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Revisiting the genus *Photobacterium*: taxonomy, ecology and pathogenesis

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Summary. The genus *Photobacterium*, one of the eight genera included in the family *Vibrionaceae*, contains 27 species with valid names and it has received attention because of the bioluminescence and pathogenesis mechanisms that some of its species exhibit. However, the taxonomy and phylogeny of this genus are not completely elucidated; for example, *P. logei* and *P. fischeri* are now considered members of the genus *Aliivibrio*, and previously were included in the genus *Vibrio*. In addition, *P. damselae* subsp. *piscicida* was formed as a new combination for former *Vibrio damsela* and *Pasteurella piscicida*. Moreover, *P. damselae* subsp. *damselae* is an earlier heterotypic synonym of P. *histaminum*. To avoid these incovenences draft and complete genomic sequences of members of *Photobacterium* are increasingly becoming available and their use is now routine for many research laboratories to address diverse goals: species delineation with overall genomic indexes, phylogenetic analyses, comparative genomics, and phenotypic inference. The habitats and isolation source of the *Photobacterium* species include seawater, sea sediments, saline lake waters, and a variety of marine organisms with which the photobacteria establish different relationships, from symbiosis to pathogenic interactions. Several species of this genus contain bioluminescent strains in symbiosis with marine fish and cephalopods; in addition, other species enhance its growth at pressures above 1 atmosphere, by means of several high-pressure adaptation mechanisms and for this, they may be considered as piezophilic (former barophilic) bacteria. Until now, only *P. jeanii*, *P. rosenbergii*, *P. sanctipauli*, and the two subspecies of *P. damselae* have been reported as responsible agents of several pathologies on animal hosts, such as corals, sponges, fish and homeothermic animals. In this review we have revised and updated the taxonomy, ecology and pathogenicity of several members of this genus. [**Int Microbiol** 20(1): 1-10 (2017)]

Keywords: *Photobacterium* · taxonomy · symbiosis · pathogenesis · virulence factors

Taxonomic and phylogenetic perspectives

The genus *Photobacterium* has a long standing in microbiology, having received attention for more than one century by the bioluminescence that some of its species exhibit. Indeed, etymologically it means light producing bacterium. To date, it contains 27 species with valid names (Table 1). The historical development of the taxonomy of this genus is relatively easy to follow. The type species, *Photobacterium phosphoreum*, was included in the Approved Lists of Bacterial Names [79] together with *P. angustum*, *P. (Aliivibrio) fischeri* and *P. leiognathi*. The only species described in the

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following decade, *P. logei*, is now considered a member of the genus *Aliivibrio* and so is *P. fischeri* [64]. In turn, *P. damselae* [80] was formed as a new combination for former *Vibrio damsela* and *Pasteurella piscicida*. This species is the only one for which subspecies have been proposed so far with the publication of *P. damselae* subsp. *piscicida* [27]. Moreover, *P. damselae* subsp. *damselae* is an earlier heterotypic synonym of *P. histaminum* [37,60]. In the last two decades the pace of descriptions has intensified with the proposal of 20 novel species and two new combinations with valid names (Table 1), which gives an average of about two new species names per year. According to minute 17 of the Subcommittee meetings on the taxonomy of *Aeromonadaceae*, *Vibrionaceae* and related organisms held in Istanbul, Turkey, in 2008 [31], the type strain of *P. aplysiae* is not available and a neotype strain has not been proposed to date.

At the time of validation [79], the description of the genus was the one given in the 8th edition of Bergey's Manual. Although an emendation has never been formally proposed it has been revised and updated recently [84].

Phylogeny. *Photobacterium* is one of the nine genera contained in the family *Vibrionaceae* (order "Vibrionales", class *Gammaproteobacteria*). It is also the largest one after the type genus *Vibrio*. Following a practice that is common and more developed for *Vibrio* spp. [64,73], several authors have established different clades within the genus *Photobacterium* [6,73,86]. Clades are usually named after the older species name, referring to its validation date, regardless of the position of that strain into the clade. Currently, four clades have been described in the genus *Photobacterium*: **Damselae** (*P. damselae* subsp. *damselae* and *P. damselae* subsp. *piscicida*), **Phosphoreum** (*P. angustum*, *P. aquimaris*, *P. iliopiscarium*, *P. kishitanii*, *P. leiognathi*, *P. phosphoreum* and *P. piscicola*), **Profundum** (*P. aestuarii*, *P. aplysiae*, *P. frigidiphilum*, *P. indicum*, *P. lipolyticum*, *P. profundum*, *P. sanguinicancri* and *P. swingsii*), and **Rosenbergii** (*P. aphoticum*, *P. ganghwense*, *P. halotolerans*, *P. jeanii*, *P. lutimaris*, *P. marinum*, *P. rosenbergii*). But the clustering of *P. aquae*, *P. gaetbulicola*, *P. gallatheae*, *P. panuliri*, and *P. sanctipauli* has not been elucidated yet. It has to be noted that this classification into clades has no standard in nomenclature although it can make more amenable the study of large genera by grouping together lines of descents. However, this achievement requires the application of robust molecular approaches and large sets of strains (not just type strains). A comprehensive study meeting both requisites is still pending to the best of our knowledge but at least it is optimistic to see that most recent species descriptions include phylogenetic analysis using alternative genes [48,56,71,83] or MLSA schemes [7,10,26,29,45,50,92]. This means that at least for some genes there are sequences available in public repositories for most (ideally all) the type strains and even for a number of additional isolates of some of them.

The genes more frequently employed to perform phylogenetic studies within the genus *Photobacterium* are *recA* (protein RecA, recombinase A), *rpoA* (RNA polymerase α subunit), *gyrB* (DNA gyrase subunit B), *pyrH* (uridylate kinase, uridine monophosphate kinase), *gapA* (glyceraldehyde 3-phosphate dehydrogenase, NAD-dependent glyceraldehyde-3-phosphate dehydrogenase), *ftsZ* (cell division protein FstZ), *topA* (DNA topoisomerase I), and *mreB* (rod shape-determining protein MreB).

At the same time, draft and complete genomic sequences of members of the genus *Photobacterium* are increasingly becoming available and their use is becoming routine for many research laboratories to address diverse goals: species delineation with overall genomic indexes, phylogenetic analyses, comparative genomics, and phenotypic inference [2,29,50]. At the time of writing the present review (1 March, 2017), a search at the Assemblies database in NCBI [http://www.ncbi.nlm.nih.gov/] shows that there are 67 results for *Photobacterium*, 15 of which are from strains flagged as type material. A more careful examination reveals that two of these can be considered redundant entries (they are from two equivalent designations of the same strain, the type strain of *P. damselae*, sequenced in different laboratories) and another one is from "*P. marinum*" that has not been validated to date. Since there are 27 species in the genus, the resulting 13 genomic sequences represent about half of them. Thus the gap to be filled to give full coverage to the type strains of the genus in terms of availability of their genomic sequences is not too large and we can anticipate it might be reached soon. Although most of these genomic sequences are assembled into contigs or scaffolds, there are two completed, *P. gaetbulicola* Gung47^T and *P. profundum* SS9.

One advantage of having large data sets of genomes is that they can be explored to search for the most suitable single gene phylogenetic marker. This objective has been addressed at the family level by Machado and Gram [49] who concluded that the *fur* (ferric uptake regulator Fur) gene was suitable for

Table 1. Species, habitats and geographic sources of *Photobacterium* species

Species	Habitats	Geographic sources	Reference
P. aestuarii	Tidal flat sediment	Yeongam Bay (R. Korea)	[46]
P. angustum	Seawater	North Pacific Ocean (20º30'N 157º30'E)	[79]
P. aphoticum	Seawater	Malvarrosa beach, Valencia (Spain)	[48]
P. aplysiae	Eggs of sea hare (*Aplysia kurodai*)	Mogiyeo (R. Korea)	[75]
P. aquae	Malabar grouper (*Epinephelus malabaricus*) in mariculture system	Tianjin (China)	[45]
P. aquimaris	Seawater	Sagami Bay (Japan)	[92]
P. damselae	Damselfish (*Chromis punctipinnis*) skin ulcer[a]	California (USA)	[47,80]
P. frigidiphilum	Deep-sea sediments (1450 m)	Edison Seamount (western Pacific Ocean)	[74]
P. gaetbulicola	Tidal flat	Gungharbour (R. Korea)	[36]
P. galatheae	Mussel	Solomon Sea (Solomon Islands)	[50]
P. ganghwense	Seawater	Ganghwa Island (R. Korea)	[63]
P. halotolerans	Water from a subterranean saline lake	Lake Martel, Mallorca (Spain)	[71]
P. iliopiscarium	Intestines of fish (herring, coal fish, cod and salmon) living in cold seawater	Norway	[84]
P. indicum	Marine mud (400 m depth)	Indian Ocean	[32]
P. jeanii	Healthy corals (*Palythoa caribaeorum*, *Phyllogorgia dilatata* and *Merulina ampliata*)	Brazil and Australia	[10]
P. kishitanii	Light organs and skin of several marine fish species	Japan, Cape Verde, Hawaii, Florida, South Africa	[7]
P. leiognathi	Light organ of teleostean fish (*Leiognathus*)	Gulf of Thailand (Thailand)	[66]
P. lipolyticum	Intertidal sediment	Yellow Sea (R. Korea)	[91]
P. lutimaris	Tidal flat sediment	Saemankum (R. Korea)	[33]
P. panuliri	Eggs of spiny lobster (*Panulirus penicillatus*)	Andaman Sea (India)	[13]
P. phosphoreum	Skin of marine animals, intestines of marine fish, luminous organs, seawater	Hawaii (USA), Japan and other locations	[79]
P. piscicola	Skin and intestine of marine fish, spoiled packed cod	North Sea (Holland), Denmark, Aberdeen Bay (UK)	[26]
P. profundum	Deep-sea sediment (5110 m)	RyukyuTrench (24º15.23'N 126º47.30'E)	[58]
P. rosenbergii	Tissue and water extracts of coral species	Magnetic Island (Australia)	[83]
P. sanctipauli	Coral (*Madracis decactis*)	St. Peter & St. Paul Archipelago (Brazil)	[56]
P. sanguinicancri	Crab (*Maja brachydactyla*) haemolymph, mussels (*Mytilus edulis*)	Spain, Netherlands	[29]
P. swingsii	Pacific oysters (*Crassostrea gigas*), crab (*Maja brachydactyla*) haemolymph	Mexico, Spain	[28]

Additional strains are reported in Smith et al. [80] from human puncture wound, diseased shark, diseased turtle, diseased fish, aquarium seawater and fish surface.

that purpose and even developed a PCR method to be used for the amplification and sequencing of the gene. Phylogenetic analysis can also be a method to elucidate horizontal gene transfer as it was performed in the study by Urbanczyk et al. [85], who assessed the incidence of interspecies transfer of the *lux* genes (*luxCDABEG*), which encode proteins involved in luminescence and concluded that horizontal transfer of the lux genes in nature is rare and that horizontal acquisition of the lux genes apparently has not contributed to speciation in recipient taxa.

Ecology of *Photobacterium*

The members of the genus *Photobacterium* thrive worldwide in oceans and show substantial ecophysiological diversity including free-living, symbiotic, piezophilic, and parasitic life styles. The habitats and isolation source of these species include seawater, sea sediments, saline lake waters, and a variety of marine organisms with which the photobacteria establish different relationships, from symbiotic ones, such as commensalism or mutualism, to pathogenic interactions.

Generally, in the marine environment (seawater and sediment), the species of *Photobacterium* are free-life forms, but they may colonize several animal surfaces developing neutral or negative relationships with the host. These nonspecific or pathogenic associations contrast with the highly specific, mutually beneficial association of certain *Photobacterium* species in bioluminescent symbiosis with aquatic animals [17].

There is not a clear discrimination between the *Photobacterium* species regarding to their relationship with the isolation source or habitat (Table 1). Thus, most of the nonluminous photobacteria (lack of *lux* operon genes) have been isolated from marine waters or sediments, but several strains of these species have been described in association with diseased or healthy corals, zoanthids, sea hares, mollusks, crabs and fish [28,29,39,45,69,75,83]. Nevertheless, strains of luminous *Photobacterium* species harbouring genes for luminescence (*lux CDABEG*) [19], such as *P. kishitanii*, *P. leiognathi*, *P. phosphoreum* and *P. piscicola*, have also been isolated from squids, corals and fish [6,26,34]. Therefore, the luminescence production property is not a key ability of this bacterial group to the specific colonization of none habitats, excepting the light-organs of squids and fish.

Photobacteria as symbiotic of light-organs. Several species of this genus contain bioluminescent strains including *P. angustum*, *P. aquimaris*, *P. damselae*, *P. ganghwense*, *P. kishitanii*, *P. leiognathi*, *P. phosphoreum*, and *P. piscicola*. From them, *P. kishitanii* and *P. leiognathi* establish bioluminescent symbiosis with marine fish, squid and octopus [57]. These associations are typically highly specific at the animal family-bacterial species level; *P. leiognathi* with families *Leiognathidae*, *Acropomatidae* and *Apogonidae* (Perciformes), and *Moridae* (Gadiformes) [21,34,82,88]; and *P. kishitanii* with the fish families *Chloropthslmidae* (Acilopiformes), *Macrouridae*, *Sleindachneriidae* and *Moridae* (Gadiformes), *Trachichthyidae* (Beryciformes), *Opisthoprectidae* (Gemeriformes) and *Acropomatidae* (Perciformes) [6,20]. The animals accumulate dense populations of luminous bacteria in gland-like tissue complex called light organs [24], providing them with nutrients and oxygen for their growth and light production. The bacterial light in symbiotic animals is associated with sex-specific signalling, predator avoidance, locating or attracting prey, to name a few [82,86]. Symbiotic luminous bacteria have not an obligatory dependency of the host for their reproduction [23], but it seems that exist certain specificity between the symbiotic fish and the luminous *Photobacterium* species. The animals that establish a relationship with *P. leiognathi* as light-organ symbionts tend to be found in shallower waters, whereas the fish that are symbiotic with *P. kishitanii* are usually found in deeper waters [23,34]. This apparent specificity, which presumably would have a genetic basis, is believed to result from the host animal selecting its species of symbiotic bacteria and preventing that other bacteria could colonize its light organs. Several authors have proposed that the bioluminescent symbiosis might involve coevolutionary interactions [21,86], due to the animal dependence of the bacterial light, its specialized anatomical adaptations for harbouring bacteria, and the host family-bacterial species specificity.

Although bioluminescent associations appear to be highly specific, in some cases two *Photobacterium* species may be present within individual light organs of fish [23,34], representing a phenomenon named cosymbiosis. Furthermore, different species of the same fish family sometimes harbour different *Photobacterium* species or even bacteria belonging to other bacterial genera, like *Aliivibrio* or *Vibrio* [23,24]. In addition, distinct strains of a single species may be present with individual light organs of both adult and larval fish [22,24]. This species- and strain-level variation demonstrates the lack of strict specificity in bioluminescent symbiosis.

Bioluminescent symbioses of fish and squid with luminous bacteria apparently do not exhibit codivergence (cospeciation), since phylogenies for host and their symbiotic bacteria present no meaningful topological congruence [23,34]. The patterns of symbiont-host affiliation in bioluminescent symbioses observed from nature therefore are not likely to have arisen through coevolutionary interactions. However, the absence of nonluminous bacteria in light-organs of fish and squid indicates that some kind of selection must be operative, like the environmental congruence [30]. The congruence between the environmental distribution of a predominant species of luminous bacteria and the fish developmental stage at which its light-organ is receptive to bacterial colonization, determines which bacterial species and strains establish the symbiosis [23,34]. Some environmental factors, such as the temperature, influence the abundance of the different species of luminous bacteria in the marine environment. Thus, lower temperatures found in deeper waters favour the prevalence of psychrotropic species like *P. kishitanii*, which is the main light-organ symbiont in these waters. On the contrary, warmer waters favour the growth of mesophilic *Photobacterium* species, such as *P. leiognathi*

being fish larvae in these waters more receptive to acquire these bacteria as light-organ symbionts.

In short, bioluminescent symbioses, therefore, differ from endosymbiotic associations, which are mutually obligate relationships in which the symbiotic bacteria are housed intracellularly and are transferred maternally. Symbiotic luminous bacteria are housed extracellularly, and in most cases they are known not be obligately dependent on the host for their reproduction. Unlike obligate intracellular bacteria, the symbiotic luminous bacteria colonize a variety of other marine habitats, including intestinal tracts, skin, and body fluids of marine animals, sediments, and seawater, where they coexist and compete with many other kinds of microorganisms. A second major difference with endosymbiotic associations is that symbiotic luminous bacteria are acquired from the environment with each new generation of the host instead of being transferred vertically through the maternal inheritance mechanisms. Another major difference between bioluminescent symbiosis and endosymbiosis is that luminous bacteria and their host animals show no evidence of co-speciation. Endosymbiosis is generally assumed to involve coevolutionary interactions, that is, reciprocal genetic changes in host and symbiont that result from the obligate and mutual dependence of each partner on the other. Detailed molecular phylogenies of bacterially luminous fish and squids, however, are very different from the phylogenies of their symbiotic light-organ bacteria [18]. This lack of host-symbiont phylogenetic congruence demonstrates that the evolutionary divergence of symbiotic luminous bacteria has occurred independently of the evolutionary divergence of their host animals.

Bioluminescent symbioses appear to represent a paradigm of symbiosis that differs fundamentally from associations involving obligate, intracellularly transferred symbionts. While fish and squids are dependent ecologically on luminous bacteria, the bacteria are not obligately dependent on their bioluminescent hosts. The evolutionary adaptations for bioluminescent symbiosis, for example presence of light organs, accessory tissues for controlling, diffusing, and shaping the emission of light, and behaviour associated with light emission, all are borne by the animal. No genetic adaptations have been identified in the bacteria that are necessary for and specific to their existence in light organs compared to the other habitats they colonize. Therefore, luminous bacteria seem to be opportunistic colonizers, able to persist in animal light-organs as well as in a variety of other habitats to which they are adapted.

Other question unanswered is regarding to the benefit of luminescence for the non-symbiotic photobacteria. This question has not been elucidated fully, but several explanations have been arisen. One of the most commonly cited explanations is that the bioluminescence increases the propagation and dispersal of bacteria by attracting fish or other marine animals to consume luminous material. This hypothesis based mostly on the prevalence of luminous bacteria in fish gut has not been demonstrated experimentally. Nevertheless, Zarubin et al. [93] established that zooplankton that contacts and feeds on *P. leiognathi* starts to glow, and the glowing individuals are highly vulnerable to predation by nocturnal fish. Glowing photobacteria are transferred to the intestines of fish and zooplankton, when they survive digestion and gain effective means for growth and dispersal. The use of bioluminescence, therefore, appears to be highly beneficial for marine bacteria, especially in oligotrophic areas of the deep sea.

Deep-sea sediments as habitats of *Photobacterium* species. Members of the genus *Photobacterium* are common inhabitants of marine waters sediments, including *P. aestuarii*, "*P. atrarenae*", *P. frigidiphilum*, *P. gaetbulicola*, *P. indicum*, *P. lipolyticum*, *P. lutimaris*, "*P. marinum*", *P. phosphoreum*, and *P. profundum*. From them, *P. frigidiphilum*, *P. phosphoreum*, and *P. profundum* may be considered as piezophilic (former barophilic) bacteria, because these species enhance its growth at pressures above 1 atmosphere, by mean of several high-pressure adaptation mechanisms [9,74]. The adaptative traits include those related to growth, macromolecules and storage lipids, membrane and soluble proteins, the respiratory-chain compounds, replication, transcription and traslation [9,54,90]. These species are the only ones known to produce a long-chain polyunsaturated fatty acid (PUFA), the eicosapentaenoic acid (EPA) [58]. Recently, Le Bihan et al. [42] analysed the proteome of *P. profundum* under different pressure regimes, and obtained altered modes of protein function in that conditions. The authors identified differentially expressed proteins involved in high pressure adaptation; thus, proteins belonging to the glycolysis/gluconeogenesis pathway were up-regulated at high pressure, whilts several proteins involved in the oxidative phosphorylation pathway were up-regulated at atmospheric pressure. In addition, the expression of some proteins involved in nutrient transport or assimilation was also directly regulated by pressure.

Pathogenesis of *Photobacterium*

Some species of this genus, including *P. rosenbergii*, *P. jeanii*, *P. sanctipauli*, and the two subspecies of *P. damselae*, have been reported to produce several pathologies on animal hosts, such as corals, sponges, fish, and homeothermic animals [10,56,69,83]. Unfortunately, little is known on the pathogenesis mechanisms of *P. rosenbergii* and *P. sanctipauli* that cause the coral bleaching and further dead of the corals [83]; however, both *P. damselae* subspecies have received a great attention as emerging pathogens for many aquatic organisms, including fish, mollusks and crustaceans, and even for humans [41,55,69,72,89].

Photobacterium damselae subsp. *damselae* (*Pdd*) is a normal inhabitant of seawater, marine sediments, seaweeds and marine animals [41,76], and prefers warm water conditions (20–30 °C). This microorganism is considered a primary pathogen of several species of wild- and cultured-fish causing wound infections and hemorrhagic septicaemia. It is also an opportunistic human pathogen, causing necrotizing fasciitis [69]. The other subspecies, *P. damselae* subsp. *piscicida* (*Pdp*), is the causal agent of fish photobacteriosis, a serious bacterial disease affecting different economically important cultured marine fish species [72].

Virulence factors of *P. damselae*. The main bacterial iron-uptake systems include the production of iron-sequestering compounds named siderophores as well as the use of heme group as iron source. Siderophores are chemically diverse low-molecular-weight iron chelators that can effectively solubilize iron or remove it from other chelators and transport it into the cell through the corresponding membrane receptor proteins [43]. Some bacteria not only produce their own siderophores, but also express receptors capable of transport xenosiderophores produced by other organisms [11]. *Pdp* and *Pdd* are able to acquire iron from hemin and hemoglobin as unique iron sources in vitro [43]. Their heme uptake systems are encoded by a gene cluster formed by 10 genes [67]. This heme uptake system includes a TonB-dependent outer membrane receptor to transport the heme group into the periplasm, a periplasmic binding protein, and an ATP-binding cassette (ABC) to drive heme across the cytoplasmic membrane [4,67]. It is also known that in *Pdp*, the acquisition of iron from its host is efficiently achieved by means of the synthesis of the siderophore piscibactin [81], and its transport into the cell through the outer membrane receptor FrpA [62]. The synthesis and transport are encoded by a pathogenicity island, which is part of the transmissible plasmid pPHDP70. It has been demonstrated that this plasmid greatly contributes to the virulence of *Pdp* for fish, and that it can be horizontally transmitted to other marine bacteria [62]. It has also been reported that *Pdd* expresses several high-molecular-weight outer membrane proteins under iron limitation conditions [69], and that some strains likely produce the siderophore vibrioferrin [65], although other virulent strains lack this system, being its contribution to virulence yet uncertain. The presence of these or other iron uptake mechanisms in other species of *Photobacterium* is unknown, although some of the iron-uptake related genes reported in both *P. damselae* subspecies are present in other species genomes. The role of these mechanisms in non-pathogenic species is uncertain.

Bacterial extracellular products (ECP) containing phospholipase, cytotoxic, and hemolytic activities may account for the damage to infected cells, the consequent release of the microorganisms, and the invasion of adjacent cells [25]. ECP of *P. damselae* strains were shown to be lethal for different fish species and for fish and homeothermic cell lines [40]. Recently, Vences et al. [87] have demonstrated that phospholipase and collagenase activities contributed to virulence of *Pdd*. It is well known the existence of a close relationship between the ability of a microorganism to provoke diseases and the production of bacterial toxins. In the case of *Pdd*, several heat-labile cytolytic toxins have been reported, one of them named damselysin (Dly), a phospholipase-D active against sphingomyelin, presented strong hemolytic activity [38]. It has also been demonstrated that presence of gene *dly* is not a pre-requisite for the hemolytic activity and for the pathogenicity of *Pdd*, since *dly*-negative strains possess virulence potential for animals, and also show toxicity for homeotherm and poikilotherm cell lines [40,61]. Rivas et al. [68] identified and characterized a 150 kb plasmid, pPHDD1, which contains the genes for both Dly and $HlyA_{pl}$, being the lastest a small pore-forming toxin (PFT) with hemolysin activity, named phobalysin [70]. The mutation of both *dly* and $hlyA_{pl}$ genes in a pPHDD1-harbouring strain renders the strain non-virulent for fish, and only slightly virulent for mice, and the hemolytic phenotype on sheep blood agar of a *dly* and $hlyA_{pl}$ double mutant resembles that of naturally plasmidless strains [68,69]. Thus, pPHDD1-harbouring isolates of *Pdd* produce three different hemolysins, each of them individually prove to be sufficient to cause death in mice. Each hemolysin contributes to virulence in a different degree, although only

the Dly-producing strains caused death in fish, demonstrating the importance of the plasmid for the virulence of this bacterium for fish. Despite the importance of pPHDD1, many *Pdd* virulent strains are plasmidless. The hemolytic activity exhibited by these strains is due to hemolysin PhlyC, encoded by the chromosome-harbored $hlyA_{ch}$ gene [69,87], which contributes to virulence for fish [87].

In *Pdp* a key pathogenicity factor is an exotoxin, a plasmid-encoded apoptosis-inducing protein of 56 kDa (AIP56), responsible for apoptogenic activity against fish macrophages and neutrophils [16]. The AIP56 toxin is a zinc metalloprotease involved in binding and internalization into the cytosol of target cells [77], and acts inducing the activation of caspases 8, 9 and 3, the loss of mitochondrial membrane potential, the release of cytochrome c into the cytosol, and the overproduction of ROS, which suggest that the exotoxin activates both extrinsic and intrinsic apoptotic pathways [12]. Through the activation of the cell death process involving macrophages and neutrophils, the pathogen is able to subvert the immune defenses of the host and to produce infectious disease.

Little is known on the adherent properties to cells of *Pdd*, although Khouadja et al. [35] established that this subspecies possess the ability to adhere to fish mucus. On the contrary, *Pdp* is adherent mainly for fish cells [53], and the adherence is heat-sensitive, but it is not affected by proteases or by treating the bacteria with antisera raised against its LPS [53]. Nevertheless, the precise nature of the mechanism responsible for adherence and interaction with host cell receptors and virulence factors contributing to the invasion of fish nonphagocytic cells is still unknown [1,3].

Pdp is considered weakly to moderately invasive to several poikilothermic cell lines. López-Doriga et al. [44] showed that the uptake of *Pdp* by EPC cells is time and bacterial-concentration dependant. These authors have been suggested that internalization of this microorganism by EPC cells is receptor-ligand mediated (zipper mechanism). *Pdp* isolates also show the ability to spread to adjacent cells from initially infected cells, forming plaques of dead cells [53]. Similar to that previously reported for other Gram-negative pathogenic bacteria, invasion by *Pdp* can be inhibited by cytochalasin D, indicating that actin and microfilament-dependent mechanisms are required for bacterial internalization [53].

Virulent *Pdp* strains are serum resistant and can grow in fresh fish serum, whereas non-virulent strains are sensitive to serum killing and their growth is totally inhibited in fresh serum [3]. The inhibitory effect of the serum on the non-virulent strains, however, is totally lost if the complement is inactivated by heating at 56 °C for 1 h [51]. Serum resistance is also associated with capsule production, since capsulated strains prevent formation of C3 convertase (C3bBb) by failing to bind serum protein B, or by a higher affinity for serum protein H than for B. Therefore, capsulated strains evade more efficiently the bacteriolytic activity of fresh serum [53]. *Pdp* capsule formation depends on growth conditions; thus, cells grown under iron-limited conditions or old-cultures had a significantly reduced amount of capsular material [14]. Studies that describe the contribution of bacterial capsules to adhesion and invasion of host cells are contradictory [44,52]. The presence of a capsule prevents the opsonization by C3b, and bacteria will not efficiently be engulfed by fish macrophages [5]. Furthermore, the capsule plays an important role in lethality of *Pdp* to fish, as non-virulent strains induced for capsule expression resulted in a reduction of LD_{50} values [52].

The ability of *Pdp* to avoid phagocytosis and thus to cause disease, may be explained by the induction of extensive apoptosis on macrophages and neutrophils present in *Pdp*-infected foci, resulting in lysis of these leukocytes by post-apoptotic secondary necrosis [15]. There are contradictory results on the interaction of *Pdp* with phagocytes; whereas intact bacteria within phagocytes have been observed in vivo [59], suggesting that *Pdp* may survive inside macrophages, other in vitro studies indicate that fish macrophages are able to kill the bacteria by means of activation of the respiratory burst or an iron-SOD activity [5,8,78].

Future perspectives

In this review, we have described some aspects of the genus *Photobacterium*, including taxonomy, phylogeny, ecology and pathological mechanisms. There is still a lack of understanding of several features encoded by *Photobacterium* genomes, such as the novel genes involved in the adaptation to specific habitats, the study of new metabolic pathways and their involved genes, and other cellular functions and metabolites produced by these microorganisms. Moreover, the ability of several species of this genus to produce polyunsaturated fatty acids, cold-adapted

enzymes and antimicrobial compounds constitutes new ways of investigation for a potential biotechnological application of these products in the future.

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References

1. Acosta F, Vivas J, Padilla D, Vega J, Bravo J, Grasso V, Real F (2009) Invasion and survival of *Photobacterium damselae* subsp. *piscicida* in non-phagocytic cells of gilthead sea bream, Sparus aurata L. J Fish Dis 32:535-541
2. Amaral GR, Campeão ME, Swings J, Thompson FL, Thompson CC (2015) Finding diagnostic phenotypic features of *Photobacterium* in the genome sequences. Antonie van Leeuwenhoek 107:1351-1358
3. Andreoni F, Magnani M (2014) Photobacteriosis: prevention and diagnosis. J Immunol Res 2014:ID 793817
4. Andreoni F, Boiani R, Serafini G, Bianconi I, Dominici S, Gorini F, Magnani M (2009) Expression, purification, and characterization of the recombinant putative periplasmic hemin-binding protein (hutB) of *Photobacterium damselae* subsp. *piscicida*. Biosci Biotech Biochem 73:1180-1183
5. Arijo S, Borrego JJ, Zorrilla I, Balebona MC, Moriñigo MA (1998) Comparison of the immune response of gilt-head seabream (*Sparus aurata* L.) to capsulated and uncapsulated strains of *Photobacterium damselae* subsp. *piscicida*. Fish Shellfish Immunol 8:63-72
6. Ast JC, Dunlap PV (2005) Phylogenetic resolution and habitat specificity of the *Photobacterium phosphoreum* species group. Environ Microbiol 7:1641-1654
7. Ast JC, Cleenwerck I, Engelbeen K, Urbanczyk H, Thompson FL, de Vos P, Dunlap PV (2007) *Photobacterium kishitanii* sp. nov., a luminous marine bacterium symbiotic with deep-sea fishes. Int J Syst Evol Microbiol 57:2073-2078
8. Barnes AC, Balebona MC, Horne MT, Ellis AE (1999) Superoxide dismutase and catalase in *Photobacterium damselae* subsp. *piscicida* and their roles in resistance to reactive oxygen species. Microbiology 145:483-494
9. Bartlett DH, Welch TJ (1995) *ompH* gene expression is regulated by multiple environmental cues in addition to high pressure in the deep-sea bacterium *Photobacterium* species strain SS9. J Bacteriol 177:1008-1016
10. Chimetto LA, Cleenwerck I, Thompson CC, Brocchi M, Willems A, De Vos P, Thompson FL (2010) *Photobacterium jeanii* sp. nov., isolated from corals and zoanthids. Int J Syst Evol Microbiol 60:2843-2848
11. Cornelis P, Andrews SC (eds) (2010) Iron uptake and homeostasis in microorganisms. Caister Academic Press (Horizon Press), Norfolk, UK
12. Costa-Ramos C, do Vale A, Ludovico P, dos Santos NMS, Silva MT (2011) The bacterial exotoxin AIP56 induces fish macrophage and neutrophil apoptosis using mechanisms of the extrinsic and intrinsic pathways. Fish Shellfish Immunol 30:173-181
13. Deep K, Poddar A, Das SK (2014) *Photobacterium panuliri* sp. nov., an alkalitolerant marine bacterium isolated from eggs of spiny lobster, Panulirus penicillatus from Andaman Sea. Curr Microbiol 69:660-668
14. do Vale A, Ellis AE, Silva MT (2001) Electron microscopic evidence that expression of capsular polysaccharide by *Photobacterium damselae* subsp. *piscicida* is dependent on iron availability and growth phase. Dis Aquat Org 44:237-240
15. do Vale A, Marques F, Silva MT (2003) Apoptosis of sea bass (*Dicentrarchus labrax* L.) neutrophils and macrophages induced by experimental infection with *Photobacterium damselae* subsp. *piscicida*. Fish Shellfish Immunol 15:129-144
16. do Vale A, Silva MT, dos Santos NMS, Nascimiento PS, Reis-Rodrigues P, Costa-Ramos C, Ellis AE, Azevedo JE (2005) AIP56, a novel plasmid-encoded virulence factor of *Photobacterium damselae* subsp. *piscicida* with apoptogenic activity against sea bass macrophages and neutrophils. Mol Microbiol 58:1025-1038
17. Dunlap PV (2009) Bioluminescence, microbial. In: Schaechter M (ed) Encyclopedia of Microbiology. Elsevier, Oxford, pp 45-61
18. Dunlap PV (2012) Bacterial bioluminescence. In: Schmidt TM, Schaechter M (eds) Topics in Ecological and Environmental Microbiology. Academic Press, Waltham, MA, pp 233-250
19. Dunlap, P.V. (2014) Biochemistry and genetics of bacterial bioluminescence. In: Thouand G, Marks R (eds) Bioluminescence: Fundamentals and Applications in Biotechnology. Springer-Verlag, Berlin, pp 37-64
20. Dunlap PV, Ast JC (2005) Genomic and phylogenetic characterization of luminous bacteria symbiotic with the deep-sea fish *Chlorophthalmus albatrossis* (Aulopiformes: *Chlorophthalmidae*). Appl Environ Microbiol 71:930-939
21. Dunlap PV, Kita-Tsukamoto K (2006) Luminous bacteria. In: Dworkin M, Falkow S, Rosenberg E, Schleifer KH, Stackebrandt E (eds) The Prokaryotes, 3rd ed, Vol 2, Springer, New York, pp 863-892
22. Dunlap PV, Jiemjit A, Ast JC, Pearce MM, Marques RR, Lavilla-Pitogo CR (2004) Genomic polymorphism in symbiotic populations of *Photobacterium leiognathi*. Environ Microbiol 6:145-158
23. Dunlap PV, Ast JC, Kimura S, Fukui A, Yoshino T, Endo H (2007) Phylogenetic analysis of host-symbiont specificity and codivergence in bioluminescent symbioses. Cladistics 23:507-532
24. Dunlap PV, Davis KM, Tomiyama S, Fujino M, Fukui A (2008) Developmental and microbiological analysis of the inception of bioluminescent symbiosis in the marine fish *Nuchequula nuchalis* (Perciformes: Leiognathidae). Appl Environ Microbiol 74:7471-7481
25. Elgendry MY, Abdelsalam M, Moustafa M, Kenawy AM, Seida A (2015) *Caligus elongates* and *Photobacterium damselae* subsp. *piscicida* concomitant infections affecting broodstock European seabass, *Dicentrarchus labrax*, with special reference to histopathological responses. J Aquac Res Dev 6:346
26. Figge MJ, Cleenwerck I, van Uijenc A, De Vosb P, Huys G, Robertson L (2014) *Photobacterium piscicola* sp. nov., isolated from marine fish and spoiled packed cod. Syst Appl Microbiol 37:329-335
27. Gauthier G, Lafay B, Ruimy R, Breittmayer V, Nicolas JL, Gauthier M, Christen R (1995) Small-subunit rRNA sequences and whole DNA relatedness concur for the reassignment of *Pasteurella piscicida* (Snieszko et al.) Janssen and Surgalla to the genus *Photobacterium* as *Photobacterium damsela* subsp. *piscicida* comb. nov. Int J Syst Bacteriol 45:139-144
28. Gómez-Gil B, Roque A, Rotllant G, Peinado L, Romalde JL, Doce A, Cabanillas-Beltrán H, Chimetto L, Thompson FL (2011) *Photobacterium swingsii* sp. nov. isolated from marine organisms. Int J Syst Evol Microbiol 61:315-319
29. Gómez-Gil B, Roque A, Rotllant G, Romalde JL, Doce A, Eggermont M, Defoirdt T (2016) *Photobacterium sanguinicancri* sp. nov. isolated from marine animals. Antoine van Leeuwehoek J Microbiol 109:817-825
30. Hastings JW, Nealson KH (1981) The symbiotic luminous bacteria. In: Starr MP, Stolp H, Truper HG, Balows A, Schlegel HG (eds) The Prokaryotes. A Handbook on Habitats, Isolation, and Identification of Bacteria. Springer-Verlag, New York, pp 1332-1345

31. Holmes B, Farmer JJ III (2009) International Committee on Systematics of Prokaryotes Subcommittee on the taxonomy of *Aeromonadaceae*, *Vibrionaceae* and related organisms. Minutes of the meetings, 6 August 2008, Istanbul, Turkey. Int J Syst Evol Microbiol 59:2638-2640
32. Johnson RM, Weisrock WP (1969) *Hyphomicrobium indicum* sp. nov. (*Hyphomicrobiaceae* Douglas). Int J Syst Bacteriol 19:295-307
33. Jung SY, Jung YT, Oh TK, Yoon JH (2007) *Photobacterium lutimaris* sp. nov., isolated from a tidal flat sediment in Korea. Int J Syst Evol Microbiol 57:332-336
34. Kaeding AJ, Ast JC, Pearce MM, Urbanczyk H, Kimura S, Endo H, Nakamura M, Dunlap PV (2007) Phylogenetic diversity and cosymbiosis in the bioluminescent symbioses of '*Photobacterium mandapamensis*'. Appl Environ Microbiol 73:3173-3182
35. Khouadja S, Lamari F, Bakhrouf A, Gaddour K (2014) Virulence properties, biofilm formation and random amplified polymorphic DNA analysis of *Photobacterium damselae* subsp. *damselae* isolates from cultured sea bream (*Sparus aurata*) and sea bass (*Dicentrarchus labrax*). Microb Pathog 69-70:13-19
36. Kim YO, Kim KK, Park S, Kang SJ, Lee JH, Lee SJ, Oh TK, Yoon JH (2010) *Photobacterium gaetbulicola* sp. nov., a lipolytic bacterium isolated from a tidal flat sediment. Int J Syst Evol Microbiol 60:2587-2591
37. Kimura B, Hokimoto S, Takahashi H, Fujii T (2000) *Photobacterium histaminum* Okuzumi et al. 1994 is a later subjective synonym of *Photobacterium damselae* subsp. *damselae* (Love et al. 1981) Smith et al. 1991. Int J Syst Evol Microbiol 50:1339-1342
38. Kothary MH, Kreger AS (1985) Purification and characterization of an extracellular cytolysin produced by *Vibrio damsela*. Infect Immun 49:25-31
39. Labella A, Vida M, Alonso MC, Infante C, Cárdenas S, López-Romalde S, Manchado M, Borrego JJ (2006) First isolation of *Photobacterium damselae* ssp. *damselae* from cultured redbanded seabream, *Pagrus auriga* Valenciennes, in Spain. J Fish Dis 29:175-179
40. Labella A, Sánchez-Montes N, Berbel C, Aparicio M, Castro D, Manchado M, Borrego JJ (2010) Toxicity of *Photobacterium damselae* subsp. *damselae* strains isolated from new cultured marine fish. Dis Aquat Org 92:31-40
41. Labella A, Berbel C, Manchado M, Castro D, Borrego JJ (2011) *Photobacterium damselae* subsp. *damselae*, an emerging pathogen affecting new cultured marine fish species in Southern Spain. In: Aral F, Doggu Z Recent Advances in Fish Farms. InTech, Rijeka, pp 135-152
42. Le Bihan T, Rayner J, Roy MM, Spagnolo L (2013) *Photobacterium profundum* under pressure: A MS-based label-free quantitative proteomics study. PlosOne 8:e60897
43. Lemos ML, Osorio CR (2007) Heme, an iron supply for vibrios pathogenic for fish. BioMetals 20:615-626
44. López-Doriga MV, Barnes AC, dos Santos NM, Ellis AE (2000) Invasion of fish epithelial cells by *Photobacterium damselae* subsp. *piscicida*: evidence for receptor specificity, and effect of capsule and serum. Microbiology 146:21-30
45. LiuY, Liu LZ, Song L, Zhou YG, Qi FJ, Liu ZP (2014) *Photobacterium aquae* sp. nov., isolated from a recirculating mariculture system. Int J Syst Evol Microbiol 64:475-480
46. Lo N, Jin HM, Che Ok Jeon CO (2014) *Photobacterium aestuarii* sp. nov., a marine bacterium isolated from a tidal flat. Int J Syst Evol Microbiol 64:625-630
47. Love M, Teebken-Fisher D, Hose JE, Farmer JJ III, Hickman FW, Fanning GR (1981) *Vibrio damsela*, a marine bacterium, causes skin ulcers on the damselfish *Chromis punctipinnis*. Science 214:1139-1140
48. Lucena T, Ruvira MA, Pascual J, Garay E, Macián MC, Arahal DR, Pujalte MJ (2011) *Photobacterium aphoticum* sp. nov., isolated from coastal water. Int J Syst Evol Microbiol 61:1579-1584
49. Machado H, Gram L (2015) The fur gene as a new phylogenetic marker for *Vibrionaceae* species identification. Appl Environ Microbiol 81:2745-2752
50. Machado H, Giubergia S, Mateiu RV, Gram L (2015) *Photobacterium galatheae* sp. nov., a bioactive bacterium isolated from a mussel in the Solomon Sea. Int J Syst Evol Microbiol 65:4503-4507
51. Magariños B, Romalde JL, Lemos ML, Barja JL, Toranzo AE (1994) Iron uptake by *Pasteurella piscicida* and its role in pathogenicity for fish. Appl Environ Microbiol 60:2990-2998
52. Magariños B, Bonet R, Romalde JL, Martínez MJ, Congregado F, Toranzo AE (1996) Influence of the capsular layer on the virulence of *Pasteurella piscicida* for fish. Microb Pathog 21:289-297
53. Magariños B, Romalde JL, Noya M, Barja JL, Toranzo AE (1996) Adherence and invasive capacities of the fish pathogen *Pasteurella piscicida*. FEMS Microbiol Lett 138:29-34
54. Martini S, Ali BA, Garel M, Nerini D, Grossi V, Pacton M, Casalot L, Curry P, Tamburini C (2013) Effects of hydrostatic pressure on growth and luminescence of a moderately-piezophilic luminous bacterium *Photobacterium phosphoreum* ANT-2200. PlosOne 8:e66580
55. Moi IM, Roslan NN, Leow ATC, Ali MSM, Rahman RNZ, Rahimpour A, Sabri S (2017) The biology and the importance of *Photobacterium* species. Appl Microbiol Biotechnol, doi:10.1007/s00253-017-8300-y
56. Moreira APB, Duytschaever G, Chimetto Tonon LA, Froes AM, de Oliveira ML, Amado-Filho GM, Francini-Filho RB, De Vos P, Swings J, Thompson CC, Thompson FL (2014) *Photobacterium sanctipauli* sp. nov. isolated from bleached *Madracis decactis* (Scleractinia) in the St Peter & St Paul Archipelago, Mid-Atlantic Ridge, Brazil. Peer J 2:e427
57. Naguit MAA, Plata KC, Abisado RG, Calugay RJ (2014) Evidence of bacterial luminescence in a Philippine squid and octopus hosts. AACL Bioflux 7:497-507
58. Nogi Y, Masui N, Kato C (1998) *Photobacterium profundum* sp. nov., a new, moderately barophilic bacterial species isolated from a deep-sea sediment. Extremophiles 2:1-7
59. Noya M, Magariños B, Lamas J (1995) Interactions between peritoneal exudate cells (PECs) of gilthead seabream (*Sparus aurata*) and *Pasteurella piscicida*. A morphological study. Aquaculture 131:11-21
60. Okuzumi M, Hiraishi A, Kobayashi T, Fujii T (1994) *Photobacterium histaminum* sp. nov., a histamine-producing marine bacterium. Int J Syst Bacteriol 44:631-636
61. Osorio CR, Romalde JL, Barja JL, Toranzo AE (2000) Presence of phospholipase-D (*dly*) gene coding for damselysin production is not a prerequisite for pathogenicity in *Photobacterium damselae* subsp. *damselae*. Microb Pathog 28:119-126
62. Osorio, CR, Rivas AJ, Balado M, Fuentes-Monteverde JC, Rodríguez J, Jiménez C, Lemos ML, Waldor MK (2015) A transmissible plasmid-borne pathogenicity island confers piscibactin biosynthesis in the fish pathogen *Photobacterium damselae* subsp. *piscicida*. Appl Environ Microbiol 81:5867-5879
63. Park YD, Baik KS, Seong CN, Bae KS, Kim S, Chun J (2006) *Photobacterium ganghwense* sp. nov., a halophilic bacterium isolated from sea water. Int J Syst Evol Microbiol 56:745-749
64. Pérez-Cataluña A, Lucena T, Tarazona E, Arahal DR, Macián MC, Pujalte MJ (2016) An MLSA approach for the taxonomic update of the Splendidus clade, a lineage containing several fish and shellfish pathogenic *Vibrio* spp. Syst Appl Microbiol 39:361-369
65. Puentes, B, Balado M, Bermúdez-Crespo J, Osorio CR, Lemos ML (2017) A proteomic analysis of the iron response of *Photobacterium*

damselae subsp. *damselae* reveals metabolic adaptations to iron levels changes and novel potential virulence factors. Vet Microbiol. 201:257-264

66. Reichelt JL, Baumann P (1975) *Photobacterium mandapamensis* Hendrie et al., a later subjective synonym of *Photobacterium leiognathi* Boisvert et al. Int J Syst EvolMicrobiol 25:208-209
67. Rio SJ, Osorio CR, Lemos ML (2005) Heme uptake genes in human and fish isolates of *Photobacterium damselae*: existence of *hutA* pseudogenes. Arch Microbiol 183:347-358
68. Rivas AJ, Balado M, Lemos ML, Osorio CR (2011) The *Photobacterium damselae* subsp. *damselae* hemolysins damselysin and HlyA are encoded within a new virulence plasmid. Infect Immun 79:4617-4627
69. Rivas AJ, Lemos ML, Osorio CR (2013) *Photobacterium damselae* subsp. *damselae*, a bacterium pathogenic for marine animals and humans. Front Microbiol 4:283-289
70. Rivas AJ, von Hoven G, Neukirch C, Meyenburg M, Qin Q, Füser S, Boller K, Lemos ML, Osorio CR, Husmann (2015) Phobalysin, a small ß-pore forming toxin of *Photobacterium damselae* subsp. *damselae*. Infect Immun 83:4335-4348
71. Rivas R, García-Fraile P, Mateos PF, Martínez-Molina E, Velasquez E (2006) *Photobacterium halotolerans* sp. nov., isolated from Lake Martel in Spain. Int J Syst Evol Microbiol 56:1067-1071
72. Romalde JL (2002) *Photobacterium damselae* subsp. *piscicida*: an integrated view of a bacterial fish pathogen. Int Microbiol 5:3-9
73. Sawabe T, Ogura Y, Matsumura Y, Feng G, Rohul Amin AKM, Mino S, Nakagawa S, Sawabe T, Kumar R, Fukui Y, Satomi M, Matsushima R, Thompson FL, Gómez-Gil B, Christen R, Maruyama F, Kurokawa K, Hayashi T (2013) Updating the *Vibrio* clades defined by multilocus sequence phylogeny: Proposal of eight new clades, and the description of *Vibrio tritonius* sp. nov. Front Microbiol 4:1-14
74. Seo HJ, Bae SS, Lee JH, Kim SJ (2005a) *Photobacterium frigidiphilum* sp. nov., a psychrophilic, lipolytic bacterium isolated from deep-sea sediments of Edison Seamount. Int J Syst Evol Microbiol 55:1661-1666
75. Seo HJ, Bae SS, Yang SH, Lee JH, Kim SJ (2005b) *Photobacterium aplysiae* sp. nov., a lipolytic marine bacterium isolated from eggs of the sea hare *Aplysia kurodai*. Int J Syst Evol Microbiol 55:2293-2296
76. Serracca L, Ercolini C, Rossini I, Battistini R, Giorgi I, Prearo M (2011) Occurrence of both subspecies of *Photobacterium damselae* in mullets collected in the river Magra (Italy). Can J Microbiol 57:437-440
77. Silva DS, Pereira LMG, Moreira AR, Ferreira da Silva F, Brito RM, Faria TQ, Zornetta I, Montecucco C, Oliveira P, Azevedo JE, Pereira PJB, Marcelo-Ribeiro S, do Vale A, dos Santos NMS (2013) The apoptogenic toxin AIP56 is a metalloprotease A-B toxin that cleaves NF-kappab P65. PLoS Pathog 9:e1003128
78. Skarmeta AM, Bandin I, Santos Y, Toranzo AE (1995) In vitro killing of *Pasteurella piscicida* by fish macrophages. Dis Aquat Org 23:51-57
79. Skerman VBD, McGowan V, Sneath PHA (1980) Approved lists of bacterial names. Int J Syst Bacteriol 30:225-420
80. Smith SK, Sutton DC, Fuerst JA, Reichelt JL (1991) Evaluation of the genus *Listonella* and reassignment of *Listonella damsela* (Love et al.) MacDonell and Colwell to the genus *Photobacterium* as *Photobacterium damsela* comb. nov. with an emended description. Int J Syst Bacteriol 41:529-534
81. Souto A, Montaos MA, Rivas AJ, Balado M, Osorio CR, Rodríguez J, Lemos ML, Jiménez C (2012) Structure and biosynthetic assembly of Piscibactin, a siderophore from *Photobacterium damselae* subsp. *piscicida*, predicted from genome analysis. Eur J Org Chem 29:5693-5700
82. Sparks JS, Dunlap PV, Smith WL (2005) Evolution and diversification of a sexually dimorphic luminescent system in ponyfish (Teleostei: *Leiognathidae*), including diagnoses for two new genera. Cladistics 21:305-327
83. Thompson FL, Thompson CC, Naser S, Hoste B, Vandemeulebroecke K, Munn C, Bourne D, Swings J (2005) *Photobacterium rosenbergii* sp. nov. and *Enterovibrio coralii* sp. nov., vibrios associated with coral bleaching. Int J Syst Evol Microbiol 55:913-917
84. Thyssen A, Ollevier F (2015) *Photobacterium*. In: Bergey's Manual of Systematics of Archaea and Bacteria, pp. 1-11. Published on line. DOI: 10.1002/9781118960608.gbm01076
85. Urbanczyk H, Ast JC, Kaeding AJ, Oliver JD, Dunlap PV (2008) Phylogenetic analysis of the incidence of lux gene horizontal transfer in *Vibrionaceae*. J Bacteriol 190:3494-3504
86. Urbanczyk H, Ast JC, Dunlap PV (2011) Phylogeny, genomics, and simbiosis of *Photobacterium*. FEMS Microbiol Rev 35:324-342
87. Vences A, Rivas AJ, Lemos ML, Husmann M, Osorio CR (2017) Chromosome-encoded hemolysin, phospholipase and collagenase, contribute to virulence for fish in plasmidless isolates of *Photobacterium damselae* subsp. *damselae*. Appl Environ Microbiol 83:e00401-17
88. Wada M, Kamiya A, Uchiyama N, Yoshizawa S, Kita-Tsukamoto K, Ikejima K, Yu R, Imada C, Karatani H, Mizuno N, Suzuki Y, Nishida M, Kogure K (2006) LuxA gene of light organ symbionts of the bioluminescent fish *Acropoma japonicum* (*Acropomatidae*) and *Siphamia versicolor* (*Apogonidae*) forms a lineage closely related to that of *Photobacterium leiognathi* ssp. *mandapamensis*. FEMS Microbiol Lett 260:186-192
89. Yamane K, Asato J, Kawade N, Takahashi H, Kimura B, Arakawa Y (2004) Two cases of fatal necrotizing fasciitis caused by *Photobacterium damsela* in Japan. J Clin Microbiol 42:1370-1372
90. Yayanos AA (1995) Microbiology to 10,500 meters in the deep-sea. Annu Rev Microbiol 49:777-805
91. Yoon JH, Lee JK, Kim YO, Oh TK (2005) *Photobacterium lipolyticum* sp. nov., a bacterium with lipolytic activity isolated from the Yellow Sea in Korea. Int J Syst Evol Microbiol 55:335-339
92. Yoshizawa S, Wada M, Kita-Tsukamoto K, Yokota A, Kogure K (2009) *Photobacterium aquimaris* sp. nov., a luminous marine bacterium isolated from seawater. Int J Syst Evol Microbiol 59:1438-1442
93. Zarubin M, Belkin S, Ionescu M, Genin A (2012) Bacterial luminescence as a lure for marine zooplankton and fish. Proc Natl Acad Sci USA 109:853-857