and the
446 fish has to drink. The noticeable increase in antioxidant enzyme activity may be due to that
447 *Bacillus* act as antigen, which can stimulate the body's antioxidant enzyme system and
448 increase the amount of antioxidants (Weifen et al., 2012; Wang et al., 2017). These antioxidant
449 enzymes effectively remove excessive free radicals produced by a high metabolism and
450 adverse environmental stress; as well as regulate of the body's free radical balance, and repair
451 damages to tissues and organs (e.g. Harris, 1992; Gill et al., 2010). Recently, Gobi et al. (2018)
452 displayed that dietary administration of *B. licheniformis* significantly improved growth
453 performance, mucus and serum immune parameters, antioxidant enzyme activity, and
454 resistance to *A. hydrophila* in tilapia. It is known that increase in fish body weight gain by

455 feeding fish probiotic supplemented diets, could be contributed to the increase in digestive
456 enzyme activity, increase in appetite, increase in the production of vitamin, breakdown of
457 indigestible components, as well as possible improvement of intestinal morphology (Irianto &
458 Austin, 2002).

459 There have been numerous investigations on the immunomodulatory effect of probiotics on
460 different immune cells to enhance immune responses (e.g. Nayak et al., 2010; Das et al., 2013;
461 Sangma & Kamilya, 2015; Gobi et al., 2018). Mucus and serum protein were significantly
462 higher in rohu fed a *B. subtilis* supplemented diet, catla (*Catla catla*) fed a diet added *B.*
463 *amyloliquifaciens*, and catla fed *B. subtilis* (Nayak et al., 2010; Das et al., 2013; Sangma &
464 Kamilya, 2015). Similarly, Gobi et al. (2018) revealed that serum protein and mucus protein
465 were significantly higher in tilapia (*Oreochromis mossambicus*) fed *B. licheniformis* Dahb1
466 supplemented diets. Serum protein and mucus protein associated with agglutinins, lectins,
467 lysozyme, immunoglobulins are considered as important proteins involved in the defense
468 mechanism (Alexander & Ingram, 1992; Esteban, 2012). Gobi et al. (2018) suggested that
469 tilapia fed diets containing *B. licheniformis* Dahb1 or other probiotics increased the level of
470 these proteins, and subsequently increased serum and mucus protein concentration.

471 **6.6 Lactic acid bacteria**

472 The host-associated lactobacilli have gained much attention in aquaculture, for review see the
473 comprehensive review of Ringø et al. (2018). Harikrishnan et al. (2010) reported that kelp
474 grouper (*Epinephelus bruneus*) fed dietary *Lactobacillus sakei* isolated from olive flounder
475 intestine significantly increased macrophage phagocytic, peroxidase, serum lysozyme
476 activities, and total protein levels; as well as a resistance to *S. iniae* and *S. parauberis*. In
477 addition, Pacific red snapper (*Lutjanus peru*) fed *Lb. sakei* isolated from the mucus of spotted
478 sand bass (*Paralabrax maculatofaciatus*) significantly promoted haemoglobin,
479 myeloperoxidase, lysozyme, and total antiproteases activities; as well as IgM, serum

480 antioxidant capabilities, and vacuoles inside the enterocytes (Reyes-Becerril et al., 2014).
481 Enhanced fish growth following feeding of *Lb. sakei* may be due to the improvement of nutrient
482 digestibility and/or to the alteration of the intestinal microbiota and immunostimulation (Reyes-
483 Becerril et al., 2012). The chemical composition of microorganisms includes different
484 polysaccharides that may have potential prebiotics in the host's intestine (Ringø et al., 2010b).
485 Both bifidobacteria and lactobacilli are capable of utilizing these oligosaccharides, and increase
486 the number of beneficial bacteria in host's gut. Further benefits of dietary supplemented
487 oligosaccharides; include improved feed efficiency, enhanced growth, and increased digestive
488 enzyme activities. Furthermore, they seem able to modulate immune responses and preserve
489 the integrity of the intestinal wall (Xu et al., 2009; Dimitroglou et al., 2010).

490 *Lactobacillus plantarum* has also gained popularity in fish and shellfish farming. Kongnum &
491 Hongpattarakere (2012) revealed that *Lactobacillus plantarum* isolated from the shrimp
492 intestines significantly improved relative growth rate, feed conversion ratio, survival rate, and
493 hemocytes count as well as disease resistance to *V. harveyi* in Pacific white shrimp. Similarly,
494 significant increases in growth performance, feed utilization efficiency, survival rate, enzyme
495 activity, immune response, and disease resistance to *A. hydrophila* were observed in rohu (Giri
496 et al., 2013); and swimming crab (*Portunus pelagicus*) (Talpur et al., 2013). More recently, the
497 dietary supplementation of *Lb. plantarum*, *Weissella confuse*, *Lactococcus lactis*, and
498 *Enterococcus faecalis* were investigated (Li et al., 2018b). The bacteria were isolated from the
499 intestines of flathead grey mullet (*Mugil cephalus*), rockfish (*Sebastes schlegeli*), fat greenling
500 (*Hexagrammos otakii*), and sōhachi (*Cleisthenes herzensteini*) and significantly stimulated
501 growth performance, disease resistance against *V. splendidus*, alkaline phosphatase, acid
502 phosphatase, super oxide dismutase, lysozyme activity, and up-regulated heat shock proteins
503 genes of juvenile sea cucumber. The elevated of growth rate of aquatic animals may be related
504 to the effects of LAB actions on competitive exclusion of pathogenic bacteria, supplying

505 hydrolytic enzymes, and/or by supplying fatty acid and vitamins (Huang et al., 2014; Hai,
506 2015b). Regarding the immunostimulatory effects of *Lb. plantarum*, it was reported that
507 lactobacilli could elicit innate and adaptive immune responses in the host via binding to the
508 pattern recognition receptors (PRR) expressed on immune cells and many other tissues,
509 including the intestinal epithelium. PRR recognize the conserved molecular structures known
510 as microbe-associated molecular patterns, which induce the production of cytokines,
511 chemokines, and other innate effectors (Abreu, 2010; Kawai & Akira, 2010; Wells et al., 2010).
512 In addition to lactobacilli, are several other genera of LAB used as probiotics in aquaculture,
513 *Enterococcus*, *Lactococcus*, and *Weissella*. *Enterococcus faecium* isolated from the intestine of
514 flathead grey mullet significantly boosted nitroblue tetrazolium assay and common carp
515 resistance to *A. hydrophila* (Gopalakannan & Arul, 2011). The authors suggested that the
516 reason of the noticed results might be the extracellular products of probiotic bacteria, such as
517 bacteriocin- and nisin-like compounds, which induce the immune system of common carp.
518 Additionally, there are several mechanisms through which probiotic bacteria can induce
519 bacterial antagonism, by producing antimicrobial agents, like antibiotics, antimicrobial
520 peptides (bacteriocins), siderophore substances, or hydrogen peroxide (e.g. Sugita et al., 1998;
521 Ringø et al., 2018). Like many probiotics, *E. faecium* produce bacteriocin, which creates a
522 pore in the cell membrane of pathogens, which leads to the efflux of K⁺ ions, resulting in cell
523 death (Satish & Arul, 2009). In a study with grouper, Sun et al. (2012) reported that dietary
524 supplementation of *E. faecium* and *Lactococcus lactis*, originating from the gut of orange-
525 spotted grouper, significantly increased feed utilization, hepatopancreatic protease activities,
526 complement component-3, and serum lysozyme activities; however, no change in phagocytic,
527 serum superoxide dismutase activities, IgM, or complement component-4 were observed.
528 Similarly, significant improvements in growth performance, innate immune response, up-
529 regulation of lysozyme genes, and disease resistance to *Streptococcus* were observed in

530 kurumar shrimp (*Marsupenaeus japonicus*) and olive flounder, fed host-associated *Lactococcus*
531 *lactic* as a probiotic (Maeda et al., 2014; Nguyen et al., 2017). Allameh et al. (2014) isolated
532 an *E. faecalis* from intestine of snakehead fish (*Channa striatus*) and revealed significantly
533 improved resistance of snakehead fish against *A. hydrophila* when the *E. faecalis* was included
534 in the diet. More recently, Mouriño et al. (2016) reported that hybrid surubim catfish
535 (*Pseudoplatystoma reticulatum* ♀ × *P. corruscans* ♂), fed *Weissella cibaria* isolated from its
536 foregut intestine, showed a significant increased red blood cell count. However, no significant
537 difference occurred in white blood cells, total thrombocyte count, haematocrit percentage,
538 basophils and other leukocytes; as well as glucose levels between supplemented diets and
539 control.

540

541 **6.7 Other host-associated probiotics**

542 *Aeromonas sobria* has been used as a potential probiotic in aquaculture (Brunt & Austin, 2005).
543 The authors suggested that dietary administration of *A. sobria* isolated from GI tract of rainbow
544 trout significantly enhanced appetite, leukocytes count, phagocytic and respiratory burst
545 activities; as well as resistance to *Lactococcus garvieae* and *S. iniae*. The mode of action of *A.*
546 *sobria* involves the stimulation of cellular immunity, which directly increases the number of
547 leucocytes, and enhances phagocytic and respiratory burst activities. It remains speculative,
548 exactly how *A. sobria* stimulates this activity when used as a feed supplement (Brunt & Austin,
549 2005).

550 Senegalese sole (*Solea senegalensis*) fed diet supplemented with two *Shewanella*, Pdp11 and
551 Pdp13 isolated from gilthead sea bream skin, significantly increased growth and nutrient
552 utilization, proximate composition, and alkaline phosphatase of juvenile sole (Sáenz et al.,
553 2009). Sharifuzzaman & Austin (2009) conducted an experiment with the use of *Kocuria*
554 SM1 isolated from the digestive tract of rainbow trout. Fish fed dietary *Kocuria* SM1 at
555 concentration of 10^8 cells g^{-1} for four weeks showed significantly enhanced phagocytic,

556 peroxidase, and serum lysozyme activities. In a study with rainbow trout, [LaPatra et al. \(2014\)](#)
557 revealed that feeding host-associated *Enterobacter* sp. significantly increased survival rate,
558 antibody titers, and resistance to *Flavobacterium psychrophilum*. Similarly, significant increase
559 were noticed on growth performance, tolerance to crowding stress, microbiota, enzyme
560 activities, innate immune response, relative immune gene expressions, and disease resistance
561 in fish and shellfish fed *Shewanella putrefaciens*, *Psychrobacter namhaensis*,
562 *Pseudoalteromonas*, and *Clostridium butyricum* host- associated probiotics ([Tapia-Paniagua et](#)
563 [al., 2014](#); [Makled et al., 2017](#); [Offret et al., 2018](#); [Sumon et al., 2018](#)). The significant increase
564 in growth performance and health status of fish, as well as disease resistance within above
565 studies are possibly due to the increase in digestive enzyme activities, absorptive capacities of
566 the intestine, innate immune, relative immune gene expressions, and modulate GI tract
567 microbiota.

568 In the pioneer review devoted to “*Probiotics in man and animals*”, [Fuller \(1989\)](#) wrote,
569 “*Probiotic preparations may consist of single strains or may contain any number up to eight*
570 *strains*”. However, most probiotic studies carried out in aquaculture since the early 1990ties
571 and until today have used single administration, but during the last decade, supplementation of
572 multiple probiotics in the diets to aquatic animals has gained interest (e.g. [Mohapatra et al.,](#)
573 [2011](#); [Ibrahim, 2015](#); [Zorriehzahra et al., 2016](#)). The advantage of multiple-strain preparations
574 is; they are active against wider range of conditions and species.

575 Dietary inclusion of *Enterobacter cloacae* and *Bacillus mojavensis*, singular or combined,
576 significantly improved growth performance, cellular immunity, and disease resistance of
577 rainbow trout ([Capkin & Altinok, 2009](#)). These improvements may be due to the probiotic
578 effects of these two microorganisms. Probiotics stimulate the digestive processes through the
579 proliferation of a favorable microbiota population, enhancing microbial enzyme activity,
580 improving the intestinal microbial balance; and, consequently, improving the digestibility,

581 absorption of food, and feed utilization (El-Haroun et al., 2006; Capkin & Altinok, 2009). The
582 authors indicated that the putative probiotic bacteria isolated from intestines of rainbow trout
583 possess antibacterial abilities. Presence of such intestinal bacteria in the GI tract can protect fish
584 against infections caused by pathogenic bacteria (Capkin & Altinok 2009). The mode of action
585 of *Enterobacter* and *B. mojavensis* is to stimulate cellular immunity, specifically due to an
586 increased number of leucocytes. *E. cloacae* are listed under the same family as *Y. ruckeri*,
587 Enterobacteriaceae. This strain may not only competitively exclude *Y. ruckeri*, but also present
588 an appearance likely to trigger higher immune reactions than that of an unrelated *Bacillus*
589 (Capkin & Altinok, 2009). Similarly, the combination of three probiotics; *Bacillus coagulans*,
590 *Rhodoseudomonas palustris*, and *Lactobacillus acidophilus* isolated from intestines of common
591 carp and grass carp significantly increased weight gain, final weight, and digestive enzyme
592 activity of grass carp (Wang, 2011). Chi et al. (2014) revealed that the dietary supplementation
593 of *Aeromonas veronii*, *Vibrio lentus*, and *Flavobacterium sasangense* derived from GI tract of
594 common carp significantly boosted total serum protein, albumin and globulin levels, innate
595 immune response, and expression of IL-1b and TNF- α in common carp. Similar results
596 improving growth performance, digestive enzyme activities, stress indicators, immune
597 response, relative immune gene expressions, modulation of gut microbiota composition, and
598 disease resistance were observed in rainbow trout fed *Kocuria* SM1 and *Rhodococcus* SM2
599 (Sharifuzzaman et al., 2014), in grass carp fed *Shewanella xiamenensis* and *A. veronii* (Wu et
600 al., 2015), in sea cucumber fed *Bacillus cereus*, *B. cereus*, and *Paracoccus marcusii* (Yang et
601 al., 2015), in Malaysian mahseer (*Tor tambroides*) fed *Bacillus* sp. and *Alcaligenes* sp. or
602 *Bacillus* sp., *Alcaligenes* sp. and *Shewanella* sp. (Asaduzzaman et al., 2018a, b). In a study
603 using Pacific white shrimp, dietary administration of host-associated *Shewanella haliotis*, *B.*
604 *cereus*, and *Aeromonas bivalvium* significantly stimulated respiratory burst, superoxide
605 dismutase, respiratory burst activity, acid phosphatase activities, and up-regulated

606 prophenoloxidase and β -glucan-binding protein genes, as well as resistance to *V. harveyi* (Hao
607 et al., 2014). In recent studies with Pacific white shrimp fed host-associated probiotics
608 *Rhodobacter sphaeroides* and *Afifella marina* or *B. subtilis* and *S. algae* isolated from ponds or
609 its GI tract; significantly improvements in water quality, growth performance, resistance to
610 acute hepatopancreatic necrosis disease (AHPND), and control *Vibrio* in shrimp
611 hepatopancreas were observed (Chumpol et al., 2017; Interaminense et al., 2018). As with other
612 host-associated probiotics, significant improvements in growth performance, immune response,
613 and disease resistance of fish may be due to the increase in digestive enzyme activities,
614 absorptive capacities of the intestine, innate immune and relative immune gene expressions,
615 modulation of the GI tract microbiota, and production of antibacterial substances (Van Doan et
616 al., 2018). Additionally, a recent study reported that growth performance improvement
617 of Malaysian mahseer was governed primary by muscle fibres hypertrophy and up-regulated
618 growth related (*GH* and *IGF1*) gene expression (Asaduzzaman et al., 2018b).

619 In contrast, Allameh et al. (2016) revealed that inclusion of individual LAB strains in the diet
620 resulted in significantly improved growth performances of Javanese carps compared to fish fed
621 a diet supplemented a LAB mixture. Dietary inclusion *E. faecalis* at 10^7 cfu g^{-1} revealed higher
622 growth performance compared to other treatments. Additionally, the population levels of LAB
623 in the fish intestine significantly increased, while the levels of Gram-negative bacteria
624 significantly decreased vs. the control.

625

626 **7. Conclusions and future applications of probiotic in aquaculture**

627 The present review addressed whether or not host-associated probiotics vs. probiotics obtained
628 from other sources and commercial probiotics are more suitable to use in aquaculture. Although
629 some studies have revealed beneficial effects of host-associated probiotics on performance,
630 immune responses and disease resistance of aquatic organisms, the observed effects were
631 species-specific. Therefore, it is necessary to carry out additional studies where both host-

632 associated probiotics and probiotics obtained from other sources are used in the same study,
633 and to determine optimum inclusion levels for host-associated probiotics. In order, to
634 evaluate *in vivo* adherence and colonization of the host-associated probiotic strains within the
635 complex microbial ecosystem of the intestine, detection of green fluorescence protein (GFP)
636 tagged strains or fluorescence *in situ* hybridization (FISH) targeting 16S rRNA to identify the
637 probiotics on the mucus surface must be carried out. Furthermore, mucus associated
638 (autochthonous) microbiome must be investigated by next-generation sequencing (NGS),
639 transcriptomic or proteomic profiling, and not the allochthonous microbiome; mostly
640 investigated *per se*. In addition, we recommend that gnotobiotic approaches are used in future
641 studies, as the gnotobiotic approaches have been reported to have important roles to understand
642 the function of gut microbiota on numerous biological processes of the host. Moreover, data is
643 needed to understand the mechanisms by which the immune system of the intestinal mucosa
644 discriminates between pathogenic, probiotics and commensal microorganisms. In summary, the
645 present study revealed higher effectiveness of host-associated probiotics compared probiotics
646 obtained from other sources, but increased attention towards isolation, optimum inclusion level
647 and administration of host-associated probiotics in aquaculture is needed.

648

649 **Acknowledgements**

650 The authors acknowledge the financial assistance provided by the Functional Food Research
651 Center for Well-being, Chiang Mai University, Chiang Mai, Thailand.

652

653 **References**

- 654 Abdelkhalek NKM, Eissa IAM, Ahmed E, Kilany OE, El-Adl M, Dawood MAO, *et al.*, (2017)
655 Protective role of dietary *Spirulina platensis* against diazinon-induced Oxidative
656 damage in Nile tilapia; *Oreochromis niloticus*. *Environmental Toxicology and*
657 *Pharmacology* **54**: 99-104.
- 658 Abreu MT (2010) Toll-like receptor signaling in the intestinal epithelium: how bacterial
659 recognition shapes intestinal function. *Nature Reviews Immunology* **10**: 131.
- 660 Adel M, Yeganeh S, Dadar M, Sakai M, Dawood MAO (2016) Effects of dietary *Spirulina*
661 *platensis* on growth performance, humoral and mucosal immune responses and disease
662 resistance in juvenile great sturgeon (*Huso huso* Linnaeus, 1754). *Fish & Shellfish*
663 *Immunology* **56**: 436-444.
- 664 Ahmed E, Holmström SJM (2014) Siderophores in environmental research: roles and
665 applications. *Microbial Biotechnology* **7**: 196-208.
- 666 Alexander, J.B. & Ingram, G.A. (1992) Noncellular nonspecific defence mechanisms of fish.
667 *Annual Review of Fish Diseases* **2**: 249-279.
- 668 Allameh SK, Ringø E, Yusoff FM, Daud HM, Ideris A (2014) Properties of *Enterococcus*
669 *faecalis*, a probiotic bacterium isolated from intestine of snakehead (*Channa striatus*).
670 *African Journal of Microbiology Research* **8**: 2215-2222.
- 671 Allameh SK, Yusoff FM, Ringø E, Daud HM, Saad CR, Ideris A (2016) Effects of dietary
672 mono-, and multiprobiotic strains on growth performance, gut bacteria and body
673 composition of Javanese carp (*Puntius gonionotus*, Bleeker 1850). *Aquaculture*
674 *Nutrition* **22**: 367-373.
- 675 Altinok I, Capkin E, Karsi A (2015) Succinate dehydrogenase mutant of *Listonella anguillarum*
676 protects rainbow trout against vibriosis. *Vaccine* **33**: 5572-5577.

677 Altinok I, Ozturk RC, Kahraman UC, Capkin E (2016) Protection of rainbow trout against
678 yersiniosis by lpxD mutant *Yersinia ruckeri*. *Fish & Shellfish Immunology* **55**: 21-27.

679 Aly SM, Abd-El-Rahman AM, John G, Mohamed MF (2008) Characterization of some bacteria
680 isolated from *Oreochromis niloticus* and their potential use as probiotics. *Aquaculture*
681 **277**: 1-6.

682 Amuguni H, Tzipori S (2012) *Bacillus subtilis*: A temperature resistant and needle free delivery
683 system of immunogens. *Human Vaccines & Immunotherapeutics* **8**: 979-986.

684 Andrews SC, Robinson AK, Rodriguez-Quinones F (2003) Bacterial iron homeostasis. *FEMS*
685 *Microbiology Reviews* **27**: 215-237.

686 Araújo C, Muñoz-Atienza E, Nahuelquín Y, Poeta P, Igrejas G, Hernández PE, *et al.*, (2015)
687 Inhibition of fish pathogens by the microbiota from rainbow trout (*Oncorhynchus*
688 *mykiss*, Walbaum) and rearing environment. *Anaerobe* **32**: 7-14.

689 Ardó L, Yin G, Xu P, Váradi L, Szigeti G, Jeney Z, *et al.*, (2008) Chinese herbs (*Astragalus*
690 *membranaceus* and *Lonicera japonica*) and boron enhance the non-specific immune
691 response of Nile tilapia (*Oreochromis niloticus*) and resistance against *Aeromonas*
692 *hydrophila*. *Aquaculture* **275**: 26-33.

693 Asaduzzaman M, Iehata S, Akter S, Kader MA, Ghosh SK, Khan MNA, *et al.*, (2018a) Effects
694 of host gut-derived probiotic bacteria on gut morphology, microbiota composition and
695 volatile short chain fatty acids production of Malaysian Mahseer *Tor tambroides*.
696 *Aquaculture Reports* **9**: 53-61.

697 Asaduzzaman M, Sofia E, Shakil A, Haque NF, Khan MNA, Ikeda D, *et al.*, AB (2018b) Host
698 gut-derived probiotic bacteria promote hypertrophic muscle progression and upregulate
699 growth-related gene expression of slow-growing Malaysian mahseer *Tor tambroides*.
700 *Aquaculture Reports* **9**: 37-45.

701 Askarian F, Kousha A, Salma W, Ringø E (2011) The effect of lactic acid bacteria
702 administration on growth, digestive enzyme activity and gut microbiota in Persian
703 sturgeon (*Acipenser persicus*) and beluga (*Huso huso*) fry. *Aquaculture Nutrition* **17**:
704 488-497.

705 Assefa A, Abunna F (2018) Maintenance of fish health in aquaculture: Review of
706 epidemiological approaches for prevention and control of infectious disease of fish.
707 *Veterinary Medicine International* **2018**: 10.

708 Ausubel FM (2005) Are innate immune signaling pathways in plants and animals conserved?
709 *Nature Immunology* **6**: 973.

710 Balcázar JL, Blas Id, Ruiz-Zarzuela I, Cunningham D, Vendrell D, Múzquiz JL (2006) The role
711 of probiotics in aquaculture. *Veterinary Microbiology* **114**:173-186.

712 Balcazar JL, de Blas I, Ruiz-Zarzuela I, Vendrell D, Girones O, Muzquiz JL (2007)
713 Enhancement of the immune response and protection induced by probiotic lactic acid
714 bacteria against furunculosis in rainbow trout (*Oncorhynchus mykiss*). *FEMS*
715 *immunology and medical microbiology* **51**: 185-193.

716 Barman D, Nen P, Mandal SC, Kumar V (2013) Immunostimulants for Aquaculture Health
717 Management. *Journal of Marine Science: Research and Development* **3**: 11.

718 Blain Kennedy S, Tucker Jr JW, Neidig CL, Vermeer GK, Cooper VR, Jarrell JL, *et al.*, (1998)
719 Bacterial management strategies for stock enhancement of warmwater marine fish: a
720 case study with common snook (*Centropomus undecimalis*). *Bulletin of Marine Science*
721 **62**: 573-588.

722 Bolasina S, Pérez A, Yamashita Y (2006) Digestive enzymes activity during ontogenetic
723 development and effect of starvation in Japanese flounder, *Paralichthys olivaceus*.
724 *Aquaculture* **252**: 503-515.

725 Borges M-T, Sousa A, De Marco P, Matos A, Hönigová P, Castro PML (2008) Aerobic and
726 Anoxic Growth and Nitrate Removal Capacity of a Marine Denitrifying Bacterium
727 Isolated from a Recirculation Aquaculture System. *Microbial Ecology* **55**: 107-118.

728 Bostock J, McAndrew B, Richards R, Jauncey K, Telfer T, Lorenzen K, *et al.*, (2010)
729 Aquaculture: global status and trends. *Philosophical Transactions of the Royal Society*
730 *B: Biological Sciences* **365**: 2897-2912.

731 Boyd CE, Hollerman WD, Plumb JA, Saeed M (1984) Effect of treatment with a commercial
732 bacterial suspension on water quality in channel catfish ponds. *Progressive Fish*
733 *Culturist* **46**: 37-40.

734 Bricknell I, Dalmo RA (2005) The use of immunostimulants in fish larval aquaculture. *Fish &*
735 *Shellfish Immunology* **19**: 457-472.

736 Bron PA, van Baarlen P, Kleerebezem M (2012) Emerging molecular insights into the
737 interaction between probiotics and the host intestinal mucosa. *Nature Reviews*
738 *Microbiology* **10**: 66-78.

739 Brudeseth BE, Wiulsrød R, Fredriksen BN, Lindmo K, Løkling K-E, Bordevik M, *et al.*, K
740 (2013) Status and future perspectives of vaccines for industrialised fin-fish farming.
741 *Fish & Shellfish Immunology* **35**: 1759-1768.

742 Brunt J, Austin B (2005) Use of a probiotic to control lactococcosis and streptococcosis in
743 rainbow trout, *Oncorhynchus mykiss* (Walbaum). *Journal of Fish Diseases* **28**: 693-701.

744 Buntin N, de Vos WM, Hongpattarakere T (2017) Variation of mucin adhesion, cell surface
745 characteristics, and molecular mechanisms among *Lactobacillus plantarum* isolated
746 from different habitats. *Applied Microbiology and Biotechnology* **101**: 7663-7674.

747 Caipang CMA, Brinchmann MF, Kiron V (2010) Antagonistic activity of bacterial isolates from
748 intestinal microbiota of Atlantic cod, *Gadus morhua*, and an investigation of their
749 immunomodulatory capabilities. *Aquaculture Research* **41**: 249-256.

750 Capkin E, Altinok I (2009) Effects of dietary probiotic supplementations on
751 prevention/treatment of yersiniosis disease. *Journal of Applied Microbiology* **106**:
752 1147-1153.

753 Capkin E, Ozcelep T, Kayis S, Altinok I (2017) Antimicrobial agents, triclosan, chloroxylenol,
754 methylisothiazolinone and borax, used in cleaning had genotoxic and histopathologic
755 effects on rainbow trout. *Chemosphere* **182**: 720-729.

756 Capkin E, Ozdemir S, Ozturk RC, Altinok I (2017) Determination and transferability of
757 plasmid-mediated antibiotic resistance genes of the bacteria isolated from rainbow trout.
758 *Aquaculture Research* **48**: 5561-5575.

759 Capkin E, Terzi E, Altinok I (2015) Occurrence of antibiotic resistance genes in culturable
760 bacteria isolated from Turkish trout farms and their local aquatic environment. *Diseases*
761 *of Aquatic Organisms* **114**: 127-137.

762 Carnevali, O., Maradonna, F. & Gioacchini, G. (2017) Integrated control of fish metabolism,
763 wellbeing and reproduction: The role of probiotic. *Aquaculture* **472**: 144-155.

764 Caza M, Kronstad JW (2013) Shared and distinct mechanisms of iron acquisition by bacterial
765 and fungal pathogens of humans. *Frontiers in Cellular and Infection Microbiology* **3**:
766 80.

767 Cha J-H, Rahimnejad S, Yang S-Y, Kim K-W, Lee K-J (2013) Evaluations of *Bacillus* spp. as
768 dietary additives on growth performance, innate immunity and disease resistance of
769 olive flounder (*Paralichthys olivaceus*) against *Streptococcus iniae* and as water
770 additives. *Aquaculture* **402-403**: 50-57.

771 Cheng G, Hao H, Xie S, Wang X, Dai M, Huang L, Yuan Z (2014) Antibiotic alternatives: the
772 substitution of antibiotics in animal husbandry? *Frontiers in Microbiology* **5**: 217.

773 Chi C, Jiang B, Yu X-B, Liu T-Q, Xia L, Wang G-X (2014) Effects of three strains of intestinal
774 autochthonous bacteria and their extracellular products on the immune response and

775 disease resistance of common carp (*Cyprinus carpio*). *Fish & Shellfish Immunology* **36**:
776 9-18.

777 Chumpol S, Kantachote D, Nitoda T, Kanzaki H (2017) The roles of probiotic purple nonsulfur
778 bacteria to control water quality and prevent acute hepatopancreatic necrosis disease
779 (AHPND) for enhancement growth with higher survival in white shrimp (*Litopenaeus*
780 *vannamei*) during cultivation. *Aquaculture* **473**: 327-336.

781 Collado MC, Gueimonde M, Salminen S (2010) Chapter 23 - Probiotics in adhesion of
782 pathogens: Mechanisms of action A2 - Watson, Ronald Ross. In: *Bioactive Foods in*
783 *Promoting Health* (ed by Preedy VR). Academic Press, Boston, pp. 353-370.

784 Collins FM, Carter PB (1978) Growth of Salmonellae in orally infected germfree mice.
785 *Infection and Immunity* **21**: 41-47.

786 Cornelissen CN (2003) Transferrin-iron uptake by Gram-negative bacteria. *Frontiers in*
787 *Bioscience* **8**: d836-847.

788 Das, A., Nakhro, K., Chowdhury, S. & Kamilya, D. (2013) Effects of potential probiotic
789 *Bacillus amyloliquifaciens* FPTB16 on systemic and cutaneous mucosal immune
790 responses and disease resistance of catla (*Catla catla*). *Fish & Shellfish Immunology* **35**:
791 1547-1553.

792 Dawood MAO, Koshio S (2016) Recent advances in the role of probiotics and prebiotics in
793 carp aquaculture: A review. *Aquaculture* **454**: 243-251.

794 Dawood MAO, Koshio S, Ishikawa M, El-Sabagh M, Esteban MA, Zaineldin AI (2016)
795 Probiotics as an environment-friendly approach to enhance red sea bream, *Pagrus major*
796 growth, immune response and oxidative status. *Fish & Shellfish Immunology* **57**: 170-
797 178.

798 A.O., D.M., Shunsuke, K., M., A.-D.M. & Hien, V.D. Probiotic application for sustainable
799 aquaculture. *Reviews in Aquaculture* (In press): <https://doi.org/10.1111/raq.12272>

800 De BC, Meena DK, Behera BK, Das P, Das Mohapatra PK, Sharma AP (2014) Probiotics in
801 fish and shellfish culture: immunomodulatory and ecophysiological responses. *Fish*
802 *Physiology and Biochemistry* **40**: 921-971.

803 Decamp O, Moriarty DJW, Lavens P (2008) Probiotics for shrimp larviculture: review of field
804 data from Asia and Latin America. *Aquaculture Research* **39**: 334-338.

805 Defoirdt T, Sorgeloos P, Bossier P (2011) Alternatives to antibiotics for the control of bacterial
806 disease in aquaculture. *Current Opinion in Microbiology* **14**: 251-258.

807 Derrien M, van Hylckama Vlieg JET (2015) Fate, activity, and impact of ingested bacteria
808 within the human gut microbiota. *Trends in Microbiology* **23**: 354-366.

809 Dhanasiri AKS, Brunvold L, Brinchmann MF, Korsnes K, Bergh Ø, Kiron V (2011) Changes
810 in the intestinal microbiota of wild Atlantic cod *Gadus morhua* L. Upon captive rearing.
811 *Microbial Ecology* **61**: 20-30.

812 Dhar AK, Manna SK, Thomas Allnut FC (2014) Viral vaccines for farmed finfish. *Virus*
813 *Disease* **25**: 1-17.

814 Dimitroglou A, Merrifield DL, Spring P, Sweetman J, Moate R, Davies SJ (2010) Effects of
815 mannan oligosaccharide (MOS) supplementation on growth performance, feed
816 utilisation, intestinal histology and gut microbiota of gilthead sea bream (*Sparus*
817 *aurata*). *Aquaculture* **300**: 182-188.

818 Duc LH, Hong HA, Barbosa TM, Henriques AO, Cutting SM (2004) Characterization of
819 *Bacillus* probiotics available for human Use. *Applied and Environmental Microbiology*
820 **70**: 2161-2171.

821 El-Haroun E, Goda AS, Chowdhury K (2006) Effect of dietary probiotic Biogen®
822 supplementation as a growth promoter on growth performance and feed utilization of
823 Nile tilapia *Oreochromis niloticus* (L.). *Aquaculture Research* **37**: 1473-1480.

824 Ellermann M, Arthur JC (2017) Siderophore-mediated iron acquisition and modulation of host-
825 bacterial interactions. *Free Radical Biology and Medicine* **105**: 68-78.

826 Elshaghabee FMF, Rokana N, Gulhane RD, Sharma C, Panwar H (2017) *Bacillus* as potential
827 probiotics: Status, concerns, and future perspectives. *Frontiers in Microbiology* **8**.

828 Esteban, M.A. (2012) An Overview of the Immunological Defenses in Fish Skin. *ISRN*
829 *Immunology* **2012**: 29.

830 Fdhila K, Haddaji N, Chakroun I, Dhiaf A, Macherki MEE, Khouildi B, *et al.*, (2017) Culture
831 conditions improvement of *Crassostrea gigas* using a potential probiotic *Bacillus* sp
832 strain. *Microbial Pathogenesis* **110**: 654-658.

833 Fečkaninová A, Koščová J, Mudroňová D, Popelka P, Toropilová J (2017) The use of probiotic
834 bacteria against *Aeromonas* infections in salmonid aquaculture. *Aquaculture* **469**: 1-8.

835 Feodorova VA, Sayapina LV, Corbel MJ, Motin VL (2014) Russian vaccines against especially
836 dangerous bacterial pathogens. *Emerging Microbes & Infections* **3**: e86.

837 Fischbach MA, Segre JA (2016) Signaling in host-associated microbial communities. *Cell*
838 **164**:1288-1300.

839 Fjellheim AJ, Playfoot KJ, Skjermo J, Vadstein O (2007) Vibrionaceae dominates the
840 microflora antagonistic towards *Listonella anguillarum* in the intestine of cultured
841 Atlantic cod (*Gadus morhua* L.) larvae. *Aquaculture* **269**: 98-106.

842 Founou LL, Founou RC, Essack SY (2016) Antibiotic resistance in the food chain: A
843 developing country-perspective. *Frontiers in Microbiology* **7**: 1881.

844 Fuller R (1989) Probiotics in man and animals. *Journal of Applied Bacteriology* **66**: 365-378.

845 Gatesoupe FJ (1999) The use of probiotics in aquaculture. *Aquaculture* **180**: 147-165.

846 Gatesoupe FJ (2007) Live yeasts in the gut: Natural occurrence, dietary introduction, and their
847 effects on fish health and development. *Aquaculture* **267**: 20-30.

848 Gill R, Tsung A, Billiar T (2010) Linking oxidative stress to inflammation: Toll-like receptors.
849 *Free Radical Biology & Medicine* **48**: 1121-1132.

850 Giraffa G, Chanishvili N, Widyastuti Y (2010) Importance of lactobacilli in food and feed
851 biotechnology. *Research in Microbiology* **161**: 480-487.

852 Giri SS, Sukumaran V, Oviya M (2013) Potential probiotic *Lactobacillus plantarum* VSG3
853 improves the growth, immunity, and disease resistance of tropical freshwater fish,
854 *Labeo rohita*. *Fish & Shellfish Immunology* **34**: 660-666.

855 Gobi N, Vaseeharan B, Chen J-C, Rekha R, Vijayakumar S, Anjugam M, *et al.*, (2018) Dietary
856 supplementation of probiotic *Bacillus licheniformis* Dahb1 improves growth
857 performance, mucus and serum immune parameters, antioxidant enzyme activity as well
858 as resistance against *Aeromonas hydrophila* in tilapia *Oreochromis mossambicus*. *Fish
859 & Shellfish Immunology* **74**: 501-508.

860 Gomez D, Sunyer JO, Salinas I (2013) The mucosal immune system of fish: the evolution of
861 tolerating commensals while fighting pathogens. *Fish & shellfish immunology* **35**: 1729-
862 1739.

863 Gopalakannan A, Arul V (2011) Inhibitory activity of probiotic *Enterococcus faecium* MC13
864 against *Aeromonas hydrophila* confers protection against hemorrhagic septicemia in
865 common carp *Cyprinus carpio*. *Aquaculture International* **19**: 973-985.

866 Govender, M., Choonara, Y.E., Kumar, P., du Toit, L.C., van Vuuren, S. & Pillay, V. (2014) A
867 review of the advancements in probiotic delivery: Conventional vs. non-conventional
868 formulations for intestinal flora supplementation. *AAPS PharmSciTech* **15**: 29-43.

869 Grajek K, Sip A, Foksowicz-Flaczyk J, Dobrowolska A, Wita A 2016) Adhesive and
870 hydrophobic properties of the selected LAB isolated from the gastrointestinal tract of
871 farming animals. *Acta Biochimica Polonica* **63**: 311-314.

872 Guo M, Hao G, Wang B, Li N, Li R, Wei L, *et al.*, (2016) Dietary administration of *Bacillus*
873 *subtilis* enhances growth performance, immune response and disease resistance in
874 cherry valley ducks. *Frontiers in Microbiology* **7**: 1975.

875 Hai NV (2015a) Research findings from the use of probiotics in tilapia aquaculture: A review.
876 *Fish & Shellfish Immunology* **45**: 592-597.

877 Hai NV (2015b) The use of probiotics in aquaculture. *Journal of Applied Microbiology* **119**:
878 917-935.

879 Han B, Long W-q, He J-y, Liu Y-j, Si Y-q, Tian L-x (2015) Effects of dietary *Bacillus*
880 *licheniformis* on growth performance, immunological parameters, intestinal
881 morphology and resistance of juvenile Nile tilapia (*Oreochromis niloticus*) to challenge
882 infections. *Fish & Shellfish Immunology* **46**: 225-231.

883 Hao K, Liu J-Y, Ling F, Liu X-L, Lu L, Xia L, *et al.*, (2014) Effects of dietary administration
884 of *Shewanella haliotis* D4, *Bacillus cereus* D7 and *Aeromonas bivalvium* D15, single or
885 combined, on the growth, innate immunity and disease resistance of shrimp,
886 *Litopenaeus vannamei*. *Aquaculture* **428-429**: 141-149.

887 Harikrishnan R, Balasundaram C, Heo M-S (2010) *Lactobacillus sakei* BK19 enriched diet
888 enhances the immunity status and disease resistance to streptococcosis infection in kelp
889 grouper, *Epinephelus bruneus*. *Fish & Shellfish Immunology* **29**: 1037-1043.

890 Harris ED (1992) Regulation of antioxidant enzymes. *FASEB Journal* **6**: 2675-2683.

891 Hill M (1993) Probiotics: the scientific basis. *Gut* **34**: 863.

892 Hoare R, Ngo TPH, Bartie KL, Adams A (2017) Efficacy of a polyvalent immersion vaccine
893 against *Flavobacterium psychrophilum* and evaluation of immune response to
894 vaccination in rainbow trout fry (*Oncorhynchus mykiss* L.). *Veterinary Research* **48**: 43.

895 Hoseinifar SH, Esteban MÁ, Cuesta A, Sun Y-Z (2015) Prebiotics and fish immune response:
896 A review of current knowledge and future perspectives. *Reviews in Fisheries Science &*
897 *Aquaculture* **23**: 315-328.

898 Hoseinifar SH, Ringø E, Shenavar Masouleh A, Esteban MA (2016) Probiotic, prebiotic and
899 synbiotic supplements in sturgeon aquaculture: a review. *Reviews in Aquaculture* **8**: 89-
900 102,

901 Hoseinifar, S.H., Sun, Y.Z. & Caipang, C.M. (2017) Short-chain fatty acids as feed supplements
902 for sustainable aquaculture: an updated view. *Aquaculture Research* **48**: 1380-1391.

903 Hosoi T, Hirose R, Saegusa S, Ametani A, Kiuchi K, Kaminogawa S (2003) Cytokine responses
904 of human intestinal epithelial-like Caco-2 cells to the nonpathogenic bacterium *Bacillus*
905 *subtilis* (natto). *International Journal of Food Microbiology* **82**: 255-264.

906 Huang J-B, Wu Y-C, Chi S-C (2014) Dietary supplementation of *Pediococcus pentosaceus*
907 enhances innate immunity, physiological health and resistance to *Vibrio anguillarum* in
908 orange-spotted grouper (*Epinephelus coioides*). *Fish & Shellfish Immunology* **39**: 196-
909 205.

910 Ibrahem MD (2015) Evolution of probiotics in aquatic world: Potential effects, the current
911 status in Egypt and recent prospectives. *Journal of Advanced Research* **6**: 765-791.

912 Interaminense JA, Vogeley JL, Gouveia CK, Portela RWS, Oliveira JP, Andrade HA, *et al.*,
913 (2018) *In vitro* and *in vivo* potential probiotic activity of *Bacillus subtilis* and
914 *Shewanella algae* for use in *Litopenaeus vannamei* rearing. *Aquaculture* **488**: 114-122.

915 Irianto A, Austin B (2002) Use of probiotics to control furunculosis in rainbow trout,
916 *Oncorhynchus mykiss* (Walbaum). *Journal of Fish Diseases* **25**: 333-342.

917 Irianto A, Austin B (2003) Use of dead probiotic cells to control furunculosis in rainbow trout,
918 *Oncorhynchus mykiss* (Walbaum). *Journal of Fish Diseases* **26**: 59-62.

919 Jöborn A, Dorsch M, Olsson JC, Westerdahl A, Kjelleberg S (1999) *Carnobacterium inhibens*
920 sp. nov., isolated from the intestine of Atlantic salmon (*Salmo salar*). *International*
921 *Journal of Systematic Bacteriology* **49 Pt 4**: 1891-1898.

922 Johnson KN, van Hulten MCW, Barnes AC (2008) “Vaccination” of shrimp against viral
923 pathogens: Phenomenology and underlying mechanisms. *Vaccine* **26**: 4885-4892.

924 Kammler M, Schön C, Hantke K (1993) Characterization of the ferrous iron uptake system of
925 *Escherichia coli*. *Journal of Bacteriology* **175**: 6212-6219.

926 Kawai T, Akira S (2010) The role of pattern-recognition receptors in innate immunity: update
927 on Toll-like receptors. *Nature Immunology* **11**: 373.

928 Kennedy S, Tucker J, Thomersen M, Sennett D (1998) Current methodology for the use of
929 probiotic bacteria in the culture of marine fish larvae. Aquaculture’98 Book of
930 Abstracts. *World Aquaculture Society, Las Vegas, USA*, 286.

931 Kleerebezem M, Hols P, Bernard E, Rolain T, Zhou M, Siezen R, *et al.*, (2010) The extracellular
932 biology of the lactobacilli. *FEMS Microbiological Reviews* **34**: 199 - 230.

933 Kongnum K, Hongpattarakere T (2012) Effect of *Lactobacillus plantarum* isolated from
934 digestive tract of wild shrimp on growth and survival of white shrimp (*Litopenaeus*
935 *vannamei*) challenged with *Vibrio harveyi*. *Fish & Shellfish Immunology* **32**: 170-177.

936 Kumar R, Mukherjee SC, Ranjan R, Nayak SK (2008) Enhanced innate immune parameters in
937 *Labeo rohita* (Ham.) following oral administration of *Bacillus subtilis*. *Fish & Shellfish*
938 *Immunology* **24**: 168-172.

939 Lakshmi B, Viswanath B, Sai Gopal DVR (2013) Probiotics as antiviral agents in shrimp
940 aquaculture. *Journal of Pathogens* **2013**: 13.

941 Lalloo R, Ramchuran S, Ramduth D, Görgens J, Gardiner N (2007) Isolation and selection of
942 *Bacillus* spp. as potential biological agents for enhancement of water quality in culture
943 of ornamental fish. *Journal of Applied Microbiology* **103**: 1471-1479.

944 Langdon A, Crook N, Dantas G (2016) The effects of antibiotics on the microbiome throughout
945 development and alternative approaches for therapeutic modulation. *Genome Medicine*
946 **8**: 39.

947 LaPatra SE, Fehringer TR, Cain KD (2014) A probiotic *Enterobacter* sp. provides significant
948 protection against *Flavobacterium psychrophilum* in rainbow trout (*Oncorhynchus*
949 *mykiss*) after injection by two different routes. *Aquaculture* **433**: 361-366.

950 Larsen AM, Mohammed HH, Arias CR (2014) Characterization of the gut microbiota of three
951 commercially valuable warm water fish species. *Journal of Applied Microbiology*
952 **116**:1396-1404.

953 Latorre JD, Hernandez-Velasco X, Wolfenden RE, Vicente JL, Wolfenden AD, Menconi A, *et*
954 *al.*, (2016) Evaluation and selection of *Bacillus* species based on enzyme production,
955 antimicrobial activity, and biofilm synthesis as direct-fed microbial candidates for
956 poultry. *Frontiers in Veterinary Science* **3**: 95.

957 Lazado CC, Caipang CMA (2014a) Atlantic cod in the dynamic probiotics research in
958 aquaculture. *Aquaculture* **424-425**: 53-62.

959 Lazado CC, Caipang CMA (2014b) Mucosal immunity and probiotics in fish. *Fish & Shellfish*
960 *Immunology* **39**: 78-89.

961 Lazado CC, Caipang CMA, Estante EG (2015) Prospects of host-associated microorganisms in
962 fish and penaeids as probiotics with immunomodulatory functions. *Fish & Shellfish*
963 *Immunology* **45**: 2-12.

964 Lazado CC, Caipang CMA, Kiron V (2012) Enzymes from the gut bacteria of Atlantic cod,
965 *Gadus morhua* and their influence on intestinal enzyme activity. *Aquaculture Nutrition*
966 **18**: 423-431.

- 967 Lazado CC, Caipang CMA, Rajan B, Brinchmann MF, Kiron V (2010) Characterization of
968 GP21 and GP12: two potential probiotic bacteria isolated from the gastrointestinal tract
969 of Atlantic cod. *Probiotics and Antimicrobial Proteins* **2**: 126-134.
- 970 Lebeer S, Vanderleyden J, De Keersmaecker SCJ (2010) Host interactions of probiotic bacterial
971 surface molecules: comparison with commensals and pathogens. *Nature Reviews*
972 *Microbiology* **8**: 171.
- 973 Lee S, Katya K, Park Y, Won S, Seong M, Hamidoghli A, *et al.*, (2017) Comparative evaluation
974 of dietary probiotics *Bacillus subtilis* WB60 and *Lactobacillus plantarum* KCTC3928
975 on the growth performance, immunological parameters, gut morphology and disease
976 resistance in Japanese eel, *Anguilla japonica*. *Fish & Shellfish Immunology* **61**: 201-
977 210.
- 978 Li J, Tan B, Mai K (2009) Dietary probiotic *Bacillus* OJ and isomaltooligosaccharides influence
979 the intestine microbial populations, immune responses and resistance to white spot
980 syndrome virus in shrimp (*Litopenaeus vannamei*). *Aquaculture* **291**: 35-40.
- 981 Li X, Ringø E, Hoseinifar SH, Lauzon H, Birkbeck H, Yang D (2018a) Adherence and
982 colonisation of microorganisms in the fish gastrointestinal tract. *Reviews in Aquaculture*
983 [Epub ahead of print], doi: 10.1111/raq.12248.
- 984 Li C, Ren Y, Jiang S, Zhou S, Zhao J, Wang R, Li Y (2018b) Effects of dietary supplementation
985 of four strains of lactic acid bacteria on growth, immune-related response and genes
986 expression of the juvenile sea cucumber *Apostichopus japonicus* Selenka. *Fish &*
987 *Shellfish Immunology* **74**: 69-75.
- 988 Lilly DM, Stillwell RH (1965) Probiotics: Growth promoting factors produced by
989 microorganisms. *Science* **147**: 747-748.

- 990 Liu CH, Chiu CS, Ho PL, Wang SW (2009) Improvement in the growth performance of white
991 shrimp, *Litopenaeus vannamei*, by a protease-producing probiotic, *Bacillus subtilis* E20,
992 from natto. *Journal of Applied Microbiology* **107**: 1031-1041.
- 993 Liu H, Li Z, Tan B, Lao Y, Duan Z, Sun W, *et al.*, (2014) Isolation of a putative probiotic strain
994 S12 and its effect on growth performance, non-specific immunity and disease-resistance
995 of white shrimp, *Litopenaeus vannamei*. *Fish & Shellfish Immunology* **41**: 300-307.
- 996 Liu H, Wang S, Cai Y, Guo X, Cao Z, Zhang Y, *et al.*, (2017) Dietary administration of *Bacillus*
997 *subtilis* HAINUP40 enhances growth, digestive enzyme activities, innate immune
998 responses and disease resistance of tilapia, *Oreochromis niloticus*. *Fish & Shellfish*
999 *Immunology* **60**: 326-333.
- 1000 Llewellyn MS, Boutin S, Hoseinifar SH, Derome N (2014) Teleost microbiomes: the state of
1001 the art in their characterization, manipulation and importance in aquaculture and
1002 fisheries. *Frontiers in Microbiology* **5**.
- 1003 Luis Balcázar J, Decamp O, Vendrell D, De Blas I, Ruiz-Zarzuola I (2006) Health and
1004 nutritional properties of probiotics in fish and shellfish. *Microbial Ecology in Health*
1005 *and Disease* **18**: 65-70.
- 1006 Ma C-W, Cho Y-S, Oh K-H (2009) Removal of pathogenic bacteria and nitrogens by
1007 *Lactobacillus* spp. JK-8 and JK-11. *Aquaculture* **287**: 266-270.
- 1008 Macfarlane GT, Macfarlane S (2012) Bacteria, colonic fermentation, and gastrointestinal
1009 health. *Journal of AOAC International* **95**: 50-60.
- 1010 Maeda M, Shibata A, Biswas G, Korenaga H, Kono T, Itami T, *et al.*, (2014) Isolation of lactic
1011 acid bacteria from kuruma shrimp (*Marsupenaeus japonicus*) intestine and assessment
1012 of immunomodulatory role of a selected strain as probiotic. *Marine Biotechnology* **16**:
1013 181-192.

- 1014 Makled SO, Hamdan AM, El-Sayed A-FM, Hafez EE (2017) Evaluation of marine
1015 psychrophile, *Psychrobacter namhaensis* SO89, as a probiotic in Nile tilapia
1016 (*Oreochromis niloticus*) diets. *Fish & Shellfish Immunology* **61**: 194-200.
- 1017 Mardones FO, Paredes F, Medina M, Tello A, Valdivia V, Ibarra R, *et al.*, (2018) Identification
1018 of research gaps for highly infectious diseases in aquaculture: The case of the endemic
1019 *Piscirickettsia salmonis* in the Chilean salmon farming industry. *Aquaculture* **482**: 211-
1020 220.
- 1021 Martínez Cruz P, Ibáñez AL, Monroy Hermosillo OA, Ramírez Saad HC (2012) Use of
1022 probiotics in aquaculture. *ISRN microbiology* **2012**: 916845.
- 1023 Marzouk M, Moustafa M, Mohamed N (2008) The influence of some probiotics on the growth
1024 performance and intestinal microbial flora of *O. niloticus*. In: *Proceeding of the 8th*
1025 *International Symposium on Tilapia in Aquaculture*, pp. 1059-1071.
- 1026 Mataragas M, Metaxopoulos J, Galiotou M, Drosinos EH (2003) Influence of pH and
1027 temperature on growth and bacteriocin production by *Leuconostoc mesenteroides* L124
1028 and *Lactobacillus curvatus* L442. *Meat Science* **64**: 265-271.
- 1029 Meidong R, Khotchanalekha K, Doolgindachbaporn S, Nagasawa T, Nakao M, Sakai K, *et al.*,
1030 (2018) Evaluation of probiotic *Bacillus aerius* B81e isolated from healthy hybrid catfish
1031 on growth, disease resistance and innate immunity of Pla-mong *Pangasius bocourti*.
1032 *Fish & Shellfish Immunology* **73**: 1-10.
- 1033 Merrifield DL, Dimitroglou A, Foey A, Davies SJ, Baker RTM, Bøggwald J, *et al.*, (2010) The
1034 current status and future focus of probiotic and prebiotic applications for salmonids.
1035 *Aquaculture* **302**: 1-18.
- 1036 Miller JH, Novak JT, Knocke WR, Pruden A (2016) Survival of antibiotic resistant bacteria
1037 and horizontal gene transfer control antibiotic resistance gene content in anaerobic
1038 digesters. *Frontiers in Microbiology* **7**.

- 1039 Mohapatra, S., Chakraborty, T., Prusty, A.K., Das, P., Paniprasad, K. & Mohanta, K.N. (2011)
1040 Use of different microbial probiotics in the diet of rohu, *Labeo rohita* fingerlings: effects
1041 on growth, nutrient digestibility and retention, digestive enzyme activities and intestinal
1042 microflora. *Aquaculture Nutrition* **18**: 1-11.
- 1043 Mohapatra S, Chakraborty T, Prusty AK, PaniPrasad K, Mohanta KN (2014) Beneficial effects
1044 of dietary probiotics mixture on hemato-immunology and cell apoptosis of *Labeo rohita*
1045 fingerlings reared at higher water temperatures. *PLOS ONE* **9**: e100929.
- 1046 Montalban-Arques A, De Schryver P, Bossier P, Gorkiewicz G, Mulero V, Gatlin DM, *et al.*,
1047 (2015) Selective manipulation of the gut microbiota improves immune status in
1048 vertebrates. *Frontiers in Immunology* **6**: 512.
- 1049 Morgan-Kiss RM, Priscu JC, Pocock T, Gudynaite-Savitch L, Huner NPA (2006) Adaptation
1050 and acclimation of photosynthetic microorganisms to permanently cold environments.
1051 *Microbiology and Molecular Biology Reviews: MMBR* **70**: 222-252.
- 1052 Moriarty DJW (1998) Control of luminous *Vibrio* species in penaeid aquaculture ponds.
1053 *Aquaculture* **164**: 351-358.
- 1054 Mouriño JLP, Pereira GDV, Vieira FDN, Jatobá AB, Ushizima TT, Silva BCD, *et al.*, Seiffert
1055 WQ, Jesus GFA, Martins ML (2016) Isolation of probiotic bacteria from the hybrid
1056 South American catfish *Pseudoplatystoma reticulatum*×*Pseudoplatystoma corruscans*
1057 (Siluriformes: Pimelodidae): A haematological approach. *Aquaculture Reports* **3**: 166-
1058 171.
- 1059 Murall CL, Abbate JL, Puelma Touzel M, Allen-Vercoe E, Alizon S, Froissart R, *et al.*, (2017)
1060 Chapter five - invasions of host-associated microbiome networks. In: *Advances in*
1061 *Ecological Research* (ed. by Bohan DA, Dumbrell AJ, Massol F). Academic Press, pp.
1062 201-281.

- 1063 Nandi, A., Banerjee, G., Dan, S.K., Ghosh, K. & Ray, A.K. (2018) Evaluation of *in vivo*
1064 probiotic efficiency of *Bacillus amyloliquifaciens* in *Labeo rohita* challenged by
1065 pathogenic strain of *Aeromonas hydrophila* MTCC 1739. *Probiotics and Antimicrobial*
1066 *Proteins* **10**: 391-398.
- 1067 Nawaz, A., Bakhsh javaid, A., Irshad, S., Hoseinifar, S.H. & Xiong, H. (2018) The functionality
1068 of prebiotics as immunostimulant: Evidences from trials on terrestrial and aquatic
1069 animals. *Fish & Shellfish Immunology* **76**: 272-278.
- 1070 Navin Chandran M, Iyapparaj P, Moovendhan S, Ramasubburayan R, Prakash S, Immanuel G,
1071 *et al.*, A (2014) Influence of probiotic bacterium *Bacillus cereus* isolated from the gut
1072 of wild shrimp *Penaeus monodon* in turn as a potent growth promoter and immune
1073 enhancer in *P. monodon*. *Fish & Shellfish Immunology* **36**: 38-45.
- 1074 Nayak SK (2010) Probiotics and immunity: A fish perspective. *Fish & Shellfish Immunology*
1075 **29**: 2-14.
- 1076 Nayak SK, Swain P, Mukherjee SC (2007) Effect of dietary supplementation of probiotic and
1077 vitamin C on the immune response of Indian major carp, *Labeo rohita* (Ham.). *Fish &*
1078 *Shellfish Immunology* **23**: 892-896.
- 1079 Newaj-Fyzul A, Adesiyun AA, Mutani A, Ramsuhag A, Brunt J, Austin B (2007) *Bacillus*
1080 *subtilis* AB1 controls *Aeromonas* infection in rainbow trout (*Oncorhynchus mykiss*,
1081 Walbaum). *Journal of Applied Microbiology* **103**: 1699-1706.
- 1082 Newaj-Fyzul A, Austin B (2015) Probiotics, immunostimulants, plant products and oral
1083 vaccines, and their role as feed supplements in the control of bacterial fish diseases.
1084 *Journal of Fish Diseases* **38**: 937-955.
- 1085 Nguyen TL, Park C-I, Kim D-H (2017) Improved growth rate and disease resistance in olive
1086 flounder, *Paralichthys olivaceus*, by probiotic *Lactococcus lactis* WFLU12 isolated
1087 from wild marine fish. *Aquaculture* **471**: 113-120.

- 1088 Nikoskelainen S, Salminen S, Bylund G, Ouwehand AC (2001a) Characterization and the
1089 properties of human- and dairy-derived probiotics for prevention of infectious diseases
1090 in fish. *Applied and Environmental Microbiology* **67**: 2430-2435.
- 1091 Nikoskelainen S, Ouwehand AC, Salminen S, Bylund G (2001b) Protection of rainbow trout
1092 (*Oncorhynchus mykiss*) from furunculosis by *Lactobacillus rhamnosus*. *Aquaculture*
1093 **198**: 229-236.
- 1094 Nimrat S, Boonthai T, Vuthiphandchai V (2011) Effects of probiotic forms, compositions of
1095 and mode of probiotic administration on rearing of Pacific white shrimp (*Litopenaeus*
1096 *vannamei*) larvae and postlarvae. *Animal Feed Science and Technology* **169**: 244-258.
- 1097 Nimrat S, Suksawat S, Boonthai T, Vuthiphandchai V (2012) Potential Bacillus probiotics
1098 enhance bacterial numbers, water quality and growth during early development of white
1099 shrimp (*Litopenaeus vannamei*). *Veterinary Microbiology* **159**: 443-450.
- 1100 Nishiyama, K., Sugiyama, M. & Mukai, T. (2016) Adhesion Properties of Lactic Acid Bacteria
1101 on Intestinal Mucin. *Microorganisms* **4**: 34.
- 1102 Offret C, Rochard V, Laguerre H, Mounier J, Huchette S, Brillet B, *et al.*, (2018) Protective
1103 Efficacy of a *Pseudoalteromonas* Strain in European Abalone, *Haliotis tuberculata*,
1104 Infected with *Vibrio harveyi* ORM4. *Probiotics and Antimicrobial Proteins* doi:
1105 10.1007/s12602-018-9389-8. [Epub ahead of print]
- 1106 Ohashi Y, Ushida K (2009) Health-beneficial effects of probiotics: Its mode of action. *Animal*
1107 *Science Journal* **80**: 361-371.
- 1108 Olsson JC, Westerdahl A, Conway PL, Kjelleberg S (1992) Intestinal colonization potential of
1109 turbot (*Scophthalmus maximus*) - and dab (*Limanda limanda*)-associated bacteria with
1110 inhibitory effects against *Vibrio anguillarum*. *Applied and Environmental Microbiology*
1111 **58**: 551-556.

- 1112 Pandiyan P, Balaraman D, Thirunavukkarasu R, George EGJ, Subaramaniyan K, Manikkam S,
1113 *et al.*, (2013) Probiotics in aquaculture. *Drug Invention Today* **5**: 55-59.
- 1114 Papadimitriou K, Zoumpopoulou G, Foligné B, Alexandraki V, Kazou M, Pot B, *et al.*, (2015)
1115 Discovering probiotic microorganisms: *in vitro*, *in vivo*, genetic and omics approaches.
1116 *Frontiers in Microbiology* **6**.
- 1117 Parrow NL, Fleming RE, Minnick MF (2013) Sequestration and scavenging of iron in infection.
1118 *Infection and Immunity* **81**: 3503-3514.
- 1119 Pereira LF, Peixoto MJ, Carvalho P, Sansuwan K, Santos GA, Goncalves JFM, *et al.*, (2018)
1120 Cross-effects of dietary probiotic supplementation and rearing temperature on growth
1121 performance, digestive enzyme activities, cumulative mortality and innate immune
1122 response in seabass (*Dicentrarchus labrax*). *Aquaculture Nutrition* **24**: 453-460.
- 1123 Pérez-Sánchez T, Ruiz-Zarzuela I, de Blas I, Balcázar JL (2014) Probiotics in aquaculture: a
1124 current assessment. *Reviews in Aquaculture* **6**: 133-146.
- 1125 Pokorzynski ND, Thompson CC, Carabeo RA (2017) Ironing out the unconventional
1126 mechanisms of iron acquisition and gene regulation in chlamydia. *Frontiers in Cellular*
1127 *and Infection Microbiology* **7**.
- 1128 Ramesh D, Souissi S, Ahamed TS (2017) Effects of the potential probiotics *Bacillus aerophilus*
1129 KADR3 in inducing immunity and disease resistance in *Labeo rohita*. *Fish & Shellfish*
1130 *Immunology* **70**: 408-415.
- 1131 Ramesh D, Vinothkanna A, Rai AK, Vignesh VS (2015) Isolation of potential probiotic
1132 *Bacillus* spp. and assessment of their subcellular components to induce immune
1133 responses in *Labeo rohita* against *Aeromonas hydrophila*. *Fish & Shellfish Immunology*
1134 **45**: 268-276.
- 1135 Ramírez C, Romero J (2017) The microbiome of *Seriola lalandi* of wild and aquaculture origin
1136 reveals differences in composition and potential function. *Frontiers in Microbiology* **8**.

- 1137 Ran C, Carrias A, Williams MA, Capps N, Dan BCT, Newton JC, *et al.*, (2012) Identification
1138 of *Bacillus* strains for biological control of catfish pathogens. *PLoS ONE* **7**: e45793.
- 1139 Rengpipat S, Phianphak W, Piyatiratitivorakul S, Menasveta P (1998) Effects of a probiotic
1140 bacterium on black tiger shrimp *Penaeus monodon* survival and growth. *Aquaculture*
1141 **167**: 301-313.
- 1142 Rengpipat S, Rukpratanporn S, Piyatiratitivorakul S, Menasaveta P (2000) Immunity
1143 enhancement in black tiger shrimp (*Penaeus monodon*) by a probiont bacterium
1144 (*Bacillus* S11). *Aquaculture* **191**: 271-288.
- 1145 Reyes-Becerril M, Angulo C, Estrada N, Murillo Y, Ascencio-Valle F (2014) Dietary
1146 administration of microalgae alone or supplemented with *Lactobacillus sakei* affects
1147 immune response and intestinal morphology of Pacific red snapper (*Lutjanus peru*).
1148 *Fish & Shellfish Immunology* **40**: 208-216.
- 1149 Reyes-Becerril M, Ascencio-Valle F, Macias ME, Maldonado M, Rojas M, Esteban MÁ (2012)
1150 Effects of marine silages enriched with *Lactobacillus sakei* 5-4 on haemato-
1151 immunological and growth response in Pacific red snapper (*Lutjanus peru*) exposed to
1152 *Aeromonas veronii*. *Fish & Shellfish Immunology* **33**: 984-992.
- 1153 Ridha MT, Azad IS (2012) Preliminary evaluation of growth performance and immune
1154 response of Nile tilapia *Oreochromis niloticus* supplemented with two putative
1155 probiotic bacteria. *Aquaculture Research* **43**: 843-852.
- 1156 Ringø E, Myklebust R, Mayhew TM, Olsen RE (2007) Bacterial translocation and pathogenesis
1157 in the digestive tract of larvae and fry. *Aquaculture* **268**: 251-264.
- 1158 Ringø E, Løvmo L, Kristiansen M, Salinas I, Myklebust R, Olsen RE *et al.*, (2010a) Lactic acid
1159 bacteria vs. pathogens in the gastrointestinal tract of fish: A review. *Aquaculture*
1160 *Research* **41**: 451-467.

- 1161 Ringø E, Olsen RE, Gifstad TØ, Dalmo RA, Amlund H, Hemre GI, *et al.*, (2010b) Prebiotics
1162 in aquaculture: a review. *Aquaculture Nutrition* **16**: 117-136.
- 1163 Ringø E, Olsen RE, Gonzales Vecino JL, Wadsworth S, Song SK (2012) Use of
1164 immunostimulants and nucleotides in aquaculture: A review. *Journal of Marine*
1165 *Science: Research & Development* **2**:1.
- 1166 Ringø E, Olsen RE, Jensen I, Romero J, Lauzon HL (2014) Application of vaccines and dietary
1167 supplements in aquaculture: possibilities and challenges. *Reviews in Fish Biology and*
1168 *Fisheries* **24**: 1005-1032.
- 1169 Ringø E, Hoseinifar SH, Ghosh K, Van Doan H, Beck BR, Song SK (2018) Lactic acid bacteria
1170 – an update. *Frontiers in Microbiology* **9**: 1818.
- 1171 Rinkinen M, Mättö J, Salminen S, Westermarck E, Ouwehand AC (2000) *In vitro* adhesion of
1172 lactic acid bacteria to canine small intestinal mucus. *Journal of Animal Physiology and*
1173 *Animal Nutrition* **84**: 43-47.
- 1174 Rinkinen M, Westermarck E, Salminen S, Ouwehand AC (2003) Absence of host specificity
1175 for *in vitro* adhesion of probiotic lactic acid bacteria to intestinal mucus. *Veterinary*
1176 *Microbiology* **97**: 55-61.
- 1177 Romero J, Feijoo´ CG, Navarrete P (2012) Antibiotics in aquaculture – use, abuse and
1178 alternatives. In: Carvalho E (ed) *Health and Environment in Aquaculture*, pp. 159–198.
1179 In-Tech, ISBN 978-953-51-0497-1.
- 1180 Sabri M, Léveillé S, Dozois CM (2006) A SitABCD homologue from an avian pathogenic
1181 *Escherichia coli* strain mediates transport of iron and manganese and resistance to
1182 hydrogen peroxide. *Microbiology* **152**: 745-758.
- 1183 Sáenz de Rodrigáñez MA, DÍAZ-Rosales P, ChabrilÓN M, Smidt H, Arijo S, LeÓN-Rubio
1184 JM, *et al.*, (2009) Effect of dietary administration of probiotics on growth and intestine

1185 functionality of juvenile Senegalese sole (*Solea senegalensis*, Kaup 1858). *Aquaculture*
1186 *Nutrition* **15**: 177-185.

1187 Salma W, Zhou Z, Wang W, Askarian F, Kousha A, Ebrahimi MT, *et al.*, (2011) Histological
1188 and bacteriological changes in intestine of beluga (*Huso huso*) following *ex vivo*
1189 exposure to bacterial strains. *Aquaculture* **314**: 24-33.

1190 Salminen S, Bouley C, Boutron MC, Cummings JH, Franck A, Gibson GR, *et al.*, (2007)
1191 Functional food science and gastrointestinal physiology and function. *The British*
1192 *journal of nutrition* **80**: S147-S171.

1193 Sanchez LM, Wong WR, Riener RM, Schulze CJ, Linington RG (2012) Examining the fish
1194 microbiome: Vertebrate-derived bacteria as an environmental niche for the discovery of
1195 unique marine natural products. *PLOS ONE* **7**: e35398.

1196 Sandy M, Butler A (2009) Microbial iron acquisition: Marine and terrestrial siderophores.
1197 *Chemical reviews* **109**: 4580-4595.

1198 Sangma, T. & Kamilya, D. (2015) *In vitro* and dietary effects of chitin on cellular and humoral
1199 immune parameters of Catla, *Catla catla* (Hamilton). *Journal of the World Aquaculture*
1200 *Society* **46**: 617-623.

1201 Satish RK, Arul V (2009) Purification and characterization of phocaecin PI80: an anti-listerial
1202 bacteriocin produced by *Streptococcus phocae* PI80 Isolated from the gut of *Peneaus*
1203 *indicus* (Indian white shrimp). *Journal of microbiology and biotechnology* **19**: 1393-
1204 1400.

1205 Schrezenmeir J, de Vrese M (2001) Probiotics, prebiotics, and synbiotics—approaching a
1206 definition1–3. *The American Journal of Clinical Nutrition* **73**: 361s-364s.

1207 Serrano PH (2005) *Responsible use of antibiotics in aquaculture*, Food & Agriculture Org.

1208 Shan X, Xiao Z, Huang W, Dou S (2008) Effects of photoperiod on growth, mortality and
1209 digestive enzymes in miiuy croaker larvae and juveniles. *Aquaculture* **281**: 70-76.

- 1210 Shapiro JA, Wencewicz TA (2016) Acinetobactin isomerization enables adaptive iron
1211 acquisition in acinetobacter baumannii through pH-triggered siderophore swapping.
1212 *ACS Infectious Diseases* **2**: 157-168.
- 1213 Sharifuzzaman SM, Al-Harbi AH, Austin B (2014) Characteristics of growth, digestive system
1214 functionality, and stress factors of rainbow trout fed probiotics *Kocuria* SM1 and
1215 *Rhodococcus* SM2. *Aquaculture* **418–419**: 55-61.
- 1216 Sharifuzzaman SM, Austin B (2009) Influence of probiotic feeding duration on disease
1217 resistance and immune parameters in rainbow trout. *Fish & Shellfish Immunology* **27**:
1218 440-445.
- 1219 Sorokulova I (2013) Modern Status and Perspectives of *Bacillus* Bacteria as Probiotics.
1220 *Probiotics & Health* **2013**: 5.
- 1221 Spanggaard B, Huber I, Nielsen J, Nielsen T, Appel KF, Gram L (2000) The microflora of
1222 rainbow trout intestine: a comparison of traditional and molecular identification.
1223 *Aquaculture* **182**: 1-15.
- 1224 Srisapoome P, Areechon N (2017) Efficacy of viable *Bacillus pumilus* isolated from farmed
1225 fish on immune responses and increased disease resistance in Nile tilapia (*Oreochromis*
1226 *niloticus*): Laboratory and on-farm trials. *Fish & Shellfish Immunology* **67**: 199-210.
- 1227 Sugita H, Hirose Y, Matsuo N, Deguchi Y (1998) Production of the antibacterial substance by
1228 *Bacillus* sp. strain NM 12, an intestinal bacterium of Japanese coastal fish. *Aquaculture*
1229 **165**: 269-280.
- 1230 Sumon MS, Ahmmed F, Khushi SS, Ahmmed MK, Rouf MA, Chisty MAH, *et al.*, (2018)
1231 Growth performance, digestive enzyme activity and immune response of
1232 *Macrobrachium rosenbergii* fed with probiotic *Clostridium butyricum* incorporated
1233 diets. *Journal of King Saud University - Science* **30**: 21-28.

- 1234 Sun Y-Z, Yang H-L, Huang K-P, Ye J-D, Zhang C-X (2013) Application of autochthonous
1235 *Bacillus bioencapsulated* in copepod to grouper *Epinephelus coioides* larvae.
1236 *Aquaculture* **392**: 44-50.
- 1237 Sun Y-Z, Yang H-L, Ma R-L, Lin W-Y (2010) Probiotic applications of two dominant gut
1238 *Bacillus* strains with antagonistic activity improved the growth performance and
1239 immune responses of grouper *Epinephelus coioides*. *Fish & Shellfish Immunology* **29**:
1240 803-809.
- 1241 Sun YZ, Yang HL, Ma RL, Song K, Li JS (2012) Effect of *Lactococcus lactis* and *Enterococcus*
1242 *faecium* on growth performance, digestive enzymes and immune response of grouper
1243 *Epinephelus coioides*. *Aquaculture Nutrition* **18**: 281-289.
- 1244 Suva M, Sureja V, Kheni D (2016) Novel insight on probiotic *Bacillus subtilis*: Mechanism of
1245 action and clinical applications. *Journal of Current Research in Scientific Medicine* **2**:
1246 65-72.
- 1247 Suzer C, Çoban D, Kamaci HO, Saka Ş, Firat K, Otgucuoğlu Ö, *et al.*, (2008) *Lactobacillus*
1248 spp. bacteria as probiotics in gilthead sea bream (*Sparus aurata*, L.) larvae: Effects on
1249 growth performance and digestive enzyme activities. *Aquaculture* **280**: 140-145.
- 1250 Suzuki S, Pruden A, Virta M, Zhang T (2017) Editorial: Antibiotic resistance in aquatic
1251 systems. *Frontiers in Microbiology* **8**.
- 1252 Tal Y, Schreier HJ, Sowers KR, Stubblefield JD, Place AR, Zohar Y (2009) Environmentally
1253 sustainable land-based marine aquaculture. *Aquaculture* **286**: 28-35.
- 1254 Talpur AD, Ikhwanuddin M, Abdullah MDD, Ambok Bolong A-M (2013) Indigenous
1255 *Lactobacillus plantarum* as probiotic for larviculture of blue swimming crab, *Portunus*
1256 *pelagicus* (Linnaeus, 1758): Effects on survival, digestive enzyme activities and water
1257 quality. *Aquaculture* **416**: 173-178.

- 1258 Tan LT-H, Chan K-G, Lee L-H, Goh B-H (2016) Streptomyces Bacteria as Potential Probiotics
1259 in Aquaculture. *Frontiers in Microbiology* **7**.
- 1260 Tapia-Paniagua ST, Vidal S, Lobo C, Prieto-Álamo MJ, Jurado J, Cordero H, *et al.*, (2014) The
1261 treatment with the probiotic *Shewanella putrefaciens* Pdp11 of specimens of *Solea*
1262 *senegalensis* exposed to high stocking densities to enhance their resistance to disease.
1263 *Fish & Shellfish Immunology* **41**: 209-221.
- 1264 Timmerman HM, Koning CJM, Mulder L, Rombouts FM, Beynen AC (2004) Monostrain,
1265 multi strain and multispecies probiotics—A comparison of functionality and efficacy.
1266 *International Journal of Food Microbiology* **96**: 219-233.
- 1267 Truong Thy HT, Tri NN, Quy OM, Fotedar R, Kannika K, Unajak S, *et al.*, (2017) Effects of
1268 the dietary supplementation of mixed probiotic spores of *Bacillus amyloliquifaciens*
1269 54A, and *Bacillus pumilus* 47B on growth, innate immunity and stress responses of
1270 striped catfish (*Pangasianodon hypophthalmus*). *Fish & Shellfish Immunology* **60**: 391-
1271 399.
- 1272 Tuomola EM, Ouwehand AC, Salminen SJ (1999) Human ileostomy glycoproteins as a model
1273 for small intestinal mucus to investigate adhesion of probiotics. *Letters in Applied*
1274 *Microbiology* **28**: 159-163.
- 1275 Tuomola E, Crittenden R, Playne M, Isolauri E, Salminen S (2001) Quality assurance criteria
1276 for probiotic bacteria. *The American Journal of Clinical Nutrition* **73**: 393s-398s.
- 1277 Tzuc JT, Escalante DR, Rojas Herrera R, Gaxiola Cortés G, Ortiz MLA (2014) Microbiota from
1278 *Litopenaeus vannamei*: digestive tract microbial community of Pacific white shrimp
1279 (*Litopenaeus vannamei*). *SpringerPlus* **3**: 280.
- 1280 Ueberschär B (1995) The use of tryptic enzyme activity measurement as a nutritional condition
1281 index: laboratory calibration data and field application. In: *ICES Marine Science*

- 1282 *Symposia*. Copenhagen, Denmark: International Council for the Exploration of the Sea,
1283 1991, pp. 119-129.
- 1284 Vadstein O, Bergh Ø, Gatesoupe F-J, Galindo-Villegas J, Mulero V, Picchiatti S, *et al.*, (2013)
1285 Microbiology and immunology of fish larvae. *Reviews in Aquaculture* **5**: S1-S25.
- 1286 Van Doan H, Hoseinifar SH, Dawood MAO, Chitmanat C, Tayyamath K (2017) Effects of
1287 *Cordyceps militaris* spent mushroom substrate and *Lactobacillus plantarum* on
1288 mucosal, serum immunology and growth performance of Nile tilapia (*Oreochromis*
1289 *niloticus*). *Fish & Shellfish Immunology* **70**: 87-94.
- 1290 Van Doan H, Hoseinifar SH, Khanongnuch C, Kanpiengjai A, Unban K, Srichaiyo S (2018)
1291 Host-associated probiotics boosted mucosal and serum immunity, disease resistance and
1292 growth performance of Nile tilapia (*Oreochromis niloticus*). *Aquaculture* **491**: 94-100.
- 1293 Van Doan H, Hoseinifar SH, Khanongnuch C, Kanpiengjai A, Unban K, Van Kim V, *et al.*,
1294 (2018) Host-associated probiotics boosted mucosal and serum immunity, disease
1295 resistance and growth performance of Nile tilapia (*Oreochromis niloticus*). *Aquaculture*
1296 **491**: 94-100.
- 1297 Verschuere L, Rombaut G, Sorgeloos P, Verstraete W (2000) Probiotic bacteria as biological
1298 control agents in aquaculture. *Microbiology and Molecular Biology Reviews: MMBR*
1299 **64**: 655-671.
- 1300 Vine NG, Leukes WD, Kaiser H (2006) Probiotics in marine larviculture. *FEMS Microbiology*
1301 *Reviews* **30**: 404-427.
- 1302 Wang L, Ge C, Wang J, Dai J, Zhang P, Li Y (2017) Effects of different combinations of
1303 *Bacillus* on immunity and antioxidant activities in common carp. *Aquaculture*
1304 *International* **25**: 2091-2099.
- 1305 Wang Y-B, Li J-R, Lin J (2008) Probiotics in aquaculture: Challenges and outlook. *Aquaculture*
1306 **281**: 1-4.

- 1307 Wang Y (2011) Use of probiotics *Bacillus coagulans*, *Rhodopseudomonas palustris* and
1308 *Lactobacillus acidophilus* as growth promoters in grass carp (*Ctenopharyngodon idella*)
1309 fingerlings. *Aquaculture Nutrition* **17**: e372-e378.
- 1310 Wang H, Wang C, Tang Y, Sun B, Huang J, Song X. (2018) *Pseudoalteromonas* probiotics as
1311 potential biocontrol agents improve survival of *Penaeus vannamei* challenged with
1312 acute hepatopancreatic necrosis (AHPND)-causing *Vibrio parahaemolyticus*.
1313 *Aquaculture* **497**: 30-36.
- 1314 Weifen L, Xiaoping Z, Wenhui S, Bin D, Quan L, Luoqin F, *et al.*, (2012) Effects of *Bacillus*
1315 preparations on immunity and antioxidant activities in grass carp (*Ctenopharyngodon*
1316 *idellus*). *Fish Physiology and Biochemistry* **38**: 1585-1592.
- 1317 Wells JM, Loonen LMP, Karczewski JM (2010) The role of innate signaling in the homeostasis
1318 of tolerance and immunity in the intestine. *International Journal of Medical*
1319 *Microbiology* **300**: 41-48.
- 1320 Wu H-J, Sun L-B, Li C-B, Li Z-Z, Zhang Z, Wen X-B, *et al.*, (2014) Enhancement of the
1321 immune response and protection against *Vibrio parahaemolyticus* by indigenous
1322 probiotic *Bacillus* strains in mud crab (*Scylla paramamosain*). *Fish & Shellfish*
1323 *Immunology* **41**: 156-162.
- 1324 Wu Z-Q, Jiang C, Ling F, Wang G-X (2015) Effects of dietary supplementation of intestinal
1325 autochthonous bacteria on the innate immunity and disease resistance of grass carp
1326 (*Ctenopharyngodon idellus*). *Aquaculture* **438**: 105-114.
- 1327 Wu ZX, Feng X, Xie LL, Peng XY, Yuan J, Chen XX (2012) Effect of probiotic *Bacillus*
1328 *subtilis* Ch9 for grass carp, *Ctenopharyngodon idella* (Valenciennes, 1844), on growth
1329 performance, digestive enzyme activities and intestinal microflora. *Journal of Applied*
1330 *Ichthyology* **28**: 721-727.

- 1331 Xu B, Wang Y, Li J, Lin Q (2009) Effect of prebiotic xylooligosaccharides on growth
1332 performances and digestive enzyme activities of allogynogenetic crucian carp
1333 (*Carassius auratus gibelio*). *Fish Physiology and Biochemistry* **35**: 351-357.
- 1334 Yan J, Guo C, Dawood MAO, Gao J (2017) Effects of dietary chitosan on growth, lipid
1335 metabolism, immune response and antioxidant-related gene expression in *Misgurnus*
1336 *anguillicaudatus*. *Beneficial Microbes* **8**: 439-449.
- 1337 Yan L, Boyd KG, Grant Burgess J (2002) Surface Attachment induced production of
1338 antimicrobial compounds by marine epiphytic bacteria using modified roller bottle
1339 cultivation. *Marine Biotechnology* **4**: 356-366.
- 1340 Yanbo W, Zirong X (2006) Effect of probiotics for common carp (*Cyprinus carpio*) based on
1341 growth performance and digestive enzyme activities. *Animal Feed Science and*
1342 *Technology* **127**: 283-292.
- 1343 Yang G, Tian X, Dong S, Peng M, Wang D (2015) Effects of dietary *Bacillus cereus* G19,
1344 *B. cereus* BC-01, and *Paracoccus marcusii* DB11 supplementation on the growth,
1345 immune response, and expression of immune-related genes in coelomocytes and
1346 intestine of the sea cucumber (*Apostichopus japonicus* Selenka). *Fish & Shellfish*
1347 *Immunology* **45**: 800-807.
- 1348 Zhang Q, Ma H, Mai K, Zhang W, Liufu Z, Xu W (2010) Interaction of dietary *Bacillus subtilis*
1349 and fructooligosaccharide on the growth performance, non-specific immunity of sea
1350 cucumber, *Apostichopus japonicus*. *Fish & Shellfish Immunology* **29**: 204-211.
- 1351 Zhao Y, Yuan L, Wan J, Sun Z, Wang Y, Sun H (2016) Effects of potential probiotic *Bacillus*
1352 *cereus* EN25 on growth, immunity and disease resistance of juvenile sea cucumber
1353 *Apostichopus japonicus*. *Fish & Shellfish Immunology* **49**: 237-242.
- 1354 Zhao Y, Zhang W, Xu W, Mai K, Zhang Y, Liufu Z (2012) Effects of potential probiotic
1355 *Bacillus subtilis* T13 on growth, immunity and disease resistance against *Vibrio*

- 1356 *splendidus* infection in juvenile sea cucumber *Apostichopus japonicus*. *Fish & Shellfish*
1357 *Immunology* **32**: 750-755.
- 1358 Zheng X, Tang J, Ren G, Wang Y (2017) The effect of four microbial products on production
1359 performance and water quality in integrated culture of freshwater pearl mussel and
1360 fishes. *Aquaculture Research* **48**: 4897-4909.
- 1361 Zhou Z, Wang W, Liu W, Gatlin DM, Zhang Y, Yao B, *et al.*, (2012) Identification of highly-
1362 adhesive gut *Lactobacillus* strains in zebrafish (*Danio rerio*) by partial *rpoB* gene
1363 sequence analysis. *Aquaculture* **370-371**: 150-157.
- 1364 Zhou T, Zheng XF, Tang JY, Qin JG, Wang Y (2017) Effect of three commercial microbial
1365 products on bacterial community in a freshwater polyculture system. *Aquaculture*
1366 *Research* **48**: 4449-4460.
- 1367 Ziaei-Nejad S, Rezaei MH, Takami GA, Lovett DL, Mirvaghefi A-R, Shakouri M (2006) The
1368 effect of *Bacillus* spp. bacteria used as probiotics on digestive enzyme activity, survival
1369 and growth in the Indian white shrimp *Fenneropenaeus indicus*. *Aquaculture* **252**: 516-
1370 524.
- 1371 Zorriehzahra MJ, Delshad ST, Adel M, Tiwari R, Karthik K, Dhama K, Lazado CC (2016)
1372 Probiotics as beneficial microbes in aquaculture: an update on their multiple modes of
1373 action: a review. *Veterinary Quarterly* **36**: 228-241.
- 1374
1375
1376