



**HAL**  
open science

# **Porphyromonas spp. have an extensive host range in ill and healthy individuals and an unexpected environmental distribution: A systematic review and meta-analysis**

Luis Acuña-Amador, Frédérique Barloy-Hubler

## ► To cite this version:

Luis Acuña-Amador, Frédérique Barloy-Hubler. Porphyromonas spp. have an extensive host range in ill and healthy individuals and an unexpected environmental distribution: A systematic review and meta-analysis. *Anaerobe*, 2020, 66, pp.102280. 10.1016/j.anaerobe.2020.102280 . hal-02974793

**HAL Id: hal-02974793**

**<https://hal.science/hal-02974793>**

Submitted on 16 Nov 2020

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 ***Porphyromonas* spp. have an extensive host range in ill and healthy individuals and an**  
2 **unexpected environmental distribution: a systematic review and meta-analysis.**

3

4 Luis Acuña-Amador<sup>a,\*</sup> and Frédérique Barloy-Hubler<sup>b</sup>

5

6 <sup>a</sup>Laboratorio de Investigación en Bacteriología Anaerobia, Centro de Investigación en  
7 Enfermedades Tropicales, Facultad de Microbiología, Universidad de Costa Rica, San José,  
8 Costa Rica

9 <sup>b</sup>Institut de Génétique et Développement de Rennes, IGDR-CNRS, UMR6290, Université de  
10 Rennes 1, Rennes, France

11 \* luisalberto.acuna@ucr.ac.cr, +506 2511-8616

12 **ABSTRACT**

13 Studies on the anaerobic bacteria *Porphyromonas*, mainly focused on *P. gingivalis*, have  
14 revealed new bacterial structures, metabolic pathways, and physiologic functionalities.  
15 *Porphyromonas* are mainly described as being associated with mammals and involved in  
16 chronic oral infections and secondary pathologies such as cancers or neurodegenerative  
17 diseases. In this review, we collected and analyzed information regarding *Porphyromonas*  
18 isolation sites and associated conditions and showed that *Porphyromonas* are detected in  
19 numerous pristine and anthropic environments and that their host range appears wider than  
20 previously believed, including aquatic animals, arthropods, and birds, even if their predominant  
21 hosts remain humans, pets, and farm animals. Our analyses also revealed their presence in  
22 multiple organs and in a substantial proportion of healthy contexts. Overall, the growing  
23 numbers of microbiota studies have allowed unprecedented advances in the understanding of  
24 *Porphyromonas* ecology but raise questions regarding their phylogenetic assignment. In  
25 conclusion, this systematic and meta-analysis provides an overview of current knowledge  
26 regarding *Porphyromonas* ecological distribution and encourages additional research to fill the  
27 knowledge gaps to better understand their environmental distribution and inter- and intra-  
28 species transmission.

29

30 **KEYWORDS:** *Porphyromonas*, host, organ, ecological distribution

31

## 32 **Introduction**

33 The study of anaerobic bacteria, one of the oldest life forms, could enhance our knowledge  
34 regarding life origins [1]. These microorganisms are characterized by atmospheric oxygen  
35 intolerance [2], which hinders their isolation and culture [3]. In addition, their high nutritional  
36 requirements and slow growth [4] hamper evaluation of their metabolism, physiology, genetics,  
37 and ecology. Nevertheless, recent studies of animal and environmental microbiota have  
38 emphasized the importance of generating and integrating knowledge about anaerobic  
39 microorganisms [5,6] owing to their prevalence [7] and roles in microbial communities [1,8].

40 The Bacteroidetes phylum is predominant among human [9] and veterinary-associated  
41 microbiota [10] and, to a lower extent, in environmental communities [11]. This group exhibits  
42 novel features [12] such as their type IX secretion system [13,14] and type V fimbriae [15],  
43 both described for the first time in genus *Porphyromonas*. In 1921, Oliver and Wherry  
44 described black colonies on solid medium containing blood and proposed the name *Bacteroides*  
45 *melaninogenicum* [16]. In the 1970s and 1980s, this species was divided into three subspecies:  
46 *B. m. melaninogenicus*, *B. m. intermedius*, and *B. m. asaccharolyticus* [17] along with two  
47 others termed *B. m. macacae* [18] and *B. m. levii* [19]. This group was then renamed  
48 *Bacteroides levii*, *B. macacae*, and *B. asaccharolyticus* and the latter subsequently subdivided  
49 into two subgroups: *B. asaccharolyticus* and *B. gingivalis* [19,20], and a fifth species,  
50 *Bacteroides endodontalis*, was later described [21].

51 In 1988, Shah and Collins proposed creating a new genus, *Porphyromonas*, to group  
52 *Porphyromonas asaccharolytica*, *P. gingivalis*, and *P. endodontalis* [22]; subsequently, both  
53 *Porphyromonas macacae* [23] and *Porphyromonas levii* [24] were reclassified into this genus.  
54 The taxonomy of *P. macacae* was confusing until the mid 1990s, with two close species  
55 designated as *P. macacae* isolated in 1980 from macaques [18] and *P. salivosa* isolated in 1987  
56 from cats [25]. These were considered as representing two distinctive heterotypic biovars  
57 [23,26,27], but are now considered a single species [28,29].

58 Between 1992 and 1994, six new species were described: *P. circumdentaria* [28], *P. canoris*  
59 [30], *P. cangingivalis* [31], *P. crevioricanis*, and *P. gingivicanis* [32]. Finally, a sixth non-  
60 pigmented species initially called *Oribaculum catoniae* [33] was renamed *Porphyromonas*  
61 *catoniae* [34]. In 2001, Fournier *et al.* divided *P. gingivalis* into *P. gingivalis* (human strains)  
62 and *P. gulae* (animal strains) [35]. Finally, eight new species completed the list: *P. uenonis*  
63 [36], *P. somerae* [37], *P. bennonis* [38], *P. pasteri* [39], *P. pogonae* [40], *P. bronchialis* [41],  
64 *P. loveana* [42], and *P. katsikii* [43]. Notably, *Falsiporphyromonas endometrii*, described in

65 2014 [44], is considered as a *Porphyromonas* in this study. Moreover, *P. canis* [45], and *P.*  
66 *cansulci* [31] have been reassigned respectively to *P. gingivicanis* [46], and *P. crevioricanis*  
67 [47]. These changes may cloud the analysis of the species, especially when some recent  
68 publications still use the old names (e.g. see [48–50]).

69 Most of the described *Porphyromonas* species are associated with mammal oral microbiota  
70 and implicated in pathological processes such as periodontitis [46,50,51]. Recently, *P.*  
71 *gingivalis* has been cited in a number of studies for its possible role in orodigestive cancers [52–  
72 54]. Other studies suggest contributions of *P. somerae* in endometrial cancer [55], *P.*  
73 *asaccharolytica* in colorectal cancer [56,57], and *P. endodontalis* in gastric adenocarcinoma  
74 [58]. Notably, *P. pasteri* was inversely correlated with cancer progression in oral squamous cell  
75 carcinoma [59].

76 In this context, the purpose of this review was to clarify the ecological distribution of  
77 *Porphyromonas*. To address this issue, we analyzed 844 studies, focusing on the sites (e.g.,  
78 organ, host, and environment) and associated conditions (e.g. pathologies vs health) of  
79 isolation.

80

## 81 **Material and methods**

82 The literature search was conducted in accordance with the PRISMA [60] using a four-  
83 step strategy (Figure S1):

84

### 85 ***Question formulation and checking for existing reviews***

86 When searching for reviews summarizing knowledge on the *Porphyromonas* genus,  
87 their hosts, infected organs, and associated pathologies, we noted that apart from *P. gingivalis*,  
88 no literature review existed. To our knowledge, this review is the first on this subject.

89

### 90 ***Searching and selecting the relevant studies***

91 Three databases, PubMed, Google Scholar and Google image were searched to retrieve all  
92 records relevant to the study. The search was limited to publications after 1988, date of  
93 *Porphyromonas-Bacteroides* separation, with the exception of 2 articles describing *P.*  
94 *circumdentaria* and *P. macacae* [18,20]. Documents regarding *P. gingivalis* in the human oral  
95 sphere were excluded. The search was performed using key terms [All fields] in various  
96 combinations using a Boolean search technique as follows: 1) “*Porphyromonas*” AND one of  
97 the 20 species (e.g. “*Porphyromonas*” AND “*gulae*”); 2) “*P.*” AND one of the 20 species; 3)

98 “*Porphyromonas*” NOT *gingivalis*; and 4) “*Porphyromonas*” OR “P.” AND “*gingivalis*” NOT  
99 “oral”.

100 Peer-reviewed studies were retrieved including scientific articles, poster (n=4), abstracts,  
101 and conference proceedings along with theses. Review articles, opinions, editorials, and blogs  
102 were not included. Only studies written in English and French (n=4) were considered. Relevant  
103 results were downloaded, and their reference lists manually checked to identify missing  
104 documents using the search terms mentioned above. Duplicate records were deleted. Finally,  
105 844 unique studies were included.

106

### 107 ***Data extraction***

108 Information was organized in synthesis tables (Table S1 to S5) that included the  
109 *Porphyromonas* species name, organ or ecosystem as well as host or place of isolation, study  
110 authors and publication year, sample types, and situation of isolation (pathology or health  
111 status). Both authors independently assessed each study. Due to their very large number,  
112 references relating to these tables are not cited in this text but in the additional tables.

113

### 114 ***Data analysis***

115 Hosts were categorized into three large taxonomic groups: most frequently mentioned hosts  
116 (humans, pets, farm animals and monkeys), aquatic animals, and less common hosts like  
117 rodents, birds, and arthropods. Organs were categorized into 9 major categories (Figure S2).  
118 *Porphyromonas* species names received an acronym (e.g. GUL for *P. gulae*, Figure 1 and Table  
119 S1). For the meta-analysis, bioinformatics and statistical analyses were carried out. The number  
120 of publications associated with a specific host, organ, and pathology were calculated for each  
121 *Porphyromonas*. The number of cases could not be utilized as this information is missing in the  
122 vast majority of articles. The statistical analysis was carried out using R Studio 1.2.5029 and R  
123 packages for correlation map and network generation (corrplot [61] and corrr R [62]); factorial  
124 correspondence analysis [63], hierarchical clustering [64] (FactoMineR [65] and factoextra  
125 [66]) and graphics generation (webr [67], wordcloud [68], and ggplot2 [69]).

126 When nucleotide sequences were accessible, we checked the taxonomic assignment using  
127 BlastN or mapping against *Porphyromonas* 16S and whole-genome in-house databases. For  
128 16S rDNA analysis, sequences were extracted manually from each genome, the phylogenetic  
129 tree built using PhyML [70] (substitution model K80, bootstrap=20) based on MAFFT  
130 alignment [71] (algorithm: G-INS-1, scoring matrix: 200PAM/k=2), the evolutionary model

131 selected by Modeltest [72] (TPM3+I+G), and the corresponding distance matrix visualized  
132 using the superheat R package [73].

133

## 134 **Results and discussion**

### 135 ***Information sources***

136 The 21 recognized *Porphyromonas* species are described in an extremely variable  
137 number of publications (Figure 1, Table S1). Over 90% of the documents focused on *P.*  
138 *gingivalis* in human oral pathologies. Consequently, the vast majority of current knowledge  
139 about *Porphyromonas* actually relates to human oral *P. gingivalis*, which is unlikely to  
140 represent the comprehensive genus biology. In the remaining 10% (844 documents), 407  
141 documents described *Porphyromonas* without attribution of species (termed *P. spp.*). The 437  
142 articles with species descriptions are also distributed unevenly with over half limited to three  
143 species: *P. asaccharolytica*, *P. gingivalis* in animal or non-oral human isolates, and *P.*  
144 *endodontalis*. Conversely, only the initial description is available for two species (*P.*  
145 *bronchiolis* and *F. endometrii*).

146 Additionally, publication frequency for each species is uneven (Figure S3). *P. gingivalis*  
147 (in the oral human context) registers hundreds of publications per year, whereas publication  
148 frequency for other *Porphyromonas* is variable and often minimal (averaging <10 papers  
149 annually). Such differences lead to a bias in the knowledge of *Porphyromonas* biology, with  
150 little if any information being produced for 20 non-*P. gingivalis* species. Nevertheless, we  
151 observed a general trend of increased publication frequencies since 2014, which corresponds to  
152 the application of next generation sequencing (NGS) in *Porphyromonas* studies (Figure S4).  
153 This technology has become an invaluable tool for their ecological study, as discussed below.

154

### 155 ***Environmental Porphyromonas***

156 Notably, 103 scientific articles state the presence of *Porphyromonas* in environmental  
157 samples, in the vast majority with no species assignment except in 13 articles that proposed a  
158 species name based on the “best match” (Table S2). To verify these “best hits”, we performed  
159 a new BlastN search and confirmed only *P. gingivalis* found on indoor climbing walls [74] and  
160 *P. asaccharolytica* in cow manure [75] whereas for three studies [76–78], we identified  
161 *Macellibacteroides fermentans* and *Fermentimonas caenicola*, respectively instead of  
162 *Porphyromonas*. However, most studies do not provide access to raw data and taxonomic  
163 designation cannot be verified. This highlights the importance of depositing sequencing data in

164 open databases to allow reproducibility and re-analysis, with the fast-growing databases  
165 enabling updates of the results. Moreover, when the “best hits” results are low, especially in the  
166 Porphyromonadaceae family for which taxonomy is frequently revised [79], it is therefore  
167 preferable to limit the description to the genus level. Owing to such possible errors in species  
168 assignment and lack of verification capability, we chose to consider environmental  
169 *Porphyromonas* as unknown species (*P. spp.*).

170 A non-exhaustive description of the environmental diversity of *Porphyromonas* is presented  
171 in Figure 2 and Table S2. In pristine environments (27%), *Porphyromonas* have been isolated  
172 from air samples (4%); from soils (10%) like agricultural lands and crops, alpine meadows,  
173 sediments and seafloor, and in fresh- and sea- water (13%). In anthropogenic environments  
174 (73%), *Porphyromonas* have been detected in healthcare facilities as well as in indoor buildings  
175 and transport systems that constitute potential sites for microbial transmission between human  
176 and animal populations. Additionally, *Porphyromonas* were detected in various personal use  
177 objects. Finally, the most important source of environmental *Porphyromonas* derives from  
178 waste-management settings.

179 In summary, the environmental component of *Porphyromonas* is far from negligible. In  
180 some studies, *Porphyromonas* constitute “rare taxons” (< 1%) whereas in others they are  
181 abundant and described as part of the “core microbiome”. Such environmental detection of  
182 *Porphyromonas* raises issues including whether they result from cross-contamination or are  
183 persistent in the environment or continually transmitted by oral and/or fecal material. These  
184 questions are inherent in all studies carried out by detecting DNA (PCR or NGS) that do not  
185 guarantee viability of the identified bacteria.

186 This review does not answer these questions but suggests that *Porphyromonas* have a  
187 capacity to persist in pristine and man-polluted environments, indicative of resistance to  
188 stressors such as atmospheric oxygen, UV radiation, or nutrient depletion, possibly via  
189 dormancy mechanisms leading to viable non-cultivable forms (VBNCs). It is also possible that  
190 in free-form, biotic interactions are harmful to *Porphyromonas* as these are not very competitive  
191 but in favorable situations such as biofilms, these bacteria are protected in a nutrient-rich  
192 microenvironment and may benefit from cooperation with other bacteria to maintain and/or  
193 thrive. Thus, environmental niches may be temporarily utilized by *Porphyromonas*, which then  
194 re-colonize and re-infect human or animal hosts.

195

196 ***Host-associated Porphyromonas***



197 All *Porphyromonas* species, except for *P. bronchialis* and *Falsiporphyromonas* described  
198 only a few times, are detected in both disease and health conditions, in various proportions  
199 (Figure 3). Until 2012, *Porphyromonas* research had been focused on clinical microbiology and  
200 therefore biased toward pathological contexts with scarce descriptions in healthy contexts. This  
201 bias gradually disappeared concomitant with recent “without *a priori*” NGS studies that  
202 reported proportions of *Porphyromonas* spp. (*P. spp.*, Figure S3) at 58.7% in healthy states  
203 versus 41.3% in disease conditions. This may be interpreted as these species constituting not  
204 true pathogens (according to Pasteur or Koch) but rather key bacteria (“keystone pathogen” or  
205 “alpha bug theory” [80,81]), orchestrating, even at low abundance, host immune response or  
206 serving as pathobionts (“bacterial passengers theory” [82]) that profit from altered homeostasis  
207 to thrive and trigger disease. Evaluation of the frequency of the major pathologies described for  
208 all species (Figure 4) reveals the preponderance of inflammatory diseases (suffix “-itis”),  
209 followed by cancers, degenerative and autoimmune diseases. These observations confirm a  
210 complex pathological pattern for *Porphyromonas* including an assortment of primary diseases  
211 and secondary morbidities.

212 In the literature, *Porphyromonas* host range is often dichotomic with opposing human and  
213 veterinary strains (e.g. see [83–85]), which may be interpreted as host specificity. However, it  
214 is important to reassess host range to address several major epidemiological issues including  
215 whether two or more *Porphyromonas* species can cohabite within a single microbiota, whether  
216 zoonosis is possible, and, if so, whether this provokes colonization, infection, adaptation, and  
217 propagation to new hosts or only transitory infection. Answers to these questions are necessary  
218 to assess the possible threat to public health and food safety. For example, the presence of  
219 *Porphyromonas* in bovine milk has been described [86,87] but it remains unknown whether **its**  
220 consumption may result in exogenous transmission. The possibility of *Porphyromonas* transfer  
221 between humans and pets is also unresolved. In order to reexamine *Porphyromonas* host range,  
222 we classified all animal isolation sources as minority/newly cited or main/historically known  
223 hosts, as follows.

224

#### 225 *Minor or newly cited hosts of Porphyromonas*

226 Minor *Porphyromonas* hosts include aquatic wildlife (Table S3), arthropods, birds,  
227 small and/or wild mammals (Table S4). Briefly, in aquatic wildlife, *Porphyromonas* can  
228 survive and multiply in amoebas and endure physical and chemical stresses in their cysts. This  
229 intracellular existence can help *Porphyromonas* escape from macrophages in healthcare

230 facilities [88]. Marine life interactions have been noted in ciliates, corals, copepods, and oysters,  
231 playing a possible role in *Porphyromonas* survival and potential transfer along the food chain,  
232 as these bacteria are also found in fish, cetaceans, and penguins. This presence in aquatic  
233 animals should be contextualized with their presence in pristine aquatic environments.  
234 *Porphyromonas* were also detected in intestinal microbiota of arthropods (ectoparasites and  
235 insects), in birds' intestinal and respiratory microbiota and appears frequent in the oral, genital,  
236 anal, ocular, and nasal microbiota of wild and captive marsupials and mammals.

237

### 238 *Frequent or frequently studied hosts of Porphyromonas*

239 The major studied hosts all constitute mammals; in descending order: humans, dogs,  
240 cats, cattle, sheep, pigs, and monkeys. Using a contingency table for each *Porphyromonas*  
241 species phenotypic marker (health status, host, and organ, Table S1), significant correlations  
242 were visualized as a correlogram (Figure 5A) which revealed six isolated species, alone or in  
243 pairs. With the exception of *P. levii*, we suspect that this was largely due to the small number  
244 of publications (from one to six). The segregated species are as follows.

245

246 *P. levii*. Previously known as *Bacteroides melaninogenicus subsp. levii* then as *Bacteroides*  
247 *levii* [19] and reclassified as *Porphyromonas* in 1995 [24]. To avoid confusion, only  
248 publications after 1995 were considered for this species. However, some publications after 1995  
249 still used the old *Bacteroides levii* name [89] or the terminology *P. levii*-like organisms (PLLO)  
250 [90,91], which might correspond to *P. somerae* [27,37,92]. For example, only one publication  
251 recorded *P. levii* in human vaginitis [93], a typical isolation site of *P. somerae*; this may  
252 therefore be a case of misidentification. Considering only accurate *P. levii* designations, we  
253 found that this species is quite specific to ovine infections [94] (Table S1). Despite its high  
254 prevalence, *P. levii* distribution within lesions suggests its role as a secondary colonizer rather  
255 than a main etiologic agent [95]. Additionally, in some cases, its presence in non-affected  
256 animals has been described [96,97]. As this species was initially isolated from healthy cattle  
257 rumen [19,98] and is occasionally re-detected in this organ [99,100], it can be hypothesized that  
258 the skin and genital colonization might be due to fecal contamination and/or hematogenous  
259 propagation [101].

260

261 *Falsiporphyromonas endometrii*. Originally isolated from cow endometrium [44] and in  
262 intestinal microbiota from sows, this species had been relegated to a new genus at the time of

263 this publication as its phylogenetic distance from other *Porphyromonas* was deemed excessive.  
264 However, rebuilding the rRNA 16S tree and distance matrix (Figures 5B & 5C) indicated a  
265 *Porphyromonas* typical identity percentage. We therefore considered *Falsiporphyromonas* as  
266 a *Porphyromonas* in the absence of an official reclassification. Moreover, searching against  
267 BLAST gave *Porphyromonas* sp. 2069 and 2070 along with *P. levii* [102] and *Porphyromonas*  
268 sp. clone 1M9 [103] as best hits.

269

270 *P. katsikii*. Published only once after its isolation from sheep with pneumonia. BLAST search  
271 using its 16S sequence (accession number: KM360064) revealed four hits (99% identity)  
272 corresponding to uncultured *Porphyromonas* sp. isolated from the uterus of healthy or metric  
273 cows [97].

274

275 *P. loveana*. Cited in three articles, two of which recorded five strains in Australian marsupials  
276 and one defining two strains in New Zealand sheep. Only partial 16S gene sequences are  
277 available from the Australian strains that form an Oceania endemic group (97 to 100% identity).

278

279 *P. pogonae*. Described in six articles, first isolated from different polymicrobial infections in  
280 *Pogona* [104]. This species has also been described from the wounds of a crowned crane  
281 (*Balearica* sp.) and in human infections [40,105–107].

282

283 *P. bronchialis*. Only the initial description article for this species is available as a source of  
284 information, including four strains isolated from bronchial liquid from a single patient [41]. No  
285 nucleic acid sequence is available.

286

287 For the remaining 15 species, correspondence analysis using a host contingency table  
288 (Figure 6A) revealed a clear separation in 4 clusters (axis 1, 80% variance) between species  
289 dominant in human versus those of pets (Figure 6B):

290 Cluster 1 contains five species essentially described in humans: *P. uenonis* and *P. somerae*  
291 yet described in cattle infections [102,108], and *P. asaccharolytica*, *P. catoniae*, and *P.*  
292 *endodontalis* also described in pets, cattle, and primates.

293 *P. gingivalis*, clusters with *P. pasteri* and *P. bennonis* in a strongly human-associated group  
294 (Cluster 2). However, *P. pasteri* (exclusively human) and *P. bennonis* (also cited in pig feces  
295 [109]) are poorly studied (Figure 1).

296 *P. gulae*, *P. gingivalis* closest relative (Figure 5B), grouped in Cluster 4 with *P. macacae*,  
297 *P. canoris*, and *P. circumdentaria*. As such, *P. gingivalis* and *P. gulae* appear as two ecotypes  
298 separated according to number of human and canine cases [110,111] and distinguishable by the  
299 catalase test, *P. gulae* being positive and *P. gingivalis* negative [35]. Nevertheless, these two  
300 species contain similar virulence factors [85,112]. *P. gulae* can invade human cells *in vitro*  
301 [113] but with less adherence to human cells than *P. gingivalis* [114].

302 Some articles recorded *P. gulae* in humans. A study showed that its high prevalence in  
303 aborigines, may be associated with their traditional diet (primate meat) and/or use of capuchin  
304 as pets, facilitating transmission from primate to human. Notably, the authors hypothesize that  
305 *P. gulae* may be a competitor of *P. gingivalis* and that both species might rarely or inefficiently  
306 cohabit [115]. Yet, both species have been identified in biofilms from periodontitis [116].  
307 Moreover, *P. gulae* have been detected in the oral cavities and skin of dog owners, which may  
308 potentially result from dog-to-human transfer [117,118], poster). Conversely, *P. gulae* was not  
309 detected in cat owners [119]. Additionally, *P. gulae* have been reported in fecal samples from  
310 patients with colorectal cancer [120] and with *P. gingivalis* in cervical microbiota from infertile  
311 women [121]. It is difficult to synthesize colonization of humans by *P. gulae* as few studies  
312 exist and as this species is highly similar to *P. gingivalis*. Therefore, several questions remain,  
313 such as whether the absence of co-detection is legitimate or owing to inadequate analyses that  
314 underestimate the presence of *P. gulae* in human microbiota, or, if such cohabitation is indeed  
315 rare. However, if both species can coexist in humans, the issue of *P. gulae* zoonotic transfer  
316 (Table S1; Fig 6B) should be addressed considering the involvement of *Porphyromonas* in  
317 oncologic and neurologic diseases.

318 Correspondingly, *P. gingivalis* has been reported in animal oral cavities either with or  
319 without periodontitis, and in bite wounds and fecal material (Table S1). However, as *P.*  
320 *gingivalis* remains isolated predominantly from human medicine contexts, its study in animals  
321 is therefore necessary to elucidate whether these reports correspond to opportunistic  
322 colonization, occasional and transitory transfer from human to animals, or whether this species  
323 is not exclusively human-based.

324 All canine and feline species clustered with *P. gulae* (Cluster 4, Fig 6B), and are also  
325 occasionally reported in humans (from 6 to 15% of cases). *P. canoris* in human skin (Table S1),  
326 *P. circumdentaria* in healthy liver biopsies [122] and in fecal and genital microbiomes  
327 [121,123]. *P. macacae* have been reported in breast cancer [124] and infected wound bites

328 [27,125,126], which was expected as this species is frequently identified in pet oral microbiota  
329 (Table S1).

330 The last cluster (Cluster 3, Fig 6B) groups *P. gingivicanis*, *P. crevioricanis*, and *P.*  
331 *cangingivalis*, originally described in dog oral microbiota but also detected in cat, human, and  
332 cattle pathologies (Table S1).

333 In conclusion, we found that *Porphyromonas* was present in almost all animal orders. This  
334 information raises new questions about their epidemiology and host-specificities. Indeed, the  
335 only studies regarding *Porphyromonas* host-to-host transmission are between humans,  
336 specifically interfamily transmission [127–135], and from oral sources, with saliva as the  
337 vehicle [136]. Epidemiological studies of *Porphyromonas* in animals do not appear to be a  
338 priority. However, domestic mammals (cattle, cats, and dogs) live in very close association with  
339 their owners and all their secretions (saliva, urine) are present in the everyday environment.  
340 This review thus highlights the necessity for a rigorous reassessment of *Porphyromonas* host  
341 specificities.

342 Moreover, although numerous studies have associated these bacteria with clinical  
343 observations, mostly in human dentistry, NGS studies in the past decade have revealed a much  
344 wider host range. Prior to these approaches, classical culture-based have been insufficient to  
345 broaden our knowledge regarding *Porphyromonas* host diversity, as these bacteria are  
346 fastidious, slow growing, and produce low biomass. The presence of *Porphyromonas* across  
347 numerous and varied environments renders it necessary to determine whether they constitute  
348 generalist environmental pathogens or specialized opportunists that may briefly transfer to  
349 other reservoirs. To explore these issues, we reviewed *Porphyromonas* distribution in different  
350 organs, both in healthy and pathological conditions.

351

### 352 **Organ distribution of *Porphyromonas***

353 The distribution of *Porphyromonas* in cellular compartments is likely indicative of their  
354 colonization mechanism. To summarize the information, we classified the anatomical sites in  
355 nine categories with associated pathological or healthy conditions (Figure S2).

356 The objective of this investigation was to clarify and extend our knowledge regarding their  
357 cellular specificities. Generally, the scientific literature simplifies the findings and usually  
358 describes *Porphyromonas* species as expressly localized in specific body sites; e.g. *P. gingivalis*  
359 and *P. endodontalis* in the oral cavity, *P. uenonis* in the gut, and *P. somerae* in the genital tract.  
360 A contingency table registering the number of articles citing each of the nine organ categories

361 was used to generate a hierarchical clustering and waffle plots (Figure 7). Analysis of these  
362 plots revealed that none of the 15 species of *Porphyromonas* exhibits organ specificity but  
363 rather preferences for certain anatomical sites.

364 *P. asaccharolytica* and *P. gingivalis*, the two most published *Porphyromonas* (Figure 1),  
365 are the only species to be found in all 9 sites, albeit at variable proportion. This suggested that  
366 the number and diversity of publications constitute important factors that likely bias the results  
367 of less-reported species. Nevertheless, currently available data reveal three different types of  
368 profiles. The first cluster (Figure 7) corresponds to “multiple organ” behavior involving *P.*  
369 *asaccharolytica*, *P. somerae*, *P. bennonis*, and *P. uenonis*. The second cluster includes *P.*  
370 *macacae*, *P. cangingivalis*, *P. canoris*, *P. circumdentaria*, and *P. crevioricanis* found in the  
371 oral cavity and skin. As these species are often isolated from pets, the hypothesis of secondary  
372 opportunistic infection of bite and scratches wounds by oral *Porphyromonas* after licking  
373 represents the most obvious route of transmission. Finally, the third group (Figure 7) includes  
374 essentially oral bacteria such as *P. gulae*, *P. gingivalis*, *P. endodontalis*, *P. gingivicanis*, *P.*  
375 *catoniae*, and *P. pasteuri*, which are also occasionally detected in other organs.

376 This descriptive analysis suggested the capacity of *Porphyromonas* species to propagate in  
377 and on different body sites, thus allowing consideration of primary sites and various invasion  
378 routes allowing secondary colonization. However, the research needed to understand these  
379 routes of transmission is lacking. Although numerous analyses have been published regarding  
380 *Porphyromonas* adhesion to host cells, these are predominantly of *P. gingivalis*;  
381 complementary investigation must therefore be achieved for the other species. Mechanisms that  
382 allow the establishment and maintenance of an intracellular lifestyle along with the diversity of  
383 intracellular compartments used for *Porphyromonas* replication and crossing of host barriers  
384 need to be specifically studied in all species if possible. This knowledge would allow more  
385 precise definition of the threshold between *Porphyromonas* commensalism and pathogenicity,  
386 which constitutes a relevant issue as demonstrated in this review because these bacteria belong  
387 to the host microbiota and can therefore be considered commensal but can become pathogenic  
388 when they escape from their original niche or when their growth rate increases.

389

### 390 **Concluding remarks**

391 The initial objective of this review was to summarize the knowledge regarding the host and  
392 organ range in addition to associated conditions (pathological or healthy) for the 21 species of  
393 the *Porphyromonas* genus currently described. However, the marked heterogeneity in the

394 knowledge between *P. gingivalis*, the predominantly reported species with several studies per  
395 week and that of the large majority of species, associated with only 5 to 10 articles annually,  
396 along with the "exotic" species such as *P. bronchialis* or *P. katsikii* that have accumulated < 5  
397 papers over the past 20 years, was immediately apparent. We also observed that approximately  
398 half of the eligible studies described *Porphyromonas* spp. This inevitably resulted in "gray  
399 areas" and biases that rendered the interpretation of the results difficult and imprecise.  
400 However, the number of cases of cancers or systemic diseases associated directly or indirectly  
401 with *Porphyromonas* is accumulating, in addition to the previously well documented cases of  
402 infections and inflammations. A more thorough understanding of this bacterial genus therefore  
403 appears important for enhancing human and veterinary health with various complementary  
404 experiments, as discussed throughout this review, appearing necessary to clarify the taxonomic  
405 descriptions and refine the biological characterizations of the less-reported species. The  
406 summary schematic (Figure 8) showing their presence in numerous environments, hosts, and  
407 biological niches is thus incomplete and biased but nevertheless indicates the extremely  
408 widespread albeit poorly studied ecological distribution of this important bacterial genus.  
409

410 **Funding details**

411 L.A-A. was supported by Vicerrectoría de Investigación from Universidad de Costa Rica (VI-  
412 UCR) under grants 803-B8-118 and 803-B9-455. Additionally, this work was supported by the  
413 mobility program from l’Institut Français d’Amérique Centrale (IFAC). Neither VI-UCR nor  
414 IFAC had any role in the design of the study and collection, analysis, and interpretation of data,  
415 nor in writing the manuscript.

416

417 **Disclosure statement**

418 The authors declare that they have no competing interests.

419



420 **Figure legends**

421 **Figure 1.** Number of documents (scientific articles, doctoral theses, posters, and conference  
422 abstracts; total = 437) related to *Porphyromonas* species. *P. gingivalis* studied in the human  
423 oral biotope (GIN\_o) does not appear because its records exceeded 8000 documents. Only  
424 records citing this species in non-human (animals) or human non\_oral contexts (GIN\_no) are  
425 represented. Records for which the species was not identified, i.e. *Porphyromonas* spp. (*P.*  
426 spp.), are not presented (407 records).

427  
428 **Figure 2.** Pie chart sub-categorized with a donut diagram representing the proportion of the  
429 different environments in which *Porphyromonas* were detected. Pristine environments  
430 correspond to undisturbed ecosystems and thus unmodified by human activity as opposed to  
431 anthropogenic environments, reflecting those modified by human activities.

432  
433 **Figure 3.** Polar chart representing the proportion of records associated with each  
434 *Porphyromonas* species along with *Porphyromonas* spp. and either healthy (green) or disease  
435 (red) conditions. The total number of records corresponds to that presented in Figure 1. For *P.*  
436 *gingivalis*, the oral human records (GIN\_o) were totaled using PubMed abstracts whereas oral  
437 and non-oral animal cases in addition to non-oral human cases (GIN\_no) were fully analyzed  
438 similarly to the other *Porphyromonas* species.

439  
440 **Figure 4.** Word cloud representing all the pathologies and/or keywords associated with all  
441 *Porphyromonas* species as recorded in this analysis. The word size corresponds its number and  
442 is proportional to the total of pathologies/keywords mentioned; colors are used in accordance  
443 with the word size (from the most frequent to the least frequent: warm colors to cool colors).

444  
445 **Figure 5.** Relationship between *Porphyromonas* species phenotypic traits and phylogenetic  
446 relatedness. **A.** Top panel. Correlogram displaying the phenotypic correlation matrix (organ,  
447 host distribution, and pathology association). Color intensity and dot size indicate the Pearson  
448 coefficient values from light (0) to dark (1). Bottom panel. Correlation network to visualize  
449 pairwise correlations between *Porphyromonas* species inside each of the three clusters  
450 presented in the top panel. Each edge stands for a Spearman correlation  $> 0.90$  ( $p < 0.05$ ). Color  
451 of the edges is related to the coefficient of correlation from light to dark. Isolated species, alone  
452 or in pairs, are marked with an asterisk. **B.** 16S rDNA phylogenetic tree. The number between

453 brackets corresponds to the number of strains used to generate each consensus sequence by  
454 species. Colors represent the clusters of correlograms in panel A. *P. bronchialis* is absent as its  
455 16S sequence is not available. C. Distance matrix used for the 16S rDNA phylogenetic tree in  
456 B.

457

458 **Figure 6.** Major host distribution for the three *Porphyromonas* species clusters identified based  
459 on phenotypic traits. A. Factorial correspondence analysis of *Porphyromonas* species according  
460 to the number of cases for each category of major hosts (see details in the text). B. Host-range  
461 repartition detailed for each *Porphyromonas* species and each identified cluster. Green, Cluster  
462 I; red, Cluster 2; blue, Cluster 3; purple, Cluster 4.

463

464 **Figure 7.** Hierarchical clustering of *Porphyromonas* species according to the isolation site or  
465 organ separated by category (see details in Figure S4). The waffle charts reflect the relative  
466 abundances in each organ group described above (one block = 1%).

467

468 **Figure 8.** Overview of *Porphyromonas* isolation and/or description in all habitats including the  
469 environment and all its hosts. Within hosts, organs or body sites from which *Porphyromonas*  
470 have been described are detailed.

471

472 **Supplemental Figure S1.** Preferred reporting elements for systematic reviews and meta-  
473 analyzes (PRISMA), flowchart and checklist detailing documents search (from 01-1988 to 09-  
474 2019) and selection process applied in this systematic review and meta-analysis about  
475 *Porphyromonas* ecology.

476

477 **Supplemental Figure S2.** Categories used in this meta-analysis corresponding to the isolation  
478 site or organ in which *Porphyromonas* species have been described; a full description of all  
479 terms is presented for each category.

480

481 **Supplemental Figure S3.** Number of records included in this study for each *Porphyromonas*  
482 species by year from 01–1988 until 09–2019. For *P. gingivalis*, the oral human records (GIN\_o)  
483 were totaled using PubMed abstracts whereas oral and non-oral animal cases in addition to non-  
484 oral human cases (GIN\_no) have been referenced based on full records for the meta-analysis,  
485 as for the other *Porphyromonas* species.

486

487 **Supplementary Figure S4.** Number of records according to method of *Porphyromonas*  
488 identification and year. For each record included in this study, the identification method for any  
489 *Porphyromonas* isolate was classified into four categories: traditional identification and  
490 culturomics, immunologic or other wet lab method, specific 16S rDNA PCR to identify  
491 *Porphyromonas* species and related methods, and microbiota and metagenomics studies (NGS).

492

493 **References**

- 494 [1] W.F. Martin, F.L. Sousa, Early Microbial Evolution: The Age of Anaerobes, Cold Spring Harb Perspect  
 495 Biol. 8 (2015) a018127. <https://doi.org/10.1101/cshperspect.a018127>.
- 496 [2] I. Slesak, M. Kula, H. Slesak, Z. Miszalski, K. Strzalka, How to define obligatory anaerobiosis? An  
 497 evolutionary view on the antioxidant response system and the early stages of the evolution of life on  
 498 Earth, Free Radic Biol Med. (2019). <https://doi.org/10.1016/j.freeradbiomed.2019.03.004>.
- 499 [3] E. Nagy, L. Boyanova, U.S. Justesen, How to isolate, identify and determine antimicrobial susceptibility of  
 500 anaerobic bacteria in routine laboratories, Clin Microbiol Infect. 24 (2018) 1139–1148.  
 501 <https://doi.org/10.1016/j.cmi.2018.02.008>.
- 502 [4] P. Hugon, J.C. Dufour, P. Colson, P.E. Fournier, K. Sallah, D. Raoult, A comprehensive repertoire of  
 503 prokaryotic species identified in human beings, Lancet Infect Dis. 15 (2015) 1211–1219.  
 504 [https://doi.org/10.1016/s1473-3099\(15\)00293-5](https://doi.org/10.1016/s1473-3099(15)00293-5).
- 505 [5] B. La Scola, S. Khelaifia, J.C. Lagier, D. Raoult, Aerobic culture of anaerobic bacteria using antioxidants: a  
 506 preliminary report, Eur J Clin Microbiol Infect Dis. 33 (2014) 1781–1783.  
 507 <https://doi.org/10.1007/s10096-014-2137-4>.
- 508 [6] L.M. Mauerhofer, P. Pappenreiter, C. Paulik, A.H. Seifert, S. Bernacchi, S.K.R. Rittmann, Methods for  
 509 quantification of growth and productivity in anaerobic microbiology and biotechnology, Folia  
 510 Microbiol (Praha). 64 (2019) 321–360. <https://doi.org/10.1007/s12223-018-0658-4>.
- 511 [7] D.L. Church, Selected Topics in Anaerobic Bacteriology, Microbiol Spectr. 4 (2016).  
 512 <https://doi.org/10.1128/microbiolspec.DMIH2-0015-2015>.
- 513 [8] I.A. Podolsky, S. Seppala, T.S. Lankiewicz, J.L. Brown, C.L. Swift, M.A. O'Malley, Harnessing Nature's  
 514 Anaerobes for Biotechnology and Bioprocessing, Annu Rev Chem Biomol Eng. 10 (2019) 105–128.  
 515 <https://doi.org/10.1146/annurev-chembioeng-060718-030340>.
- 516 [9] G. Gibiino, L.R. Lopetuso, F. Scaldaferrì, G. Rizzatti, C. Binda, A. Gasbarrini, Exploring Bacteroidetes:  
 517 Metabolic key points and immunological tricks of our gut commensals, Dig Liver Dis. 50 (2018) 635–  
 518 639. <https://doi.org/10.1016/j.dld.2018.03.016>.
- 519 [10] P. Deng, K.S. Swanson, Gut microbiota of humans, dogs and cats: current knowledge and future  
 520 opportunities and challenges, Br J Nutr. 113 Suppl (2015) S6-17.  
 521 <https://doi.org/10.1017/s0007114514002943>.
- 522 [11] J.M. Grondin, K. Tamura, G. Dejean, D.W. Abbott, H. Brumer, Polysaccharide Utilization Loci: Fueling  
 523 Microbial Communities, J Bacteriol. 199 (2017). <https://doi.org/10.1128/jb.00860-16>.
- 524 [12] P. Manfredi, F. Lauber, F. Renzi, K. Hack, E. Hess, G.R. Cornelis, New iron acquisition system in  
 525 Bacteroidetes, Infect Immun. 83 (2015) 300–310. <https://doi.org/10.1128/iai.02042-14>.
- 526 [13] M.J. McBride, Bacteroidetes Gliding Motility and the Type IX Secretion System, Microbiol Spectr. 7  
 527 (2019). <https://doi.org/10.1128/microbiolspec.PSIB-0002-2018>.
- 528 [14] K. Sato, M. Naito, H. Yukitake, H. Hirakawa, M. Shoji, M.J. McBride, R.G. Rhodes, K. Nakayama, A  
 529 protein secretion system linked to bacteroidete gliding motility and pathogenesis, Proc. Natl. Acad. Sci.  
 530 U. S. A. 107 (2010) 276–281. <https://doi.org/10.1073/pnas.0912010107>.
- 531 [15] T. Onoe, C.I. Hoover, K. Nakayama, T. Ideka, H. Nakamura, F. Yoshimura, Identification of  
 532 Porphyromonas gingivalis prefimbrilin possessing a long leader peptide: possible involvement of  
 533 trypsin-like protease in fimbrilin maturation, Microb Pathog. 19 (1995) 351–364.
- 534 [16] W.W. Oliver, W.B. Wherry, Notes on some bacterial parasites of the human mucous membranes, J. Infect.  
 535 Dis. (1921) 341–344.
- 536 [17] S.M. Finegold, E.M. BARNES, Proposal that the saccharolytic and asaccharolytic strains at present classified  
 537 in the species Bacteroides melaninogenicus (Oliver and Wherry) should be reclassified in two species as  
 538 Bacteroides melaninogenicus and Bacteroides asaccharolyticus, Int. J. Syst. Bacteriol. 27 (1977) 388–  
 539 391.
- 540 [18] J. Slots, R.J. Genco, Bacteroides melaninogenicus subsp. macacae, a new subspecies from monkey  
 541 periodontopathic indigenous microflora, Int. J. Syst. Bacteriol. 30 (1980) 82–85.  
 542 <https://doi.org/10.1099/00207713-30-1-82>.
- 543 [19] J.L. Johnson, L. V Holdeman, Bacteroides intermedius comb. nov. and descriptions of Bacteroides corporis  
 544 sp. nov. and Bacteroides levii sp. nov, Int. J. Syst. Evol. Microbiol. 33 (1983) 15–25.
- 545 [20] A.L. Coykendall, F.S. Kaczmarek, J. Slots, Genetic heterogeneity in Bacteroides asaccharolyticus  
 546 (Holdeman and Moore 1970) Finegold and Barnes 1977 (Approved Lists, 1980) and proposal of  
 547 Bacteroides gingivalis sp. nov. and Bacteroides macacae (Slots and Genco) comb. nov., Int. J. Syst.  
 548 Bacteriol. 30 (1980) 559–564. <https://doi.org/10.1099/00207713-30-3-559>.
- 549 [21] T.J.M. Van Steenberg, A.J. Van Winkelhoff, D. Mayrand, D. Grenier, J. De Graaff, Bacteroides  
 550 endodontalis sp. nov., an asaccharolytic black-pigmented Bacteroides species from infected dental root

- 551 canals, *Int. J. Syst. Evol. Microbiol.* 34 (1984) 118–120.
- 552 [22] H.N. Shah, M.D. Collins, Proposal for reclassification of *Bacteroides asaccharolyticus*, *Bacteroides*  
553 *gingivalis*, and *Bacteroides endodontalis* in a new genus, *Porphyromonas*, *Int. J. Syst. Evol. Microbiol.*  
554 38 (1988) 128–131.
- 555 [23] D.N. Love, *Porphyromonas macacae* comb. nov., a consequence of *Bacteroides macacae* being a senior  
556 synonym of *Porphyromonas salivosa*, *Int. J. Syst. Evol. Microbiol.* 45 (1995) 90–92.
- 557 [24] H.N. Shah, M.D. Collins, I. Olsen, B.J. Paster, F.E. Dewhirst, Reclassification of *Bacteroides levii*  
558 (Holdeman, Cato, and Moore) in the Genus *Polphyromonas*, as *Porphyromonas levii* comb. nov., *Int. J.*  
559 *Syst. Bacteriol.* 45 (1995) 586–588.
- 560 [25] D.N. Love, J.L. Johnson, R.F. Jones, A. Calverley, *Bacteroides salivosus* sp. nov., an Asaccharolytic,  
561 Black-Pigmented Species from Cats, *Int. J. Syst. Bacteriol.* 37 (1987) 307–309.  
562 <https://doi.org/10.1099/00207713-37-4-307>.
- 563 [26] M.E. Mulligan, D.M. Citron, R.Y. Kwok, E.J.C. Goldstein, Immunoblot Characterization of  
564 *Porphyromonas* species from infected dog and cat bite wounds in humans, *CID.* 25 (1997) S98–S99.  
565 <https://doi.org/10.1086/516236>.
- 566 [27] D.M. Citron, S. Hunt Gerardo, M.C. Claros, F. Abrahamian, D. Talan, E.J.C. Goldstein, S.H. Gerardo, M.C.  
567 Claros, F. Abrahamian, D. Talan, E.J.C. Goldstein, Frequency of Isolation of *Porphyromonas* Species  
568 from Infected Dog and Cat Bite Wounds in Humans and Their Characterization by Biochemical Tests  
569 and Arbitrarily Primed- Polymerase Chain Reaction Fingerprinting, *Clin. Infect. Dis.* 23 (1996) S77–82.  
570 [https://doi.org/10.1093/clinids/23.supplement\\_1.s78](https://doi.org/10.1093/clinids/23.supplement_1.s78).
- 571 [28] D.N. Love, G.D. Bailey, S. Collings, D.A. Briscoe, Description of *Porphyromonas circumdentaria* sp. nov.  
572 and reassignment of *Bacteroides salivosus* (Love, Johnson, Jones, and Calverley 1987) as  
573 *Porphyromonas* (Shah and Collins 1988) *salivosa* comb. nov., *Int. J. Syst. Bacteriol.* 42 (1992) 434–  
574 438. <https://doi.org/10.1099/00207713-42-3-434>.
- 575 [29] B.J. Paster, F.E. Dewhirst, I. Olsen, G.J. Fraser, Phylogeny of *Bacteroides*, *Prevotella*, and *Porphyromonas*  
576 spp. and related bacteria., *J. Bacteriol.* 176 (1994) 725–732. [https://doi.org/10.1128/jb.176.3.725-](https://doi.org/10.1128/jb.176.3.725-732.1994)  
577 [732.1994](https://doi.org/10.1128/jb.176.3.725-732.1994).
- 578 [30] D.N. Love, J. Karjalainen, A. Ivlnervo, B. Forsblom, E. Sarkiala, G.D. Bailey, D.I. Wigney, H. Jousimies-  
579 Somer, A. Kanervo, B. Forsblom, E. Sarkiala, G.D. Bailey, D.I. Wigney, H. Jousimies-Somer,  
580 *Porphyromonas canoris* sp. nov., an Asaccharolytic, Black-Pigmented Species from the Gingival Sulcus  
581 of Dogs, *Int. J. Syst. Bacteriol.* 44 (1994) 204–208. <https://doi.org/10.1099/00207713-44-2-204>.
- 582 [31] M.D. Collins, D.N. Love, J. Karjalainen, A. Kanervo, B. Forsblom, A. Willems, S. Stubbs, E. Sarkiala,  
583 G.D. Bailey, D.I. Wigney, et al., H. Jousimies-Somer, Phylogenetic analysis of members of the genus  
584 *Porphyromonas* and description of *Porphyromonas cangingivalis* sp. nov. and *Porphyromonas cansulci*  
585 sp. nov., *Int. J. Syst. Bacteriol.* 44 (1994) 674–679. <https://doi.org/10.1099/00207713-44-4-674>.
- 586 [32] M. Hirasawa, K. Takada, *Porphyromonas gingivicanis* sp. nov. and *Porphyromonas crevioricanis* sp. nov.,  
587 isolated from beagles, *Int J Syst Bacteriol.* 44 (1994) 637–640. [https://doi.org/10.1099/00207713-44-4-](https://doi.org/10.1099/00207713-44-4-637)  
588 [637](https://doi.org/10.1099/00207713-44-4-637).
- 589 [33] L.V.H. Moore, W.E.C. Moore, *Oribaculum catoniae* gen. nov., sp. nov.; *Catonella morbi* gen. nov., sp.  
590 nov.; *Hallella seregens* gen. nov., sp. nov.; *Johnsonella ignava* gen. nov., sp. nov.; and *Dialister*  
591 *pneumosintes* gen. nov., comb. nov., nom. rev., anaerobic gram-negative bacilli from , *Int. J. Syst. Evol.*  
592 *Microbiol.* 44 (1994) 187–192.
- 593 [34] A. Willems, M.D. Collins, Reclassification of *Oribaculum catoniae* (Moore and Moore 1994) as  
594 *Porphyromonas catoniae* comb. nov. and emendation of the genus *Porphyromonas*, *Int J Syst Bacteriol.*  
595 45 (1995) 578–581. <https://doi.org/10.1099/00207713-45-3-578>.
- 596 [35] D. Fournier, C. Mouton, P. Lapierre, T. Kato, K. Okuda, C. Menard, C. Ménard, *Porphyromonas gulae* sp.  
597 nov, an anaerobic, Gram-negative coccobacillus from gingival sulcus of various animal hosts, *Int. J.*  
598 *Syst. Evol. Microbiol.* 51 (2001) 1179–1189. <https://doi.org/10.1099/00207713-51-3-1179>.
- 599 [36] S.M. Finegold, M.L. Vaisanen, M. Rautio, E. Eerola, P. Summanen, D. Molitoris, Y. Song, C. Liu, H.  
600 Jousimies-Somer, *Porphyromonas uenonis* sp. nov., a pathogen for humans distinct from *P.*  
601 *asaccharolytica* and *P. endodontalis*, *J. Clin. Microbiol.* 42 (2004) 5298–5301.  
602 <https://doi.org/10.1128/JCM.42.11.5298-5301.2004>.
- 603 [37] P.H. Summanen, B. Durmaz, M.L. Vaisanen, C. Liu, D. Molitoris, E. Eerola, I.M. Helander, S.M. Finegold,  
604 *Porphyromonas somerae* sp. nov., a pathogen isolated from humans and distinct from *Porphyromonas*  
605 *levii*, *J Clin Microbiol.* 43 (2005) 4455–4459. <https://doi.org/10.1128/jcm.43.9.4455-4459.2005>.
- 606 [38] P.H. Summanen, P.A. Lawson, S.M. Finegold, *Porphyromonas bennonis* sp. nov., isolated from human  
607 clinical specimens, *Int. J. Syst. Evol. Microbiol.* 59 (2009) 1727–1732.  
608 <https://doi.org/10.1099/ijs.0.001909-0>.
- 609 [39] M. Sakamoto, D. Li, Y. Shibata, T. Takeshita, Y. Yamashita, M. Ohkuma, *Porphyromonas pasteri* sp. Nov.,

- 610 isolated from human saliva, *Int. J. Syst. Evol. Microbiol.* 65 (2015) 2511–2515.  
611 <https://doi.org/10.1099/ijms.0.000294>.
- 612 [40] Y. Kawamura, S. Kuwabara, S.A. Kania, H. Kato, M. Hamagishi, N. Fujiwara, T. Sato, J. Tomida, K.  
613 Tanaka, D.A. Bemis, *Porphyromonas pogonae* sp. nov., an anaerobic but low concentration oxygen  
614 adapted coccobacillus isolated from lizards (*Pogona vitticeps*) or human clinical specimens, and  
615 emended description of the genus *Porphyromonas* Shah and Collins 1988, *Syst. Appl. Microbiol.* 38  
616 (2015) 104–109. <https://doi.org/10.1016/j.syapm.2014.11.004>.
- 617 [41] T. Sato, J. Tomida, T. Naka, N. Fujiwara, A. Hasegawa, Y. Hoshikawa, J. Matsuyama, N. Ishida, T. Kondo,  
618 K. Tanaka, *Porphyromonas bronchialis* sp. nov. isolated from intraoperative bronchial fluids of a patient  
619 with non-small cell lung cancer, *Tohoku J. Exp. Med.* 237 (2015) 31–37.
- 620 [42] P.S. Bird, D.J. Trott, D. Mikkelsen, G.J. Milinovich, K.M. Hillman, P.C. Burrell, L.L. Blackall,  
621 *Porphyromonas loveana* sp. Nov., isolated from the oral cavity of Australian marsupials, *Int. J. Syst.*  
622 *Evol. Microbiol.* 66 (2016) 3771–3778. <https://doi.org/10.1099/ijsem.0.000898>.
- 623 [43] G. Filioussis, E. Petridou, E. Karavanis, J. Frey, Pyogranulomatous pneumonia in goats caused by an  
624 undescribed *Porphyromonas* species: “*Porphyromonas katsikii*” *J Clin Microbiol.* 53 (2015) 795–8.  
625 <https://doi.org/10.1128/JCM.02682-14>.
- 626 [44] K. Wagener, M. Drillich, S. Baumgardt, P. Kämpfer, H.J. Busse, M. Ehling-Schulz, *Falsiporphyromonas*  
627 *endometrii* gen. nov., sp. nov., isolated from the post-partum bovine uterus, and emended description of  
628 the genus *Porphyromonas* Shah and Collins 1988, *Int. J. Syst. Evol. Microbiol.* 64 (2014) 642–649.  
629 <https://doi.org/10.1099/ijms.0.057307-0>.
- 630 [45] *Porphyromonas canis* gene for 16S rRNA - Nucleotide - NCBI, (n.d.).  
631 <https://www.ncbi.nlm.nih.gov/nuccore/AB034799.1> (accessed January 24, 2020).
- 632 [46] N.R. Krieg, W. Ludwig, J. Euzéby, W.B. Whitman, Phylum XIV. Bacteroidetes phyl. nov, in: N.R. Krieg,  
633 J.T. Staley, D.R. Brown, B.P. Hedlund, B.J. Paster, N.L. Ward, W. Ludwig, W.B. Whitman (Eds.),  
634 *Bergey’s Manual® Syst. Bacteriol. Vol. Four Bacteroidetes, Spirochaetes, Tenericutes (Mollicutes),*  
635 *Acidobacteria, Fibrobacteres, Fusobacteria, Dictyoglomi, Gemmatimonadetes, Lentisphaerae,*  
636 *Verrucomicrobia, Chlamydiae, Planctomycetes,* Springer New York, New York, NY, 2010: pp. 25–469.  
637 [https://doi.org/10.1007/978-0-387-68572-4\\_3](https://doi.org/10.1007/978-0-387-68572-4_3).
- 638 [47] F.E. Dewhirst, E.A. Klein, E.C. Thompson, J.M. Blanton, T. Chen, L. Milella, C.M.F. Buckley, I.J. Davis,  
639 M.L. Bennett, Z. V. Marshall-Jones, The canine oral microbiome, *PLoS One.* 7 (2012) 1–12.  
640 <https://doi.org/10.1371/journal.pone.0036067>.
- 641 [48] Y. Koyata, K. Watanabe, T. Toyama, S. Haruka, N. Hamada, Purification and characterization of a fimbrial  
642 protein from *Porphyromonas salivosa* ATCC 49407, *J. Vet. Med. Sci.* 81 (2019) 916–923.  
643 <https://doi.org/10.1292/jvms.19-0067>.
- 644 [49] J.H.Y.J.Y.H. Lee, J.H. Moon, J.I. Ryu, S.W. Kang, K.H. Kwack, J.H.Y.J.Y.H. Lee, Antibacterial effects of  
645 sodium tripolyphosphate against *Porphyromonas* species associated with periodontitis of companion  
646 animals, *J Vet Sci.* 20 (2019) e33. <https://doi.org/10.4142/jvs.2019.20.e33>.
- 647 [50] A. do Nascimento Silva, E.D. de Avila, V. Nakano, M.J. Avila-Campos, Pathogenicity and genetic profile  
648 of oral *Porphyromonas* species from canine periodontitis, *Arch. Oral Biol.* 83 (2017) 20–24.  
649 <https://doi.org/10.1016/j.archoralbio.2017.07.001>.
- 650 [51] C. Damgaard, A.K. Danielsen, C. Enevold, L. Massarenti, C.H. Nielsen, P. Holmstrup, D. Belstrom,  
651 *Porphyromonas gingivalis* in saliva associates with chronic and aggressive periodontitis, *J Oral*  
652 *Microbiol.* 11 (2019) 1653123. <https://doi.org/10.1080/20002297.2019.1653123>.
- 653 [52] I. Lafuente Ibáñez de Mendoza, X. Maritxalar Mendia, A.M. García de la Fuente, G. Quindós Andrés, J.M.  
654 Aguirre Urizar, Role of *Porphyromonas gingivalis* in oral squamous cell carcinoma development: A  
655 systematic review, *J. Periodontal Res.* (2019) jre.12691. <https://doi.org/10.1111/jre.12691>.
- 656 [53] I. Olsen, Ö. Yilmaz, Possible role of *Porphyromonas gingivalis* in orodigestive cancers, *J. Oral Microbiol.*  
657 11 (2019). <https://doi.org/10.1080/20002297.2018.1563410>.
- 658 [54] Y. Zhou, G.H. Luo, *Porphyromonas gingivalis* and digestive system cancers, *World J. Clin. Cases.* 7 (2019)  
659 819–829. <https://doi.org/10.12998/wjcc.v7.i7.819>.
- 660 [55] E. Caselli, I. Soffritti, M. D’Accolti, I. Piva, P. Greco, G. Bonaccorsi, *Atopobium vaginae* and  
661 *Porphyromonas somerae* induce proinflammatory cytokines expression in endometrial cells: A possible  
662 implication for endometrial cancer? *Cancer Manag. Res.* 11 (2019) 8571–8575.  
663 <https://doi.org/10.2147/CMAR.S217362>.
- 664 [56] N.T. Baxter, M.T. Ruffin, M.A.M. Rogers, P.D. Schloss, Microbiota-based model improves the sensitivity  
665 of fecal immunochemical test for detecting colonic lesions, *Genome Med.* 8 (2016) 37.  
666 <https://doi.org/10.1186/s13073-016-0290-3>.
- 667 [57] Z. Dai, O.O. Coker, G. Nakatsu, W.K.K.K. Wu, L. Zhao, Z. Chen, F.K.L.L. Chan, K. Kristiansen, J.J.Y.Y.  
668 Sung, S.H. Wong, J. Yu, Multi-cohort analysis of colorectal cancer metagenome identified altered

- 669 bacteria across populations and universal bacterial markers, *Microbiome*. 6 (2018) 70.  
670 <https://doi.org/10.1186/s40168-018-0451-2>.
- 671 [58] Y.L. Hu, W. Pang, Y. Huang, Y. Zhang, C.J. Zhang, The Gastric Microbiome Is Perturbed in Advanced  
672 Gastric Adenocarcinoma Identified Through Shotgun Metagenomics, *Front. Cell. Infect. Microbiol.* 8  
673 (2018) 433. <https://doi.org/10.3389/fcimb.2018.00433>.
- 674 [59] C.Y. Yang, Y.M. Yeh, H.Y. Yu, C.Y. Chin, C.W. Hsu, H. Liu, P.J. Huang, S.N. Hu, C.T. Liao, K.P. Chang,  
675 Y.L. Chang, Oral microbiota community dynamics associated with oral squamous cell carcinoma  
676 staging, *Front. Microbiol.* 9 (2018). <https://doi.org/10.3389/fmicb.2018.00862>.
- 677 [60] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, Preferred reporting items for systematic reviews and meta-  
678 analyses: the PRISMA statement., *PLoS Med.* 6 (2009) e1000097.  
679 <https://doi.org/10.1371/journal.pmed.1000097>.
- 680 [61] T. Wei, V. Simko, R package “corrplot”: Visualization of a Correlation Matrix, (2017).  
681 <https://github.com/taiyun/corrplot>.
- 682 [62] M. Kuhn, S. Jackson, J. Cimentada, R package “corr”: Correlations in R, (2020). [https://cran.r-](https://cran.r-project.org/package=corr)  
683 [project.org/package=corr](https://cran.r-project.org/package=corr).
- 684 [63] N. Sourial, C. Wolfson, B. Zhu, J. Quail, J. Fletcher, S. Karunanathan, K. Bandeen-Roche, F. Béland, H.  
685 Bergman, Correspondence analysis is a useful tool to uncover the relationships among categorical  
686 variables, *J. Clin. Epidemiol.* 63 (2010) 638–646. <https://doi.org/10.1016/j.jclinepi.2009.08.008>.
- 687 [64] A.S. Vijaya, R. Bateja, A Review on Hierarchical Clustering Algorithms, *J. Eng. Appl. Sci.* 12 (2017)  
688 7501–7507.
- 689 [65] S. Lê, J. Josse, F. Husson, FactoMineR: A Package for Multivariate Analysis, *J. Stat. Softw.* 25 (2008) 1–  
690 18. <https://doi.org/10.18637/jss.v025.i01>.
- 691 [66] A. Kassambara, F. Mundt, R package “factoextra”: Extract and Visualize the Results of Multivariate Data  
692 Analyses, (2020). <https://cran.r-project.org/package=factoextra>.
- 693 [67] K.-W. Moon, T. Martino, R package “webr”: Data and Functions for Web-Based Analysis, (2020).  
694 <https://cran.r-project.org/package=webr>.
- 695 [68] I. Fellows, R package “wordcloud”: Word Clouds, (2018). <https://cran.r-project.org/package=wordcloud>.
- 696 [69] H. Wickham, *ggplot2: Elegant Graphics for Data Analysis*, Springer-Verlag New York, 2016.  
697 <https://ggplot2.tidyverse.org>.
- 698 [70] S. Guindon, J.-F. Dufayard, V. Lefort, M. Anisimova, W. Hordijk, O. Gascuel, New algorithms and  
699 methods to estimate maximum-likelihood phylogenies: assessing the performance of PhyML 3.0., *Syst.*  
700 *Biol.* 59 (2010) 307–321. <https://doi.org/10.1093/sysbio/syq010>.
- 701 [71] K. Katoh, K. Misawa, K. Kuma, T. Miyata, MAFFT: a novel method for rapid multiple sequence alignment  
702 based on fast Fourier transform, *Nucleic Acids Res.* 30 (2002) 3059–3066.
- 703 [72] D. Posada, K.A. Crandall, MODELTEST: testing the model of DNA substitution., *Bioinformatics.* 14  
704 (1998) 817–818. <https://doi.org/10.1093/bioinformatics/14.9.817>.
- 705 [73] R. Barter, B. Yu, R package “superheat”: A Graphical Tool for Exploring Complex Datasets Using  
706 Heatmaps, (2017). <https://cran.r-project.org/package=superheat>.
- 707 [74] S.L. Bräuer, D. Vuono, M.J. Carmichael, C. Pepe-Ranney, A. Strom, E. Rabinowitz, D.H. Buckley, S.H.  
708 Zinder, S.L. Brauer, D. Vuono, M.J. Carmichael, C. Pepe-Ranney, A. Strom, E. Rabinowitz, D.H.  
709 Buckley, S.H. Zinder, Microbial Sequencing Analyses Suggest the Presence of a Fecal Veneer on  
710 Indoor Climbing Wall Holds, *Curr. Microbiol.* 69 (2014) 681–689. [https://doi.org/10.1007/s00284-014-](https://doi.org/10.1007/s00284-014-0643-3)  
711 [0643-3](https://doi.org/10.1007/s00284-014-0643-3).
- 712 [75] P.M. Christy, L.R. Gopinath, D. Divya, Microbial dynamics during anaerobic digestion of cow dung, in:  
713 *Interanational J. Plant, Anim. Environ. Sci.*, 2014: pp. 86–94. [www.ijpaes.com](http://www.ijpaes.com).
- 714 [76] T. Shimoyama, A. Yamazawa, Y. Ueno, K. Watanabe, Phylogenetic analyses of bacterial communities  
715 developed in a cassette-electrode microbial fuel cell, *Microbes Environ.* 24 (2009) 188–192.  
716 <https://doi.org/10.1264/jsme2.ME09108>.
- 717 [77] T.-S. Song, H.-Y. Cai, Z.-S. Yan, Z.-W. Zhao, H.-L. Jiang, Various voltage productions by microbial fuel  
718 cells with sedimentary inocula taken from different sites in one freshwater lake, *Bioresour. Technol.*  
719 108 (2012) 68–75. <https://doi.org/10.1016/J.BIORTECH.2011.11.136>.
- 720 [78] R. Snell-Castro, J.-J.J. Godon, J.-P.P. Delgenès, P. Dabert, Characterisation of the microbial diversity in a  
721 pig manure storage pit using small subunit rDNA sequence analysis, *FEMS Microbiol. Ecol.* 52 (2005)  
722 229–242. <https://doi.org/10.1016/j.femsec.2004.11.016>.
- 723 [79] M. Sakamoto, The Family Porphyromonadaceae, in: E. Rosenberg, E.F. DeLong, S. Lory, E. Stackebrandt,  
724 F. Thompson (Eds.), *Prokaryotes Other Major Lineages Bact. Archaea*, Springer Berlin Heidelberg,  
725 Berlin, Heidelberg, 2014: pp. 811–824. [https://doi.org/10.1007/978-3-642-38954-2\\_132](https://doi.org/10.1007/978-3-642-38954-2_132).
- 726 [80] C.L. Sears, D.M. Pardoll, Perspective: alpha-bugs, their microbial partners, and the link to colon cancer., *J.*  
727 *Infect. Dis.* 203 (2011) 306–11. <https://doi.org/10.1093/jinfdis/jiq061>.

- 728 [81] G. Hajishengallis, R.P. Darveau, M.A. Curtis, The keystone-pathogen hypothesis, *Nat Rev Microbiol.* 10  
729 (2012) 717–725. <https://doi.org/10.1038/nrmicro2873>.
- 730 [82] H. Tjalsma, A. Boleij, J.R. Marchesi, B.E. Dutilh, A bacterial driver-passenger model for colorectal cancer:  
731 Beyond the usual suspects, *Nat. Rev. Microbiol.* 10 (2012) 575–582.  
732 <https://doi.org/10.1038/nrmicro2819>.
- 733 [83] G.N.A. Senhorinho, V. Nakano, C. Liu, Y. Song, S.M. Finegold, M.J. Avila-Campos, Detection of  
734 *Porphyromonas gulae* from subgingival biofilms of dogs with and without periodontitis, *Anaerobe.* 17  
735 (2011) 257–258. <https://doi.org/10.1016/j.anaerobe.2011.06.002>.
- 736 [84] R. Nomura, M. Shirai, Y. Kato, M. Murakami, K. Nakano, N. Hirai, T. Mizusawa, S. Naka, Y. Yamasaki,  
737 M. Matsumoto-Nakano, T. Ooshima, F. Asai, Diversity of fimbriin among *Porphyromonas gulae*  
738 clinical isolates from Japanese dogs, *J Vet Med Sci.* 74 (2012) 885–891.
- 739 [85] J.C. Lenzo, N.M. O'Brien-Simpson, R.K. Orth, H.L. Mitchell, S.G. Dashper, E.C. Reynolds,  
740 *Porphyromonas gulae* Has Virulence and Immunological Characteristics Similar to Those of the Human  
741 Periodontal Pathogen *Porphyromonas gingivalis*, *Infect Immun.* 84 (2016) 2575–2585.  
742 <https://doi.org/10.1128/iai.01500-15>.
- 743 [86] M.F. Addis, A. Tanca, S. Uzzau, G. Oikonomou, R.C. Bicalho, P. Moroni, The bovine milk microbiota:  
744 Insights and perspectives from -omics studies, *Mol. Biosyst.* 12 (2016) 2359–2372.  
745 <https://doi.org/10.1039/c6mb00217j>.
- 746 [87] C. Catozzi, A. Sanchez Bonastre, O. Francino, C. Lecchi, E. De Carlo, D. Vecchio, A. Martucciello, P.  
747 Fraulo, V. Bronzo, A. Cuscó, S. D'Andrea, F. Cecilian, The microbiota of water buffalo milk during  
748 mastitis, *PLoS One.* 12 (2017) 1–20. <https://doi.org/10.1371/journal.pone.0184710>.
- 749 [88] Y. Wagner, B. Noack, T. Hoffmann, E. Jacobs, P. Christian Lück, Periodontopathogenic bacteria multiply  
750 in the environmental amoeba *Acanthamoeba castellanii*, *Int. J. Hyg. Environ. Health.* 209 (2006) 535–  
751 539. <https://doi.org/10.1016/j.ijheh.2006.05.006>.
- 752 [89] R.J. Collighan, M.J. Woodward, Spirochaetes and other bacterial species associated with bovine digital  
753 dermatitis, *FEMS Microbiol. Lett.* 156 (1997) 37–41. [https://doi.org/10.1016/S0378-1097\(97\)00399-6](https://doi.org/10.1016/S0378-1097(97)00399-6).
- 754 [90] S.M. Finegold, H. Jousimies-Somer, Recently Described Clinically Important Anaerobic Bacteria: Medical  
755 Aspects, *Clin. Infect. Dis.* 25 (1997) S88–S93. <https://doi.org/10.1086/516237>.
- 756 [91] C.L. Haggerty, P.A. Totten, M. Ferris, D.H. Martin, S. Hoferka, S.G. Astete, R. Ondondo, J. Norori, R.B.  
757 Ness, Clinical characteristics of bacterial vaginosis among women testing positive for fastidious  
758 bacteria., *Sex. Transm. Infect.* 85 (2009) 242–248. <https://doi.org/10.1136/sti.2008.032821>.
- 759 [92] M.K. Hudspeth, S. Hunt Gerardo, D.M. Citron, E.J. Goldstein, Growth characteristics and a novel method  
760 for identification (the WEE-TAB system) of *Porphyromonas* species isolated from infected dog and cat  
761 bite wounds in humans., *J. Clin. Microbiol.* 35 (1997) 2450–3. [https://doi.org/10.1128/jcm.35.10.2450-  
762 2453.1997](https://doi.org/10.1128/jcm.35.10.2450-2453.1997).
- 763 [93] M. Zeb, H. Tariq, W. Khan, E. Khan, A. Hussain, B. Jehan Farooqi, S. Khan Sherwani,  
764 H.T.W.K.E.K.A.H.B.J.F.S.K.S. Mubarak Zeb, An Emerging Trend of Anaerobes: *Porphyromonas levii*  
765 Causing Necrotic Vulvo Vaginitis. A Case Report, *Int. J. Basic Med. Sci. Pharm.* 4 (2014) 15–18.  
766 [www.ijbmsp.org](http://www.ijbmsp.org) (accessed February 26, 2020).
- 767 [94] L.R.V. Knudsen, Molecular characterisation of the uterine microbiome of dairy cows suffering from  
768 endometritis, metritis, and pyometra, Technical University of Denmark, 2014.
- 769 [95] T.F. Moreira, E.J. Facury Filho, A.U. Carvalho, M.L. Strube, M.W. Nielsen, K. Klitgaard, T.K. Jensen,  
770 Pathology and bacteria related to digital dermatitis in dairy cattle in all year-round grazing system in  
771 Brazil, *PLoS One.* 13 (2018) 1–15. <https://doi.org/10.1371/journal.pone.0193870>.
- 772 [96] S. Blum, J. Brenner, O. Friedgut, Y. Stram, O. Koren, I. Dagoni, A. Munbaz, D. Elad, Isolation of  
773 *Porphyromonas levii* from vaginal samples from cows in herds negative for bovine necrotic  
774 vulvovaginitis, *Vet. Rec.* 163 (2008) 745–747. <https://doi.org/10.1136/vr.163.25.745>.
- 775 [97] Y. Peng, Y.H. Wang, S.Q. Hang, W.Y. Zhu, Microbial diversity in uterus of healthy and metritic  
776 postpartum Holstein dairy cows, *Folia Microbiol. (Praha).* 58 (2013) 593–600.  
777 <https://doi.org/10.1007/s12223-013-0238-6>.
- 778 [98] M. Lev, Apparent requirement for vitamin K of rumen strains of *Fusiformis nigrescens* [36], *Nature.* 181  
779 (1958) 203–204. <https://doi.org/10.1038/181203a0>.
- 780 [99] S.E. Dowd, T.R. Callaway, R.D. Wolcott, Y. Sun, T. McKeehan, R.G. Hagevoort, T.S. Edrington,  
781 Evaluation of the bacterial diversity in the feces of cattle using 16S rDNA bacterial tag-encoded FLX  
782 amplicon pyrosequencing (bTEFAP), *BMC Microbiol.* 8 (2008) 1–8. [https://doi.org/10.1186/1471-  
783 2180-8-125](https://doi.org/10.1186/1471-2180-8-125).
- 784 [100] P.G. Koringa, J.R. Thakkar, R.J. Pandit, A.T. Hinsu, M.J. Parekh, R.K. Shah, S.J. Jakhesara, C.G. Joshi,  
785 Metagenomic characterisation of ruminal bacterial diversity in buffaloes from birth to adulthood using  
786 16S rRNA gene amplicon sequencing, *Funct. Integr. Genomics.* 19 (2019) 237–247.



- 787 <https://doi.org/10.1007/s10142-018-0640-x>.
- 788 [101] S.J. Jeon, F. Cunha, A. Vieira-Neto, R.C. Bicalho, S. Lima, M.L. Bicalho, K.N. Galvão, Blood as a route  
789 of transmission of uterine pathogens from the gut to the uterus in cows, *Microbiome*. 5 (2017) 109.  
790 <https://doi.org/10.1186/s40168-017-0328-9>.
- 791 [102] M. Sweeney, J. Watts, E. Portis, M. Lucas, R. Nutsch, D. Meeuwse, D. Bade, V. Oliver, D.W. Morck, D.  
792 Shinabarger, S. Poppe, M. Peterson, D. Sweeney, M. Knechtel, G. Zurenko, Identification of  
793 *Porphyromonas levii* isolated from clinical cases of bovine interdigital necrobacillosis by 16S rRNA  
794 sequencing, *Vet. Ther.* 10 (2009) E1-10. <http://www.ncbi.nlm.nih.gov/pubmed/20425726> (accessed  
795 February 27, 2020).
- 796 [103] T.M.A. Santos, R. Gilbert, R.C. Bicalho, Metagenomic analysis of the uterine bacterial microbiota in  
797 healthy and metritic postpartum dairy cows, *J. Dairy Sci.* 94 (2011) 291–302.  
798 <https://doi.org/10.3168/jds.2010-3668>.
- 799 [104] D.A. Bemis, C.B. Greenacre, M.J. Bryant, R.D. Jones, S.A. Kania, Isolation of a variant *Porphyromonas*  
800 sp. from polymicrobial infections in central bearded dragons (*Pogona vitticeps*), *J. Vet. Diagnostic*  
801 *Investig.* 23 (2011) 99–104. <https://doi.org/10.1177/104063871102300116>.
- 802 [105] B. Kim, H. Pai, K.T. Hwang, Y. Lee, *Porphyromonas pogonae* identification from a soft tissue infection:  
803 The first human case, *Anaerobe*. 42 (2016) 37–39. <https://doi.org/10.1016/j.anaerobe.2016.08.002>.
- 804 [106] P. Schröttner, K. Heidrich, W.W. Rudolph, F. Stölzel, E. Jacobs, F. Gunzer. First report on sepsis caused  
805 by *Porphyromonas pogonae*, *Anaerobe*. 44 (2017) 96–98.  
806 <https://doi.org/10.1016/j.anaerobe.2017.02.016>.
- 807 [107] A. Romero de Oliveira, J.M. Nürmberger, M. Issa, V. Pinto, M.M.K. Bond, J.T. Rabelato, M.B. Meirelles,  
808 L. Miglioli, C.S. Abboud, Late ascending aortic prosthesis infection by *Porphyromonas pogonae*: An  
809 unexpected infectious complication, *Anaerobe*. 56 (2019) 106–108.  
810 <https://doi.org/10.1016/j.anaerobe.2019.01.006>.
- 811 [108] T. Yano, K.K. Moe, K. Yamazaki, T. Ooka, T. Hayashi, N. Misawa, Identification of candidate pathogens  
812 of papillomatous digital dermatitis in dairy cattle from quantitative 16S rRNA clonal analysis, *Vet.*  
813 *Microbiol.* 143 (2010) 352–362. <https://doi.org/10.1016/j.vetmic.2009.12.009>.
- 814 [109] D. Lu, F. Tiezzi, C. Schillebeeckx, N.P. McNulty, C. Schwab, C. Shull, C. Maltecca, Host contributes to  
815 longitudinal diversity of fecal microbiota in swine selected for lean growth, *Microbiome*. 6 (2018) 1–  
816 15. <https://doi.org/10.1186/s40168-017-0384-1>.
- 817 [110] Y. Oishi, K. Watanabe, H. Kumada, E. Ishikawa, N. Hamada, Purification and characterization of a novel  
818 secondary fimbrial protein from *Porphyromonas gulae*, *J Oral Microbiol.* 4 (2012).  
819 <https://doi.org/10.3402/jom.v4i0.19076>.
- 820 [111] C. O’Flynn, O. Deusch, A.E. Darling, J.A. Eisen, C. Wallis, I.J. Davis, S.J. Harris, C. O’Flynn, O. Deusch,  
821 A.E. Darling, J.A. Eisen, C. Wallis, I.J. Davis, S.J. Harris, Comparative Genomics of the Genus  
822 *Porphyromonas* Identifies Adaptations for Heme Synthesis within the Prevalent Canine Oral Species  
823 *Porphyromonas cangingivalis*, *Genome Biol. Evol.* 7 (2015) 3397–3413.  
824 <https://doi.org/10.1093/gbe/evv220>.
- 825 [112] S. Arastu-Kapur, M. Nguyen, D. Raha, F. Ermini, U. Haditsch, J. Araujo, I.A.M. De Lannoy, M.I. Ryder,  
826 S.S. Dominy, C. Lynch, L.J. Holsinger, Treatment of *Porphyromonas gulae* infection and downstream  
827 pathology in the aged dog by lysine-gingipain inhibitor COR388, *Pharmacol. Res. Perspect.* 8 (2020)  
828 e00562. <https://doi.org/10.1002/prp2.562>.
- 829 [113] H. Inaba, R. Nomura, Y. Kato, H. Takeuchi, A. Amano, F. Asai, K. Nakano, R.J. Lamont, M. Matsumoto-  
830 Nakano, Adhesion and invasion of gingival epithelial cells by *Porphyromonas gulae*, *PLoS One*. 14  
831 (2019) e0213309. <https://doi.org/10.1371/journal.pone.0213309>.
- 832 [114] N. Hamada, Y. Takahashi, K. Watanabe, H. Kumada, Y. Oishi, T. Umemoto, Molecular and antigenic  
833 similarities of the fimbrial major components between *Porphyromonas gulae* and *P. gingivalis*, *Vet*  
834 *Microbiol.* 128 (2008) 108–117. <https://doi.org/10.1016/j.vetmic.2007.09.014>.
- 835 [115] E. Gaetti-Jardim, M.F. Pereira, E.M.M. Vieira, C.M. Schweitzer, A.C. Okamoto, M.J. Ávila-Campos,  
836 Occurrence of periodontal pathogens in ethnic groups from a native Brazilian reservation, *Arch. Oral*  
837 *Biol.* 60 (2015) 959–965. <https://doi.org/10.1016/j.archoralbio.2015.01.002>.
- 838 [116] N. Noguchi, Y. Noiri, M. Narimatsu, S. Ebisu, Identification and localization of extraradicular biofilm-  
839 forming bacteria associated with refractory endodontic pathogens, *Appl. Environ. Microbiol.* 71 (2005)  
840 8738–8743. <https://doi.org/10.1128/AEM.71.12.8738-8743.2005>.
- 841 [117] Y. Yamasaki, R. Nomura, K. Nakano, S. Naka, M. Matsumoto-Nakano, F. Asai, T. Ooshima, Distribution  
842 of periodontopathic bacterial species in dogs and their owners, *Arch. Oral Biol.* 57 (2012) 1183–1188.  
843 <https://doi.org/10.1016/j.archoralbio.2012.02.015>.
- 844 [118] F.E. Dewhirst, Canine oral bacteria identified in human skin microbiome libraries, 324 (2012) 36067.  
845 <ftp://www.homd.org/poster/2012c.pdf>.

- 846 [119] H.E. Booij-Vrieling, W.A. van der Reijden, D.J. Houwers, W.E.A.J. de Wit, C.J. Bosch-Tijhof, L.C.  
847 Penning, A.J. van Winkelhoff, H.A.W. Hazewinkel, Comparison of periodontal pathogens between cats  
848 and their owners, *Vet. Microbiol.* 144 (2010) 147–152. <https://doi.org/10.1016/J.VETMIC.2009.12.046>.
- 849 [120] S. Yachida, S. Mizutani, H. Shiroma, S. Shiba, T. Nakajima, T. Sakamoto, H. Watanabe, K. Masuda, Y.  
850 Nishimoto, M. Kubo, F. Hosoda, H. Rokutan, M. Matsumoto, H. Takamaru, M. Yamada, T. Matsuda,  
851 M. Iwasaki, T. Yamaji, T. Yachida, T. Soga, K. Kurokawa, A. Toyoda, Y. Ogura, T. Hayashi, M.  
852 Hatakeyama, H. Nakagama, Y. Saito, S. Fukuda, T. Shibata, T. Yamada, Metagenomic and  
853 metabolomic analyses reveal distinct stage-specific phenotypes of the gut microbiota in colorectal  
854 cancer, *Nat. Med.* 25 (2019) 968–976. <https://doi.org/10.1038/s41591-019-0458-7>.
- 855 [121] S. Graspeuntner, The cervical microbiome in female infectious infertility: clinical trial and experimental  
856 mouse models, University of Lübeck, 2017. <https://d-nb.info/1142648095/34> (accessed March 5, 2020).
- 857 [122] V. Iebba, F. Guerrieri, V. Di Gregorio, M. Levrero, A. Gagliardi, F. Santangelo, A.P. Sobolev, S. Circi, V.  
858 Giannelli, L. Mannina, S. Schippa, M. Merli, Combining amplicon sequencing and metabolomics in  
859 cirrhotic patients highlights distinctive microbiota features involved in bacterial translocation, systemic  
860 inflammation and hepatic encephalopathy., *Sci. Rep.* 8 (2018) 8210. <https://doi.org/10.1038/s41598-018-26509-y>.
- 861 [123] S. Harakeh, S. Bahijri, G. Ajabnoor, A. Al-Hejin, M.W. Pfaffl, S. Farraj, G. Hegazy, S. Masaudi, S.  
862 Barnawi, A. Ahmed, S. Alfadul, E. Azhar, Obesity and microbiota among healthy Saudis with various  
863 degrees of obesity, in: 9th Euro Glob. Gastroenterol. Conf., Valencia, Spain, 2016.  
864 <https://doi.org/10.4172/2161-069X.C1.043>.
- 865 [124] S. Parida, D. Sharma, The power of small changes: Comprehensive analyses of microbial dysbiosis in  
866 breast cancer., *Biochim. Biophys. Acta. Rev. Cancer.* 1871 (2019) 392–405.  
867 <https://doi.org/10.1016/j.bbcan.2019.04.001>.
- 868 [125] D.A. Talan, D.M. Citron, F.M. Abrahamian, G.J. Moran, E.J. Goldstein, Bacteriologic analysis of infected  
869 dog and cat bites. Emergency Medicine Animal Bite Infection Study Group., *N. Engl. J. Med.* 340  
870 (1999) 85–92. <https://doi.org/10.1056/NEJM199901143400202>.
- 871 [126] J. Dhillon, J. Hoopes, T. Epp, Scoping decades of dog evidence: a scoping review of dog bite-related  
872 sequelae, *Can. J. Public Heal.* (2018) 1–12.
- 873 [127] M.D.A. Petit, T.J.M. van Steenberg, L.M.H. Scholte, U. van der Velden, J. de Graaff, Epidemiology and  
874 transmission of *Porphyromonas gingivalis* and *Actinobacillus actinomycetemcomitans* among children  
875 and their family members: A report of 4 surveys, *J. Clin. Periodontol.* 20 (1993) 641–650.  
876 <https://doi.org/10.1111/j.1600-051X.1993.tb00709.x>.
- 877 [128] M. Saarela, B. von Troll-Lindén, H. Torkko, A. -M Stucki, S. Alaluusua, H. Jousimies-Somer, S.  
878 Asikainen, Transmission of oral bacterial species between spouses, *Oral Microbiol. Immunol.* 8 (1993)  
879 349–354. <https://doi.org/10.1111/j.1399-302X.1993.tb00610.x>.
- 880 [129] T.J.M. van Steenberg, M.D.A. Petit, L.H.M. Scholte, U. van der Velden, J. de Graaff, Transmission of  
881 *Porphyromonas gingivalis* between spouses, *J. Clin. Periodontol.* 20 (1993) 340–345.  
882 <https://doi.org/10.1111/j.1600-051X.1993.tb00370.x>.
- 883 [130] M. Tuite-McDonnell, A.L. Griffen, M.L. Moeschberger, R.E. Dalton, P.A. Fuerst, E.J. Leys, Concordance  
884 of *Porphyromonas gingivalis* Colonization in Families Downloaded from, 1997. <http://jcm.asm.org/>  
885 (accessed March 9, 2020).
- 886 [131] H. Asano, K. Ishihara, T. Nakagawa, S. Yamada, K. Okuda. Relationship Between Transmission of  
887 *Porphyromonas gingivalis* and fimA Type in Spouses, *J. Periodontol.* 74 (2003) 1355–1360.  
888 <https://doi.org/10.1902/jop.2003.74.9.1355>.
- 889 [132] M.C. Rijnsburger, S. Delwel, K. Boutaga, T.J.M. Van Steenberg, P.H.M. Savelkoul, A.J. Van  
890 Winkelhoff, Comparison of restriction enzyme analysis and amplified fragment length polymorphism  
891 typing of *Porphyromonas gingivalis* isolated from spouses, *Oral Microbiol. Immunol.* 22 (2007) 369–  
892 373. <https://doi.org/10.1111/j.1399-302X.2007.00372.x>.
- 893 [133] M. Belcheva, Transmission of *Porphyromonas gingivalis* from caregivers to children, *J. IMAB - Annu.*  
894 *Proceeding (Scientific Pap.* 18, 2 (2012) 157–162. <https://doi.org/10.5272/jimab.2012182.157>.
- 895 [134] X. Feng, L. Zhu, L. Xu, H. Meng, L. Zhang, X. Ren, R. Lu, Y. Tian, D. Shi, X. Wang, Distribution of 8  
896 periodontal microorganisms in family members of Chinese patients with aggressive periodontitis, *Arch.*  
897 *Oral Biol.* 60 (2015) 400–407. <https://doi.org/10.1016/j.archoralbio.2014.11.015>.
- 898 [135] K. Adhikari, C.S. Saimbi, B.P. Gupta, Estimation of Transmission of *Porphyromonas gingivalis* from  
899 Mother to Child through Saliva., *JNMA. J. Nepal Med. Assoc.* 56 (2018) 781–786.  
900 <http://www.ncbi.nlm.nih.gov/pubmed/30387469> (accessed March 9, 2020).
- 901 [136] S. Asikainen, C. Chen, S. Alaluusua, J. Slots, Can one acquire periodontal bacteria and periodontitis from  
902 a family member? *J. Am. Dent. Assoc.* 128 (1997) 1263–1271.  
903 <https://doi.org/10.14219/jada.archive.1997.0403>.
- 904