



HAL
open science

Fish skin pigmentation in aquaculture: The influence of rearing conditions and its neuroendocrine regulation

Paula G. Vissio, Maria J. Darias, María P. Di Yorio, Daniela I. Pérez Sirkin,
Tomás H. Delgadin

► **To cite this version:**

Paula G. Vissio, Maria J. Darias, María P. Di Yorio, Daniela I. Pérez Sirkin, Tomás H. Delgadin. Fish skin pigmentation in aquaculture: The influence of rearing conditions and its neuroendocrine regulation. *General and Comparative Endocrinology*, 2021, *General and Comparative Endocrinology*, 301, pp.113662. 10.1016/j.ygcen.2020.113662 . ird-03183177

HAL Id: ird-03183177

<https://ird.hal.science/ird-03183177v1>

Submitted on 27 Mar 2021

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.

Article published in:
General and Comparative Endocrinology
Volume 301, 15 January 2021, 113662
<https://doi.org/10.1016/j.ygcen.2020.113662>

Fish skin pigmentation in aquaculture: the influence of rearing conditions and its neuroendocrine regulation

Paula G. Vissio^{1,2*+}, Maria J. Darias³⁺, María P. Di Yorio^{1,2+}, Daniela I. Pérez Sirkin^{1,2+},
Tomás H. Delgadin^{1,2}

+Authors with equal contribution

Affiliations:¹ Universidad de Buenos Aires. Facultad de Ciencias Exactas y Naturales.
Departamento de Biodiversidad y Biología Experimental. Buenos Aires, Argentina.

²CONICET – Universidad de Buenos Aires. Instituto de Biodiversidad y Biología Experimental y Aplicada (IBBEA), CONICET. Buenos Aires, Argentina.

³MARBEC, Univ Montpellier, CNRS, Ifremer, IRD, Montpellier, France.

*Corresponding author: Paula G. Vissio. E-mail: pvissio@gmail.com

1 **Abstract**

2 Skin pigmentation pattern is a species-specific characteristic that depends on the
3 number and the spatial combination of several types of chromatophores. This feature
4 can change during life, for example in the metamorphosis or reproductive cycle, or as a
5 response to biotic and/or abiotic environmental cues (nutrition, UV incidence,
6 surrounding luminosity, and social interactions). Fish skin pigmentation is one of the
7 most important quality criteria dictating the market value of both aquaculture and
8 ornamental species because it serves as an external signal to infer its welfare and the
9 culture conditions used. For that reason, several studies have been conducted aiming to
10 understand the mechanisms underlying fish pigmentation as well as the influence
11 exerted by rearing conditions. In this context, the present review focuses on the current
12 knowledge on endocrine regulation of fish pigmentation as well as on the aquaculture
13 conditions affecting skin coloration. Available information on Iberoamerican fish
14 species cultured is presented.

15

16 **Keywords:** Fish pigmentation; Chromatophore; Hormones; Aquaculture

17

18 **1 Introduction**

19 Aquaculture contributes significantly to global seafood supply, accounting for 46% of
20 the total production in 2018, and has had the fastest growth rate among major food
21 production sectors for several decades (FAO, 2020a). Today, aquaculture plays an
22 important role in income generation and food and nutrition security, particularly in
23 developing countries (Belton et al., 2018), and promotes local biodiversity and the
24 preservation of cultural traditions. Fish skin pigmentation is one of the most important
25 quality criteria dictating the market value of fish for human consumption and
26 ornamental use (Harpaz and Padowicz, 2007). For instance, colors in food are linked to
27 anticipated quality and are cues that allow consumers to make judgements about
28 desirability (Bjerkeng, 2008). However, aquaculture conditions can negatively affect the
29 natural skin coloration of fish (Lim et al., 2018), thus hampering successful
30 commercialization. Indeed, skin pigmentation in fish is regulated by both external
31 (biotic and abiotic) and internal (genetic, cellular, nervous, and hormonal) factors
32 (Pittman et al., 2013). For that reason, several studies have been conducted aiming to
33 understand the mechanisms underlying fish pigmentation as well as the influence
34 exerted by rearing conditions.

35 Aquaculture in Iberoamerica (IA), the Spanish- and Portuguese-speaking nations of the
36 Americas and Europe, represents 3.05% of the world's global production with nearly
37 3.5 million tons produced in 2018 (FAO, 2020b), and several studies have addressed
38 skin pigmentation in fish species cultivated in these countries. Reared flatfish species
39 (Pleuronectiformes), which are known for their asymmetric pigmentation and their
40 ability to adapt to background color changes by adjusting their ocular-side pigmentation

41 (Inui and Miwa, 2012), frequently present pigmentation anomalies, such as albinism
42 and ambicoloration. Research on pigmentation has been conducted on flatfish species
43 that either are cultivated or have been identified as candidate species for aquaculture
44 diversification in IA, such as turbot, *Scophthalmus maximus* (also known as *Psetta*
45 *maxima*; e.g., Reitan et al., 1994; Estévez and Kanazawa, 1995; Estévez et al., 1999),
46 Senegalese sole, *Solea senegalensis* (e.g., Villalta et al., 2005; Darias et al., 2013a;
47 Boglino et al., 2014), common sole, *Solea solea* (Lund et al., 2008, 2010), California
48 halibut, *Paralichthys californicus* (Vizcaíno-Ochoa et al., 2010), *Paralichthys*
49 *adpersus* (Orihuela et al., 2018), *Paralichthys orbignyanus* (López et al., 2009; Vieira
50 Rodrigues et al., 2012) or *Paralichthys woolmani* (Benetti, 1997; Bohórquez-Cruz et al.,
51 2018). Further studies have dealt with other fish species cultivated in IA, such as
52 salmonids (Colihueque, 2010), red porgy, *Pagrus pagrus* (e.g., Kalinowski et al., 2007;
53 Tejera et al., 2010), gilthead sea bream, *Sparus aurata* (e.g., Gouveia et al., 2002;
54 Ribeiro et al., 2017), Nile tilapia, *Oreochromis niloticus* (Ponce-Palafox et al., 2004;
55 Valente et al., 2016) or ornamental species like *Hyphessobrycon eques* (Berchielli-
56 Morais et al., 2016), which require dietary carotenoid supplementation in order to
57 maintain their natural skin coloration (Bjerkeng, 2008). Besides, the influence of rearing
58 conditions such as tank color, light intensity or social interactions on skin pigmentation
59 has been studied in other IA fish species, such as *Lophiosilurus alexandri* (Costa et al.,
60 2017, Santos et al., 2019), *Paralichthys woolmani* (Benetti, 1997; Venizelos and
61 Benetti, 1999; Han et al., 2005), Neon tetra, *Paracheirodo ninnesi* (Kasai and Oshima,
62 2006) or *Cichlasoma dimerus* (Alonso et al., 2011; Cánepa et al., 2006, 2012, Delgadin
63 et al., 2020).

64 In this context, the present review focuses on the current knowledge on endocrine
65 regulation of fish pigmentation as well as on the aquaculture conditions affecting skin
66 coloration. Available information on species cultured in IA is presented.

67

68 **2 An overview on fish skin pigmentation**

69 Skin pigmentation pattern is a species-specific characteristic that depends on the
70 number and spatial combination of several types of chromatophores included in the
71 epidermis and in the dermis (Aspengren et al., 2012; Darias et al., 2013a). Compared to
72 other vertebrates, it has been suggested that this great variety of pigmentation patterns
73 in fish is due to the fish-specific genome duplication which gave rise to about 30% more
74 pigmentation-related genes (Braasch et al. 2008; reviewed in Pittman et al., 2013).
75 Furthermore, the skin pigmentation pattern can change during life time, for example,
76 during metamorphosis or the reproductive cycle, or as a response to biotic and/or abiotic
77 environmental cues (nutrition, UV incidence, surrounding luminosity, and social
78 interactions) (Price et al., 2008; Leclercq et al., 2010; Darias et al., 2013a, b; Parichy
79 and Spiewak, 2015). Studies performed in flatfish species have shown that there is a
80 sensitive period during pre- and pro-metamorphosis, named pigmentation window, in
81 which different external factors can disrupt the normal development of pigmentation
82 (Darias et al., 2013a, b; Pittman et al., 2013).

83 In vertebrates, chromatophores cells derive from one of the most fascinating cells of
84 vertebrate development biology: the neural crest cells (NCC). These cells arise from a
85 region between the border of the neural plate and the non-neural ectoderm and, after
86 undergoing an epithelial-to-mesenchymal transition, they migrate throughout the
87 embryo, colonizing different tissues and organs where they settle and differentiate
88 (Bronner and LeDouarin, 2012; Theveneau and Mayor, 2012). It has been proposed that

89 all chromatophores are generated from a common chromatoblast (Bagnara et al., 1979)
90 through progressive fate-restriction processes (Le Douarin and Dupin, 2003; Dupin et
91 al., 2007; Kimura et al., 2014). Different chromatophores have been described in fish,
92 classified into light-absorbing chromatophores (melanophores, erythrophores,
93 xanthophores, and cyanophores) and light-reflecting chromatophores (leucophores and
94 iridophores) (Fujii, 2000; Sugimoto, 2002). While melanophores, iridophores, and
95 xanthophores are widely distributed in teleosts (Schartl et al., 2016), leucophores are
96 less abundant (Menter et al., 1979; Iga and Matsuno, 1992; Nagao et al., 2018). In
97 addition, two cell types of melanophores and xanthophores, differing in size and
98 sequentially appearing during development, have been described in Japanese flounder,
99 *Paralichthys olivaceus*, and Senegalese sole (Seikai et al., 1987; Nakamura et al., 2010;
100 Darias et al., 2013a). These two different cell types have been identified as larval and
101 adult melanophores and xanthophores in Japanese flounder (Seikai et al., 1987;
102 Nakamura et al., 2010), whereas in the case of Senegalese sole melanophores, the two
103 cell types rather correspond to different morphological stages of newly differentiated
104 and melanized melanophores at post-metamorphosis (Darias et al., 2013a).

105 Melanophores are the most common and studied chromatophores and are responsible
106 for the dorsal pigmentation in vertebrates (Aspengren et al., 2012). Melanophores are
107 dendritic shaped cells that extend their projections, containing the pigmented organelles
108 (melanosomes), almost parallel to the plane of the skin (Fujii, 2000; Nüsslein-Volhard
109 and Singh, 2017). In teleosts' skin, melanophores are mostly found in the dermis,
110 although they can also be observed in the epidermis (Fujii, 2000).

111

112 **3 How does skin color change in fish?**

113 **3.1 Cellular mechanisms**

114 Skin color can vary through two different mechanisms. On the one hand, the
115 physiological color changes, which are rapid and transient, are produced by the motility
116 of pigment vesicles (chromatosomes) or by the movement of reflective structures within
117 their cells. On the other hand, the morphological color changes, which occur within
118 days and/or weeks, involve variations in skin pigment concentration or the density and
119 distribution of chromatophores in the integument (Leclercq et al., 2010).

120 The translocation of chromatosomes, which are characteristic of physiological color
121 changes, is coordinated by the microtubule and actin filament architecture of the
122 cytoskeleton and the associated motor proteins. When light-absorbing chromatophores
123 receive an input (such as hormones, neurotransmitters or environmental cues) that
124 produces the aggregation or dispersion of chromatosomes, the specific molecular motor
125 hauls pigment granules back toward the nucleus or to the cell periphery (Ligon and
126 McCartney, 2016). In general, decreases in cAMP levels and/or increases in Ca^{2+} levels
127 within chromatophores trigger aggregation responses, while the opposite changes in
128 cAMP or Ca^{2+} levels induce dispersion responses (reviewed in Fujii, 2000). Regarding
129 iridophores, which contain thin reflecting platelets in their cytoplasm, under certain
130 inputs they simultaneously change the distance between adjoining platelets, leading to a
131 shift in the spectral reflectance of the skin (Kasukawa et al., 1986).

132 Chromatophores density variation implies both differentiation and apoptosis processes.
133 It is believed that the number of melanophores increases through precursor cell
134 differentiation rather than the division of already differentiated melanophores
135 (Sugimoto et al., 2002). There is evidence that these precursors are neural crest-derived
136 stem cells that have been set aside in distinct niches, such as the ganglia of the

137 peripheral nervous system, the base of the fins, or in deep layers of the dermis, which
138 migrate and differentiate into adult-type pigment cells under specific stimuli (reviewed
139 in Sugimoto et al., 2002; Yamada et al., 2010; Darias et al., 2013a; Frohnhöfer et al.,
140 2013). This differentiation implies the molecular action of the chromatophore-
141 differentiating genes that are also implicated in the regulation of skin pigment
142 concentration. In particular, microphthalmia-associated transcription factor (*mitf*) is
143 considered the master regulator of melanophore development and controls expression of
144 genes required for melanophore development, including dopachrome tautomerase (*dct*),
145 tyrosinase (*tyr*), tyrosinase related peptides (*trp 1* and *2*) and the receptor tyrosine kinase
146 (*c-kit*) (Steingrímsson et al., 2004, Darias et al., 2013a, Nagao et al, 2018). Furthermore,
147 the sodium/potassium/calcium exchanger 5 (*slc24a5*) is crucial for proper melanin
148 synthesis. The paired box protein 3 (*pax3*) can promote or inhibit melanogenesis
149 through transcriptional regulation of *mitf* and *cKit*, the latter being necessary for
150 melanophore differentiation and responsible for the activation of *tyr*. Besides, *pax3* can
151 also modulate the expression of *trp1* and *trp2* (see model in Darias et al., 2013a).
152 Although the molecular mechanisms of fish melanophore differentiation have been well
153 characterized, those of the other chromatophores have remained largely unknown
154 (Otsuki et al., 2020). It was demonstrated that Sry-box transcription factor 5 (Sox5) acts
155 antagonistically against Sox10 in the specification of zebrafish chromatophores and in
156 melanophore and iridophore lineages in medaka. However, in this last species,
157 xanthophores and leucophores developed from a shared progenitor Pax7a positive. This
158 progenitor differentiates in xanthophore or leucophore depending on Sox5/Sox10. While
159 Sox5/10 promotes xanthophore specification, it represses leucophore formation (Kimura
160 et al., 2014; Nagao et al., 2018).

161 The decrease in chromatophore number occurs by apoptosis stimulated by specific
162 factors (Sugimoto et al., 2002; Sköld et al., 2016). Interestingly, xanthophores can
163 eliminate the surrounding melanophores, and vice versa, in zebrafish (Nakamasu et al.,
164 2009), and similarly, xanthophores in the skin of Senegalese sole pseudo-albinos
165 seemed to be responsible for the degeneration of melanophores (Darias et al., 2013b).
166 Besides, variation in melanophore morphology, which mainly implies variation in
167 dendritic process elongation, has been described as another type of morphological color
168 change (reviewed in Sugimoto et al., 2002).

169 Since morphological color changes are preceded by physiological color changes, similar
170 control mechanisms have been proposed to function both in the motile responses and in
171 the chromatophore densities (reviewed in Sugimoto, 2002).

172

173 **3.2 Hormone regulators**

174 Unlike other vertebrate taxa, it is generally accepted that teleost fish present a dual-
175 hormonal mechanism for skin color regulation (reviewed in Bertolesi et al., 2019). Two
176 hormones with opposite effects, skin lightening and darkening, have been proposed as
177 the main morphological and physiological color change regulators: the melanin-
178 concentrating hormone (Mch) and the melanophore-stimulating hormone (Msh),
179 derived from precursor Proopiomelanocortin. However, skin color regulation is more
180 complex, and other regulatory factors have been identified in studies performed on the
181 regulation over other chromatophores cells. Table 1 summarizes this complex scenario
182 with the old and new actors involved in skin color regulation in fish. In addition, figure
183 1 shows the endocrine and nervous effect over the different chromatophores. In this
184 figure, the lack of studies on the regulation of some pigmentary cells is reflected. More

185 studies will help to improve the understanding of pigment disorders in aquaculture
186 species.

187

188 **3.3 Nervous control**

189 Rapid chromatosome aggregation is mainly controlled by the sympathetic
190 postganglionic system. Chromatic information is captured by the eyes, processed in the
191 optic tectum and partly at the level of the motoneurons in the medulla, and sent to
192 chromatophores via direct nervous connections (Grove, 1994; reviewed in Fujii, 2000).
193 Since Fujii and Oshima (1994), Fujii (2000) and Sköld et al. (2016) have reviewed this
194 issue in depth, we will only point out some aspects of this regulation that are relevant
195 for the following sections. It has been proposed that there is a constant rate of firing of
196 noradrenaline (NA) from nerve terminals that increases or decreases depending on
197 different stimuli (Fujii and Oshima, 1994). Other studies have demonstrated that ATP is
198 released as a co-transmitter together with NA (true-transmitter) and that, in the synaptic
199 cleft, it is dephosphorylated to adenosine, which survives longer and reverses NA
200 action, causing re-dispersion of pigment after the cessation of the stimulus (Fujii and
201 Oshima, 1994).

202 Noradrenaline interacts with α - and β -adrenoreceptors, with α_2 -adrenoreceptor subtype
203 being more effective than α_1 -adrenoreceptor in producing pigment aggregation, while
204 β_2 -adrenoreceptor subtype induces pigment dispersion. Concerning NA effects over
205 chromatosomes, its release induces aggregation of these vesicles in melanophores,
206 xanthophores and erythrophores, but disperses the light-scattering organelles in
207 leucophores, and also produces a change in the arrangement of reflecting platelets in
208 iridophores (Fujii and Oshima, 1994; reviewed in Fujii 2000; Sköld et al., 2016).

209 Besides this action, Sugimoto (2000) observed that NA induces melanophore apoptosis
210 in medaka skin culture, and that denervation decreases melanophore density in this
211 species (Sugimoto, 1993) (Figure 1).

212

213 **4 Influence of rearing conditions on skin pigmentation**

214 Rearing conditions, such as environment and feeding, which are very different from
215 those of natural habitats, influence fish physiology and behavior (Eslamloo et al., 2015).
216 Especially in intensive farming, fish are exposed to grading, handling, transportation,
217 stocking densities, diseases, vaccination, food withdrawal or aggression, among other,
218 that affect welfare and can lead to acute or chronic stress (Sneddon et al., 2016). In this
219 sense, besides nutrition—which is a source of pigments for several species and plays an
220 essential role in morphogenesis during early development (Bjerkeng, 2008; Rønnestad
221 et al., 2013)—, stress can trigger skin pigmentation changes. During an acute stress
222 response, higher amounts of catecholamines (CA), i.e., adrenaline, noradrenaline, and
223 dopamine, are released from the chromaffin cells of the head kidney and thus, increase
224 in the bloodstream (reviewed in Wendelaar Bonga, 1997). As chromatophores express
225 CA receptors, this increase directly impacts fish coloration, generally inducing skin
226 paling (Figure 1). If the stressful stimulus continues, the chronic stress response begins
227 with the activation of the hypothalamus-pituitary-interrenal axis. Thus, corticotropin-
228 releasing hormone (Crh) and thyrotrophin-releasing hormone (Trh) produce an increase
229 in adrenocorticotrophic hormone (Acth) and α -Msh secretion, which in turn stimulates
230 cortisol release causing skin darkening or paling depending on the species. Cortisol can
231 also exert a negative feedback on α -Msh and the interrenal cells, in addition to a
232 downregulation of certain CA receptors, such as adrenergic receptors (Wendelaar

233 Bonga, 1997). Furthermore, stressor-induced cortisol production has been associated
234 with disruption of the gut microbiome in fish (Uren Webster et al., 2020). Considering
235 the major role of the gut microbiome in the regulation of the physiology of the
236 organism, including the modulation of neuronal and endocrine pathways (Lerner et al.,
237 2017), and the recent association found between the pseudo-albino phenotype and gut
238 microbiome modification in Senegalese sole (Pinto et al., 2019), deeper research
239 towards deciphering the molecular mechanisms and cellular processes of skin
240 pigmentation regulated by the gut microbiome and their link with other biological
241 processes will undoubtedly shed light into better understanding the intricate and
242 interlocked processes of physiological regulation in fish.

243 Finally, as more than one stressor can be present at the same time, different effects on
244 skin pigmentation can be observed depending on the hormonal response to each
245 stimulus

246 **4.1 Nutrition**

247 The influence of nutrition in fish skin pigmentation has been widely reported; however,
248 fewer studies have dealt with its endocrine regulation. The association between nutrition
249 and pigmentation has been mostly studied in flatfish, which can present a high
250 incidence of pigmentation anomalies under aquaculture conditions, and in fish species
251 owing their skin coloration to dietary carotenoids.

252 In flatfish, larval nutrition has been proved to be essential for proper physiological and
253 morphological transformations occurring during the complex process of metamorphosis,
254 including pigmentation (Hamre et al., 2005; Boglino et al., 2013; Darias et al., 2013b).
255 Several studies have shown higher survival rates and better pigmentation when fish are
256 fed copepods than with any other live prey (Seikai, 1985; Shields et al., 1999; Wilcox et

257 al., 2006). Several differences in nutrient composition between copepods and live preys
258 such as *Artemia* or rotifers have been suggested to account to the dissimilarities in the
259 pigmentation process of fish, such as the amount of docosahexaenoic (DHA) and
260 eicosapentaenoic acids (EPA) (and their ratios), polar lipids and amino acids, as well as
261 vitamin A (VA) and carotenoid composition (Næss and Lie, 1998). Kanazawa (1993)
262 suggested that albinism in flatfish resulted from the insufficiency of rhodopsin, the
263 production of which depends on VA, DHA and phospholipids, necessary to the
264 formation of melanin. According to this author, feeding Japanese flounder larvae fed a
265 diet deficient in those nutrients during the formation of the retina (at around 10 days
266 post hatching-dph) hampers the production of rhodopsin in the retina. The absence of
267 rhodopsin prevents the visual transmission from the retina to the central nervous system,
268 then the production of Msh is not triggered resulting in the interruption of black
269 pigment formation (Kanazawa, 1993). Copepods contain 5 times higher DHA content
270 than *Artemia* (Hamre et al., 2002), thus the involvement of DHA in vision development
271 and its importance to stimulate melanin synthesis might be the reason behind the
272 importance of DHA in pigmentation. Copepods also present higher levels of EPA.
273 Adequate levels of DHA and EPA and their ratios have shown to be necessary for the
274 correct development of skin pigmentation of turbot (Reitan et al., 1994; Estévez and
275 Kanazawa, 1995), common sole, *Solea solea* (Heatch and Moore, 1997), Atlantic
276 halibut, *Hipoglossus hipoglossus* (Hamre et al., 2005), and California halibut,
277 *Paralichthys californicus* (Vizcaíno-Ochoa et al., 2010). Besides, the lower iodine
278 content in *Artemia* compared to copepods has been suggested to decrease the level of
279 thyroid hormone (Th) in fish larvae (Hamre et al., 2005), which could in turn interfere
280 in the metamorphosis process, including pigmentation (Inui and Miwa, 2012; Wang et
281 al., 2019). VA also influences the fate of chromatophores in flatfish, high doses of

282 retinoic acid stimulating the development of chromatophores in the blind side of flatfish
283 (Miwa and Yamano, 1999). It has been suggested that interactions between VA and
284 fatty acids, as well as between VA and Th at the nuclear receptor level are key in the
285 stimulation of normal pigmentation (Hamre et al., 2005).

286 Adequate dietary arachidonic acid (ARA) content has also been demonstrated to be
287 important for proper skin pigmentation of several flatfish species such as Yellowtail
288 flounder, *Limanda ferruginea* (Copeman and Parrish, 2002), common sole (Lund et al.,
289 2008), turbot (Estévez et al., 1999), Japanese flounder (Estévez et al., 2001), Atlantic
290 halibut (Hamre et al., 2007) and Senegalese sole (Villalta et al., 2005; Darias et al.,
291 2013b; Boglino et al., 2014). Pre- and pro-metamorphosis are the sensitive periods
292 during which nutrition exerts its greatest influence on pigmentation, coinciding with the
293 time in which chromatoblast differentiation takes place towards the adult type
294 chromatophores (Bolker et al., 2005; Darias et al., 2013b). Senegalese sole larvae fed
295 with high levels of ARA becoming pseudo-albinos at later stages developed
296 pigmentation in the same way as future normally pigmented specimens, but once
297 metamorphosed, the future pseudo-albinos began to show different relative proportions,
298 allocation patterns, shapes and sizes of skin chromatophores that progressively
299 disappeared during post-metamorphosis (Darias et al., 2013b). This process was mainly
300 attributed to the down-regulation of *trp1* and *slc24a5*, which prevented melanin
301 production, and the involvement of *pax3*, *mitf* and *asip1* (agouti signaling protein) in the
302 developmental disruption of the new post-metamorphic populations of melanophores,
303 xanthophores and iridophores (Darias et al., 2013b). Melanophores in pseudo-albino
304 specimens were less abundant and not so aggregated in patches as they were in normally
305 pigmented ones, whereas their shape differed (round vs. dendrite-like shape) suggesting
306 their inability to disperse melanin (Darias et al., 2013b). Besides, high amounts of

307 dietary ARA can produce imbalances in the relative content of EPA and DHA (Moren
308 et al., 2011), which in turn modify the relative concentrations of prostaglandin E of the
309 2 (ARA-derived) and 3 (EPA-derived) series (Boglino et al., 2014). In fact, EPA and
310 DHA compete as substrates for cyclo- and lipoxygenases, which are involved in
311 prostaglandin biosynthesis pathways. Prostaglandin E2 (PEG2) and PEG3 are potent
312 regulators of metabolism with opposing effects (Bell and Sargent, 2003); thus, the
313 balance in their synthesis from both series is dependent on a balanced dietary intake of
314 both ARA and EPA (Hamre et al., 2005). ARA-induced abnormally pigmented
315 individuals have shown to present higher levels of PGE2 than normally pigmented fish
316 fed with a control diet in both Senegalese sole (Villalta et al., 2005, Boglino et al.,
317 2014) and common sole (Lund et al., 2010). Further, pseudo-albino specimens fed a
318 high ARA content diet displayed higher PGE2 concentrations than normally pigmented
319 fish fed the same diet (Boglino et al., 2014). In Senegalese sole, high dietary ARA
320 levels and altered PGE2 concentrations not only affected the pigmentation success, but
321 also disrupted the process of head remodeling during metamorphosis (Boglino et al.,
322 2013).

323 Many fish species owe their bright coloration to carotenoids, which are the predominant
324 pigments in xanthophores and erythrophores. Fish are not able to biosynthesize
325 carotenoids *de novo*, and thus must obtain them from the diet (Bjerkeng, 2008). In
326 aquaculture, several cultured fish species require carotenoid supplementation in order to
327 avoid skin paleness (Bjerkeng, 2008). The effect of carotenoids on the endocrine system
328 as well as their mechanisms of action remain to be elucidated (De Carvalho and
329 Caramujo, 2017). However, it is known that carotenoid deposition in the skin is induced
330 during the breeding season in many fish species, and gonadal hormones such as 17 β -

331 estradiol and 11-ketotestosterone have shown to play a role in carotenoid-based nuptial
332 coloration (reviewed in Leclercq et al., 2010; Lim et al., 2018).

333 Astaxanthin is the main carotenoid used in aquaculture feeds and is either obtained from
334 chemical synthesis or from natural resources such as algae, fungi, yeast and bacteria,
335 (Lim et al., 2018). Besides a source of pinkish-red pigments, astaxanthin is known to
336 improve survival, growth performance, reproductive capacity, stress tolerance, disease
337 resistance and immune related gene expression (Lim et al., 2018). Several studies have
338 analyzed the effect of dietary astaxanthin on skin coloration of cultured fish species for
339 human consumption, such as Atlantic salmon, *Salmo salar*, rainbow trout,
340 *Oncorhynchus mykiss*, red porgy, gilthead sea bream, red sea bream, *Pagrus major*,
341 Japanese flounder or Australasian snapper, *Pagrus auratus*, as well as in ornamental
342 species, such as goldfish, *Carassius auratus*, kissing gourami, *Helostoma temminckii*,
343 false clownfish, *Amphiprion ocellaris* or koi carp, *Cyprinus carpio*, among others
344 (reviewed in Lim et al., 2018). Besides, other carotenoid sources have been also
345 assessed to enhance fish skin coloration, as for example the fucoxanthin-rich microalga
346 *Phaeodactylum tricornutum* (gilthead sea bream; Ribeiro et al., 2017), China rose
347 petals, *Hibiscus rosa-sinensis* (goldfish; Sinha and Asimi, 2007), annatto, *Bixa orellana*
348 (goldfish; Fries et al., 2014), sea lettuces *Ulva rigida* and *Ulva lactuca* (Nile tilapia;
349 Valente et al., 2016) or *Spirulina* sp. (yellow tail cichlid, *Pseudotropheus acei*; Guroy et
350 al., 2012), among others.

351

352 **4.2 Tank color**

353 The characteristics of rearing tanks are an important issue to consider in aquaculture,
354 since it has been demonstrated that they can induce stress (Ishibashi et al., 2013), affect

355 growth and survival (Martinez-Cardenas and Purser, 2015; Wang et al., 2017), induce
356 skeletal anomalies (Cobcroft and Battaglione, 2009), and alter fish behavior (Höglund et
357 al., 2002; Cobcroft and Battaglione, 2009) and skin pigmentation (van der Salm et al.,
358 2005; Doolan et al., 2008b; Eslamloo et al., 2015). Despite all the evidence, tank
359 characteristics are often under-considered in aquaculture, and, for instance, the color of
360 the rearing tanks is seldom described in the scientific literature.

361 Background adaptation is widely observed in fish and refers to the ability to modify
362 body color in response to environmental luminosity, as in the case of dark or bright
363 backgrounds. This ability is exploited in aquaculture to improve skin pigmentation. For
364 example, skin darkening in sparids, which negatively affects market value (Matsui et
365 al., 1992; Kolios et al., 1997; Lin et al., 1998; Rotllant et al., 2003; Booth et al. 2004;
366 Van der Salm et al., 2004; Doolan et al., 2007), can be reversed by rearing these species
367 in white tanks (Doolan et al, 2008a, b). However, a white environment has been shown
368 to induce an increased stress response to overcrowding in *P. pagrus*, which may depend
369 on the size of the fish (Rotllant et al., 2003; Van der Salm et al., 2004). In tilapia,
370 *Oreochromis mossambicus*, white and grey backgrounds induce skin lightening,
371 whereas a black background induces skin darkening and a more stressful response (Van
372 der Salm et al., 2005). In goldfish, red and blue backgrounds are chronically stressful,
373 whereas a white background improves fish growth, but generates a skin color loss
374 (Eslamloo et al., 2015). In *Lophiosilurus alexandri* dark colored tanks promoted an
375 increase in plasma cortisol levels and a reduction in brightness of the skin, while the use
376 of light colors resulted in paler skin (Costa et al., 2017).

377 As previously mentioned, tank color not only affects fish pigmentation, but can also
378 cause other physiological changes. In several fish species, it has been observed that fish

379 adapted to a white background present better growth performance than those adapted to
380 other background color (Amiya et al. 2005; Karakatsouli et al. 2007; Strand et al. 2007;
381 Takahashi et al., 2004; Yamanome et al. 2005; Pérez Sirkin et al., 2012; Eslamloo et al.,
382 2015). In part, this could be due to the high contrast between feed and background color
383 that improves the visibility of feed in the tanks (Jentoft et al., 2006; Strand et al. 2007;
384 Eslamloo et al., 2015). Besides, white background induces high levels of Mch and, as
385 Mch has been proposed to play an orexigenic role in some species (Takahashi et al.,
386 2014; Volkoff, 2016), the increase in somatic growth could be interpreted as an increase
387 of food intake. On the other hand, in *C. dimerus*, it was demonstrated that Mch
388 stimulates Gh release in pituitary cultures, so the increase in fish growth could also be
389 related to this regulation (Pérez Sirkin et al., 2012).

390 The adaptation to black background results in the dispersion of pigment in
391 melanophores within a few hours, concomitant with an increase in plasma α -Msh levels
392 (Mizusawa et al., 2013). However, the involvement of this hormone in long-term
393 background adaptation has no consensus in fish (Cal et al., 2017). Despite what would
394 be expected, gilthead sea bream adapted to a white background for 15 days presented an
395 increase in plasma α -Msh levels compared to specimens adapted to grey or black
396 backgrounds (Arends et al., 2000). Similar results were observed in red porgy adapted
397 for one month to white or black backgrounds (Rotllant et al., 2003). However, it has
398 been hypothesized that the regulation of α -Msh acetylation may be an important
399 mechanism for background adaptation, more than total amounts of α -Msh released into
400 the blood (Arends et al., 2000).

401 The pioneering works of Zhu and Thomas (1996, 1997, 1998) and Zhu et al. (1999)
402 introduced somatolactin (Sl) as a hormone involved in background color adaptation.

403 They suggested that SI plays a role in background adaptation and possibly regulates
404 pigment movement in the chromatophores of sciaenid fishes. In *C. dimerus*, the long-
405 term exposition to a black background produces an increase in the number and area of
406 SL immunoreactive cells (Cánepa et al., 2006), even from early stages of development
407 (Delgadin et al., 2020). Moreover, growth hormone receptor 1 (GhR1; probably the SL
408 receptor) was detected in the epidermis and dermis from fish scales (Cánepa et al.,
409 2012). This receptor showed changes in its transcript level concomitant with changes in
410 melanophores, suggesting plausible evidence for the role of SI and its receptor in the
411 regulation of chromatophores in *C. dimerus* (Cánepa et al., 2012). Furthermore, it was
412 determined that medaka larvae with biallelic mutations of the GhR1 receptor failed to
413 adapt to the background, unless at the beginning of development (Delgadin et al., 2020).

414 SL has been shown to be involved in different physiological processes, including
415 reproduction, stress responses, Ca²⁺ homeostasis, acid–base balance, growth,
416 metabolism, and immune responses (reviewed in Kawauchi et al., 2009); therefore,
417 changes in tank color can influence the general physiology in different ways, thus
418 affecting fish welfare.

419

420 **4.3 Social interactions**

421 In many social species, skin pigmentation reflects the social hierarchy; for example, in
422 salmonids, social subordination is associated with skin darkening (Abbott et al., 1985;
423 O'Connor et al., 1999; Höglund et al., 2000, 2002). Subordinate fish are subjected to
424 chronic stress induced by aggressive acts from dominant fish (Winberg and Lepage,
425 1998; Øverli et al., 1999; Höglund et al., 2000, 2002). As it was previously mentioned,
426 this leads to a chronic activation of the hypothalamic–pituitary–interrenal axis, and to an
427 increase of α -Msh that induces interrenal cortisol release and skin darkening (Fujii and

428 Oshima, 1986, Höglund et al., 2000). In *Astatotilapia burtoni* it was demonstrated that
429 yellow males are more aggressive than blue ones (Korzan and Fernald, 2007; Korzan et
430 al., 2008). Later on, it was demonstrated that blue males have higher cortisol levels than
431 yellow ones, indicated by an activation of the melanocortin system in the skin (Dijkstra
432 et al., 2017).

433 In *C. dimerus*, body color pattern is associated with different social status. A relation
434 between color and dominance was observed in territorial individuals, which had bright
435 body color patterns, while non-territorial individuals were opaque grey (Alonso et al.,
436 2011). Furthermore, a negative correlation was found between plasma cortisol levels
437 and dominance; fish of lower social hierarchy rank had higher plasma cortisol levels
438 than those in higher rank (Alonso et al., 2011, 2012).

439 It is important to point out that the color of the tank can increase social agonist
440 encounters, besides inducing stress. In Nile tilapia, blue and brown tanks increased this
441 kind of behavior (Merighe et al., 2004), whereas in Arctic char, *Salvelinus alpinus*,
442 white tanks induced a more aggressive behavior than black ones (Höglund et al., 2002).

443

444 **4.4 Light and other factors**

445 It is known that chromatophores respond directly to incident light. This “primary color
446 response” can be observed during embryonic and larval stages, when chromatophores
447 are not innervated or under endocrine control, as well as in adulthood regardless of the
448 presence of both regulatory systems (reviewed in Fujii, 2000; Oshima, 2001). In this
449 sense, cone opsin expression has been detected in melanophores (Chen et al., 2013) and
450 erythrophores (Ban et al., 2005; Chen et al., 2013) in Nile tilapia and in iridophores in

451 Neon tetra (Kasai and Oshima, 2006). Melanophores respond to wavelengths between
452 380-580 nm by dispersing melanosomes (Chen et al., 2013), and erythrophores
453 aggregate or disperse pigment depending on exposure to short or middle/long
454 wavelengths, respectively (Sato et al., 2004; Ban et al., 2005; Chen et al., 2013). The
455 photo-response of iridophores depends on light intensity, with the wavelength of 500
456 nm being the most effective one (Kasai and Oshima, 2006). Besides, the photic
457 environment affects fish pigmentation by modulating nervous and endocrine systems.
458 Unfortunately, there are few studies conducted on the impact of different wavelengths
459 on fish pigmentation. For example, adults of red porgy became paler when exposed to
460 blue light compared to individuals exposed to the full spectrum, with no observed
461 changes in melanin content or α -Msh and cortisol levels (Szisch et al., 2002). These
462 authors proposed that these changes in fish coloration could be due to changes in
463 melanosome aggregation produced by the control of the nervous system. In addition,
464 Amano and Takahashi (2009) suggested that, since green light increased somatic
465 growth in barfin flounder, *Verasper moseri* (Yamanome et al., 2009), *mch* expression
466 and its secretion could be higher, so the skin color of those animals should be paler.
467 Unfortunately, the effect of green light on skin color was not analyzed in that study.

468 Light intensity has been shown to affect growth, behavior, physiology, and coloration in
469 some fish species, such as *Paralichthys woolmani* (Benetti, 1997; Venizelos and
470 Benetti, 1999; Han et al., 2005). Santos et al. (2019) showed that light influences food
471 consumption and conversion, behavior, and plasma cortisol levels of *Lophiosilurus*
472 *alexandri* juveniles; however, no effect on skin pigmentation was observed.

473 Photoperiod can also induce alterations in skin color, given that melatonin not only acts
474 directly over chromatophores but also modifies other endocrine pathways that affect

475 skin pigmentation. For example, in Neon tetra, the red and brown colors produced by
476 erythrophores and melanophores were found to be markedly reduced at night,
477 suggesting the regulation of coloration by an endogenous circadian rhythm (Lythgoe
478 and Shand, 1983). Differences in skin pigmentation due to photoperiod were also
479 observed in Japanese flounder after metamorphosis when comparing the effects of
480 continuous 24 h illumination (LL) to natural light conditions (15 h light: 9 h dark, LD)
481 during larval development. Itoh et al. (2012) found that larvae reared in LL presented
482 paler skin color, and a higher ratio of abnormal pigmentation after metamorphosis.
483 Moreover, LL conditions decreased tyrosine hydroxylase-1 (*th1*) in dopaminergic
484 neurons, but increased *α-msh* levels in melanotrophs with no changes in *mch*
485 expression levels in the lateral tuberal nucleus (NLT). Authors concluded that there
486 could be an accumulation of α-Msh in the melanotrophs because of the inhibitory
487 action of Mch over its protein secretion, causing a pale skin color. In another study,
488 Ginés et al. (2004) found that the skin luminosity of gilthead sea bream was higher
489 under the longer the photoperiod. Similar results were obtained by Lyon and Baker
490 (1993) in rainbow trout, who also described that Mch secretion reached a peak during
491 the light period and then, it gradually declined before night, when the lowest
492 concentrations were observed. These hormone variations were directly related to animal
493 skin paleness.

494 Other factors such as handling, crowding, transport, hydrostatic pressure, and variations
495 in temperature, oxygen, and salinity, can affect either directly or indirectly
496 chromatophores' physiology and thus modify fish pigment. The direct impact of some of
497 these stimuli on chromatophores is poorly studied, although, for example, it is accepted
498 that high temperatures aggregate chromatosomes, while lower temperatures disperse
499 them (Fujii and Oshima, 1994). In any case, these factors are generally considered as

500 stressors, promoting an acute or chronic stress response depending on the duration of
501 the stimuli (reviewed in Wendelaar Bonga, 1997).

502

503 **5 Conclusions and perspectives**

504 The skin pigmentation pattern in fish is species-specific and is given by the number and
505 spatial combination of several types of chromatophores. Research efforts have been
506 made to improve understanding of the underlying endocrine regulation of skin
507 pigmentation. In particular, recent studies have identified other actors besides the classic
508 color change regulators Mch and Msh, such as Sl, Asip, and Th, that seem to play an
509 important role in the regulation of pigmentation. In this sense, more studies are needed
510 to understand how these factors interact in a coordinated way to regulate skin color.
511 Furthermore, considering that most studies on the physiology of pigment cells focus on
512 melanophores and that some studies have demonstrated that cellular communication
513 between different types of chromatophores is essential in the pigmentation patterning
514 process, further research on the regulatory factors of all types of chromatophores and
515 the interactions among them is essential to understand the intricate mechanisms of skin
516 pigmentation as well as to identify the origin and the causes leading to pigmentation
517 disorders. Furthermore, as chromatophores derive from NCC, pigmentation anomalies
518 could be the visible sign of more complex physiological disruptions.

519 Skin pigmentation is one of the most important quality criteria dictating the market
520 value of fish for both human consumption and ornamental use. Rearing conditions such
521 as nutrition, tank coloration, UV incidence, surrounding luminosity, or social
522 interactions can negatively affect the natural skin coloration. In this sense, further
523 studies are needed to identify pigmentation-related endocrine factors that are being

524 modulated when fish are reared under suboptimal conditions. This knowledge will also
525 be useful to better understand the impact of rearing conditions on other biological
526 processes, as many endocrine signals affecting pigmentation are additionally regulating
527 processes such as growth, reproduction, or nutrition, among others. In this sense, skin
528 pigmentation could be considered an indicator of fish well-being.

529 New insights on the influence of stress in gut microbiome modulation and on the role of
530 gut microbiome in the regulation of skin pigmentation reinforces the need for a better
531 understanding of the influence of environmental conditions. Taken together, research on
532 the endocrine factors affecting pigmentation, the communication among different types
533 of chromatophores, the influence of nutrition and abiotic factor in the modulation of
534 these endocrine signals, and the role of gut microbiome in the regulation of these
535 physiological processes could contribute to identify the best rearing conditions for
536 species presenting pigmentation disorders and hence to improve their commercial
537 production.

538

539 **Acknowledgements**

540 This work was carried out with the collaboration of Red CYTED LARVAplus
541 (117RT0521) and was supported by Universidad de Buenos Aires (grant number:
542 20020160100110BA to PV), Consejo Nacional de Investigaciones Científicas y
543 Técnicas (CONICET) (PIP 2014-2016:11220130100501CO to PV).

544

545 **Author contribution:** PGV, MJD, MPDY, and DIPS contributed equally to the design
546 and writing of the manuscript. THD contributed to the revision of the manuscript. All
547 authors approved the final version of the manuscript.

548

549 **References**

- 550 Abbott, J.C., Dunbrack, R.L., Orr, C.D., 1985. The interaction of size and experience in dominance
551 relationships of juvenile steelhead trout (*Salmo gairdneri*). Behaviour, 241-253.
552 <https://www.jstor.org/stable/4534413>
- 553 Alonso, F., Cánepa, M., Moreira, R.G., Pandolfi, M., 2011. Social and reproductive physiology and
554 behavior of the Neotropical cichlid fish *Cichlasoma dimerus* under laboratory conditions. Neotrop.
555 Ichthyol. 9, 559-570. <https://doi.org/10.1590/S1679-62252011005000025>
- 556 Alonso, F., Honji, R.M., Moreira, R.G., Pandolfi, M., 2012. Dominance hierarchies and social status
557 ascent opportunity: anticipatory behavioral and physiological adjustments in a Neotropical cichlid
558 fish. Physiol. Behav. 106, 612-618. <https://doi.org/10.1016/j.physbeh.2012.04.003>
- 559 Amano, M., Takahashi, A., 2009. Melanin-concentrating hormone: A neuropeptide hormone affecting the
560 relationship between photic environment and fish with special reference to background color and food
561 intake regulation. Peptides 30, 1979-1984. <https://doi.org/10.1016/j.peptides.2009.05.022>
- 562 Amiya, N., Amano, M., Takahashi, A., Yamanome, T., Kawauchi, H., Yamamori, K., 2005. Effects of
563 tank color on melanin-concentrating hormone levels in the brain, pituitary gland, and plasma of the
564 barfin flounder as revealed by a newly developed time-resolved fluoroimmunoassay. Gen. Comp.
565 Endocrinol. 143, 251-256. <https://doi.org/10.1016/j.ygcen.2005.04.012>
- 566 Arends, R., Rotllant, J., Metz, J., Mancera, J. M., Bonga, S. W., Flik, G., 2000. alpha-MSH acetylation in
567 the pituitary gland of the sea bream (*Sparus aurata* L.) in response to different backgrounds,
568 confinement and air exposure. J. Endocrinol. 166, 427-435. <https://doi.org/10.1677/joe.0.1660427>

569 Aspengren, S., Hedberg, D., Sköld, H.N., Wallin, M., 2012. New Insights into Melanosome Transport in
570 Vertebrate Pigment Cells. In: Kwang Jeon. (Ed), International Review of Cell and Molecular Biology.
571 Elsevier, Volume 293. 1st Edition, pp. 245, 302

572 Bagnara, J.T., Matsumoto, J., Ferris, W., Frost, S.K., Turner, W.A., Tchen, T.T., Taylor, J.D., 1979.
573 Common origin of pigment cells. Science, 203, 410-415. <https://doi.org/10.1126/science.760198>

574 Baker, B.I., Bird, D.J., Buckingham, J.C., 1986. Effects of chronic administration of melanin-
575 concentrating hormone on corticotrophin, melanotrophin, and pigmentation in the trout. Gen. Comp.
576 Endocrinol. 63, 62-69. [https://doi.org/10.1016/0016-6480\(86\)90182-6](https://doi.org/10.1016/0016-6480(86)90182-6)

577 Ban, E., Kasai, A., Sato, M., Yokozeki, A., Hisatomi, O., Oshima, N., 2005. The signaling pathway in
578 photoresponses that may be mediated by visual pigments in erythrocytes of Nile tilapia. Pigment
579 Cell Res. 18, 360-369. <https://doi.org/10.1111/j.1600-0749.2005.00267.x>

580 Bell, J.G., Sargent, J.R., 2003. Arachidonic acid in aquaculture feeds: current status and future
581 opportunities. Aquaculture 218, 491-499. [https://doi.org/10.1016/S0044-8486\(02\)00370-8](https://doi.org/10.1016/S0044-8486(02)00370-8)

582 Belton, B., Bush, S.R., Little, D.C., 2018. Not just for the wealthy: Rethinking farmed fish consumption
583 in the Global South. Glob. Food Sec. 16, 85-92. <https://doi.org/10.1016/j.gfs.2017.10.005>

584 Benetti, D.D., 1997. Spawning and larval husbandry of flounder (*Paralichthys woolmani*) and Pacific
585 yellowtail (*Seriola mazatlanensis*), new candidate species for aquaculture. Aquaculture, 155, 307-318.
586 [https://doi.org/10.1016/S0044-8486\(97\)00099-9](https://doi.org/10.1016/S0044-8486(97)00099-9)

587 Berchielli-Morais, F.A., Fernandes, J.B.K., Sipaúba-Tavares, L.H., 2016. Diets supplemented with
588 microalgal biomass: effects on growth, survival and colouration of ornamental fish *Hyphessobrycon*
589 *eques* (Steindacher 1882). Aquac. Res. 47, 3061-3069. <https://doi.org/10.1111/are.12756>

590 Bernier, N.J., Flik, G., Klaren, P.H., 2009. Regulation and contribution of the corticotropic, melanotropic
591 and thyrotropic axes to the stress response in fishes. Fish physiol. 28, 235-311.
592 [https://doi.org/10.1016/S1546-5098\(09\)28006-X](https://doi.org/10.1016/S1546-5098(09)28006-X)

593 Bertolesi, G.E., Zhang, J.Z., McFarlane, S., 2019. Plasticity for colour adaptation in vertebrates explained
594 by the evolution of the genes pomc, pmch and pmchl. *Pigment Cell Melanoma Res.* 32, 510-527.
595 <https://doi.org/10.1111/pcmr.12776>

596 Bjerkeng, B., 2008. Carotenoids in aquaculture: fish and crustaceans, in: Britton, G., Liaaen-Jensen, S.,
597 Pfander, H. (Eds.), *Carotenoids*. Birkhäuser, Basel, pp. 237-254.

598 Blanton, M.L., Specker, J.L., 2007. The hypothalamic-pituitary-thyroid (HPT) axis in fish and its role in
599 fish development and reproduction. *Crit. Rev. Toxicol.* 37, 97-115.
600 <https://doi.org/10.1080/10408440601123529>

601 Boglino, A., Wishkerman, A., Darias, M.J., Andree, K.B., De la Iglesia, P., Estévez, A., Gisbert, E., 2013.
602 High dietary arachidonic acid levels affect the process of eye migration and head shape in pseudo-
603 albino Senegalese sole *Solea senegalensis* early juveniles. *J. Fish Biol.* 83, 1302-1320.
604 <https://doi.org/10.1111/jfb.12230>

605 Boglino, A., Wishkerman, A., Darias, M.J., de la Iglesia, P., Andree, K.B., Gisbert, E., Estévez, A., 2014.
606 Senegalese sole (*Solea senegalensis*) metamorphic larvae are more sensitive to pseudo-albinism
607 induced by high dietary arachidonic acid levels than post-metamorphic larvae. *Aquaculture* 433, 276-
608 287. <https://doi.org/10.1016/j.aquaculture.2014.06.012>

609 Bohórquez-Cruz, M., Rodríguez, S., Sonnenholzner, S., Argüello-Guevara, W., 2018. Early development
610 and Juvenile Culture Technique of Speckled Flounder, *Paralichthys woolmani* (Jordan & Williams,
611 1897) under ambient seawater. *J. Appl. Ichthyol.* 34(3), 610-616. <https://doi.org/10.1111/jai.13624>

612 Bolker, J.A., Hakala, T.F., Quist, J.E., 2005. Pigmentation development, defects, and patterning in
613 summer flounder (*Paralichthys dentatus*). *Zoology* 108(3), 183-193.
614 <https://doi.org/10.1016/j.zool.2005.05.001>

615 Booth, M.A., Warner-Smith, R.J., Allan, G.L., Glencross, B.D., 2004. Effects of dietary astaxanthin
616 source and light manipulation on the skin colour of Australian snapper *Pagrus auratus* (Bloch &
617 Schneider, 1801). *Aquac. Res.* 35, 458-464. <https://doi.org/10.1111/j.1365-2109.2004.01038.x>

618 Braasch, I., Volff, J.N., Schartl, M., 2008. The evolution of teleost pigmentation and the fish-specific
619 genome duplication. *J. Fish Biol.* 73, 191-1918. <https://doi.org/10.1111/j.1095-8649.2008.02011.x>

620 Bronner, M.E., LeDouarin, N.M., 2012. Development and evolution of the neural crest: an overview.
621 *Dev. Biol.* 366, 2-9. <https://doi.org/10.1016/j.ydbio.2011.12.042>

622 Cal, L., Suarez-Bregua, P., Cerdá-Reverter, J.M., Braasch, I., Rotllant, J., 2017. Fish pigmentation and the
623 melanocortin system. *Comp. Biochem. Physiol. A Mol. Integr. Physiol.* 211, 26-
624 33. <https://doi.org/10.1016/j.cbpa.2017.06.001>

625 Cal, L., Suarez-Bregua, P., Moran, P., Cerdá-Reverter, J.M., Rotllant, J., 2018. Fish pigmentation. A key
626 issue for the sustainable development of fish farming, in: Yufera, M. (Ed.), *Emerging issues in fish*
627 *larvae research*. Springer, Cham, pp. 229-252.

628 Cal, L., Suarez-Bregua, P., Comesaña, P., Owen, J., Braasch, I., Kelsh, R., Cerdá-Reverter, J.M., Rotllant,
629 J., 2019. Countershading in zebrafish results from an *Asip1* controlled dorsoventral gradient of
630 pigment cell differentiation. *Sci. Rep.* 9, 1-13. <https://doi.org/10.1038/s41598-019-40251-z>

631 Cánepa, M.M., Pandolfi, M., Maggese, M.C., Vissio, P.G., 2006. Involvement of somatolactin in
632 background adaptation of the cichlid fish *Cichlasoma dimerus*. *J. Exp. Zool. A Comp. Exp. Biol.* 305,
633 410-419. <https://doi.org/10.1002/jez.a.273>

634 Cánepa, M.M., Zhu, Y., Fossati, M., Stiller, J.W., Vissio, P.G., 2012. Cloning, phylogenetic analysis and
635 expression of somatolactin and its receptor in *Cichlasoma dimerus*: Their role in long-term
636 background color acclimation. *Gen. Comp. Endocrinol.*, 176, 52-61.
637 <https://doi.org/10.1016/j.ygcen.2011.12.023>

638 Ceinos, R.M., Guillot, R., Kelsh, R.N., Cerdá-Reverter, J.M., Rotllant, J., 2015. Pigment patterns in adult
639 fish result from superimposition of two largely independent pigmentation mechanisms. *Pigment Cell*
640 *Melanoma Res.* 28, 196-209. <https://doi.org/10.1111/pcmr.12335>

641 Cerdá-Reverter, J.M., Haitina, T., Schiöth, H.B., Peter, R.E., 2005. Gene structure of the goldfish agouti-
642 signaling protein: a putative role in the dorsal-ventral pigment pattern of fish. *Endocrinology*, 146,
643 1597-1610. <https://doi.org/10.1210/en.2004-1346>

- 644 Chang, J.P., Wong, A.O., 2009. Growth hormone regulation in fish: a multifactorial model with
645 hypothalamic, peripheral and local autocrine/paracrine signals. *Fish Physiol.* 28, 151-195.
646 [https://doi.org/10.1016/S1546-5098\(09\)28004-6](https://doi.org/10.1016/S1546-5098(09)28004-6)
- 647 Chen, S.C., Robertson, R.M., Hawryshyn, C.W., 2013. Possible involvement of cone opsins in distinct
648 photoresponses of intrinsically photosensitive dermal chromatophores in tilapia *Oreochromis*
649 *niloticus*. *PLoS One* 8. <https://doi.org/10.1371/journal.pone.0070342>
- 650 Cobcroft, J.M., Battaglene, S.C., 2009. Jaw malformation in striped trumpeter *Latris lineata* larvae linked
651 to walling behavior and tank color. *Aquaculture*, 289, 274-282
652 <https://doi.org/10.1016/j.aquaculture.2008.12.018>
- 653 Colihueque, N., 2010. Genetics of salmonid skin pigmentation: clues and prospects for improving the
654 external appearance of farmed salmonids. *Rev. Fish Biol. Fisher.* 20, 71-86.
655 <https://doi.org/10.1007/s11160-009-9121-6>
- 656 Copeman, L.A., Parrish, C.C., 2002. Lipid composition of malpigmented and normally pigmented newly
657 settled yellowtail flounder, *Limanda ferruginea* (Storer). *Aquac. Res.* 33, 1209-1219.
658 <https://doi.org/10.1046/j.1365-2109.2002.00761.x>
- 659 Costa, D.C., Mattioli, C.C., Silva, W.S., Takata, R., Leme, F.O.P., Oliveira, A.L., Luz, R.K., 2017. The
660 effect of environmental colour on the growth, metabolism, physiology and skin pigmentation of the
661 carnivorous freshwater catfish *Lophiosilurus alexandri*. *J. Fish Biol.* 90, 922-935.
662 <https://doi.org/10.1111/jfb.13208>
- 663 Darias, M.J., Andree, K.B., Boglino, A., Fernández, I., Estévez, A., Gisbert, E., 2013a. Coordinated
664 regulation of chromatophore differentiation and melanogenesis during the ontogeny of skin
665 pigmentation of *Solea senegalensis* (Kaup, 1858). *PLoS One*, 8, e63005.
666 <https://doi.org/10.1371/journal.pone.0063005>
- 667 Darias, M.J., Andree, K.B., Boglino, A., Rotllant, J., Cerda-Reverter, J.M., Estevez, A., Gisbert, E.,
668 2013b. Morphological and molecular characterization of dietary-induced pseudo-albinism during post-
669 embryonic development of *Solea senegalensis* (Kaup, 1858). *PLoS One*, 8, e68844.
670 <https://doi.org/10.1371/journal.pone.0068844>

671 De Carvalho, C.C., Caramujo, M.J., 2017. Carotenoids in aquatic ecosystems and aquaculture: a colorful
672 business with implications for human health. *Front. Mar. Sci.* 4, 93.
673 <https://doi.org/10.3389/fmars.2017.00093>

674 Delgado, T.H., Castaneda-Cortes, D.C., Sacks, C., Breccia, A., Fernandino, J.I., Vissio, P.G., 2020.
675 Morphological colour adaptation during development: Involvement of Growth Hormone Receptor 1.
676 bioRxiv. doi: <https://doi.org/10.1101/2020.06.01.128538>

677 Dijkstra, P.D., Maguire, S.M., Harris, R.M., Rodriguez, A.A., DeAngelis, R.S., Flores, S.A., Hofmann,
678 H.A., 2017. The melanocortin system regulates body pigmentation and social behaviour in a colour
679 polymorphic cichlid fish. *P. Roy. Soc. B-Biol. Sci.* 284, 20162838.
680 <https://doi.org/10.1098/rspb.2016.2838>

681 Doolan, B.J., Booth, M.A., Jones, P.L., Allan, G.L., 2007. Effect of cage colour and light environment on
682 the skin colour of Australian snapper *Pagrus auratus* (Bloch & Schneider, 1801). *Aquac. Res.* 38,
683 1395-1403. <https://doi.org/10.1111/j.1365-2109.2007.01818.x>

684 Doolan, B.J., Allan, G.L., Booth, M.A., Jones, P.L., 2008a. Cage colour and post-harvest K⁺
685 concentration affect skin colour of Australian snapper *Pagrus auratus* (Bloch & Schneider, 1801).
686 *Aquac. Res.* 39, 919-927. <https://doi.org/10.1111/j.1365-2109.2008.01950.x>

687 Doolan, B.J., Allan, G.L., Booth, M.A., Jones, P.L., 2008b. Effects of cage netting colour and density on
688 the skin pigmentation and stress response of Australian snapper *Pagrus auratus* (Bloch & Schneider,
689 1801). *Aquac. Res.* 39, 1360-1368. <https://doi.org/10.1111/j.1365-2109.2008.02003.x>

690 Dupin, E., Calloni, G., Real, C., Gonçalves-Trentin, A., Le Douarin, N.M., 2007. Neural crest progenitors
691 and stem cells. *C. R. Biol.* 330, 521-529. <https://doi.org/10.1016/j.crv.2007.04.004>

692 Eslamloo, K., Akhavan, S.R., Eslamifar, A., Henry, M.A., 2015. Effects of background colour on growth
693 performance, skin pigmentation, physiological condition and innate immune responses of goldfish,
694 *Carassius auratus*. *Aquac. Res.* 46, 202-215. <https://doi.org/10.1111/are.12177>

695 Estevez, A., Kanazawa, A., 1995. Effect of (n-3) PUFA and vitamin A Artemia enrichment on
696 pigmentation success of turbot, *Scophthalmus maximus* (L). Aquac. Nutr. 1, 159-168.
697 <https://doi.org/10.1111/j.1365-2095.1995.tb00040.x>

698 Estévez, A., McEvoy, L.A., Bell, J.G., Sargent, J.R., 1999. Growth, survival, lipid composition and
699 pigmentation of turbot (*Scophthalmus maximus*) larvae fed live prey enriched in arachidonic and
700 eicosapentaenoic acids. Aquaculture 180, 321–343. [https://doi.org/10.1016/S0044-8486\(99\)00209-4](https://doi.org/10.1016/S0044-8486(99)00209-4)

701 Estevez, A., Kaneko, T., Seikai, T., Dores, R.M., Tagawa, M., Tanaka, M., 2001. Ontogeny of ACTH and
702 MSH cells in Japanese flounder (*Paralichthys olivaceus*) in relation to albinism. Aquaculture, 202,
703 131-143. [https://doi.org/10.1016/S0044-8486\(01\)00571-3](https://doi.org/10.1016/S0044-8486(01)00571-3)

704 Falcon, J., Migaud, H., Munoz-Cueto, J.A., Carrillo, M., 2010. Current knowledge on the melatonin
705 system in teleost fish. Gene. Comp. Endocrinol. 165, 469-482.
706 <https://doi.org/10.1016/j.ygcen.2009.04.026>

707 Falcón, J., Besseau, L., Magnanou, E., Herrero, M.J., Nagai, M., Boeuf, G., 2011. Melatonin, the time
708 keeper: biosynthesis and effects in fish. Cybium 35, 3-18. [https://doi.org/10.26028/cybium/2011-351-](https://doi.org/10.26028/cybium/2011-351-001)
709 [001](https://doi.org/10.26028/cybium/2011-351-001)

710 FAO, 2020a. The State of World Fisheries and Aquaculture 2020. Sustainability in action. Rome, Italy.
711 <https://doi.org/10.4060/ca9229en>

712 FAO, 2020b. Fishery and Aquaculture Statistics. Global production by production source 1950-2018
713 (FishstatJ), in: FAO Fisheries and Aquaculture Department [online]. Rome. Updated 2020.
714 www.fao.org/fishery/statistics/software/fishstatj/en

715 Freeman, M.E., Kanyicska, B., Lerant, A., Nagy, G., 2000. Prolactin: structure, function, and regulation
716 of secretion. Physiol. Rev. 80, 1523-1631. <https://doi.org/10.1152/physrev.2000.80.4.1523>

717 Fries, E.M., Bittarello, A.C., Zaminhan, M., Signor, A., Feiden, A., Boscolo, W.R., 2014. Annatto in diets
718 *Carassius auratus* goldfish fingerlings: growth performance and skin pigmentation. Semin. Ciên.
719 Agrár. 35, 3401-3414. <https://doi.org/10.5433/1679-0359.2014v35n6p3401>

720 Frohnhöfer, H.G., Krauss, J., Maischein, H.M., Nüsslein-Volhard, C., 2013. Iridophores and their
721 interactions with other chromatophores are required for stripe formation in zebrafish. *Development*.
722 140, 2997-3007. <https://doi.org/10.1242/dev.096719>.

723 Fujii, R., Miyashita, Y., 1982. Receptor mechanisms in fish chromatophores--V. MSH disperses
724 melanosomes in both dermal and epidermal melanophores of a catfish (*Parasilurusasotus*). *Comp.*
725 *Biochem. Physiol. C* 71, 1-6. [https://doi.org/10.1016/0306-4492\(82\)90002-8](https://doi.org/10.1016/0306-4492(82)90002-8)

726 Fujii, R., Oshima, N., 1986. Control of chromatophore movements in teleost fishes. *Zoolog. Sci.* 3, 13-47.

727 Fujii, R., Oshima, N., 1994. Factors influencing motile activities of fish chromatophores, in: *Advances in*
728 *comparative and environmental physiology*. Springer, Berlin, Heidelberg, pp. 1-54.

729 Fujii, R., 2000. The regulation of motile activity in fish chromatophores. *Pigment Cell Res.* 13, 300-319.
730 <https://doi.org/10.1034/j.1600-0749.2000.130502.x>

731 Fukada, H., Ozaki, Y., Pierce, A.L., Adachi, S., Yamauchi, K., Hara, A., Swanson, P., Dickhoff, W. W.,
732 2005. Identification of the salmon somatolactin receptor, a new member of the cytokine receptor
733 family. *Endocrinology* 146, 2354-2361. <https://doi.org/10.1210/en.2004-1578>

734 Fukamachi, S., Sugimoto, M., Mitani, H., Shima, A., 2004. Somatolactin selectively regulates
735 proliferation and morphogenesis of neural-crest derived pigment cells in medaka. *Proc. Natl. Acad.*
736 *Sci.* 101, 10661-10666. <https://doi.org/10.1073/pnas.0401278101>

737 Fukamachi, S., Meyer, A., 2007. Evolution of receptors for growth hormone and somatolactin in fish and
738 land vertebrates: lessons from the lungfish and sturgeon orthologues. *J. Mol. Evol.* 65, 359-372.
739 <https://doi.org/10.1007/s00239-007-9035-7>

740 Fukamachi, S., Yada, T., Meyer, A., Kinoshita, M., 2009. Effects of constitutive expression of
741 somatolactin alpha on skin pigmentation in medaka. *Gene* 442, 81-87.
742 <https://doi.org/10.1016/j.gene.2009.04.010>

743 Ginés, R., Afonso, J.M., Argüello, A., Zamorano, M.J., López, J.L., 2004. The effects of long-day
744 photoperiod on growth, body composition and skin colour in immature gilthead sea bream (*Sparus*
745 *aurata* L.). *Aquac. Res.* 35, 1207-1212. <https://doi.org/10.1111/j.1365-2109.2004.01126.x>

746 Gouveia, L., Choubert, G., Pereira, N., Santinha, J., Empis, J., Gomes, E., 2002. Pigmentation of gilthead
747 seabream, *Sparus aurata* (L. 1875), using *Chlorella vulgaris* (Chlorophyta, Volvocales) microalga.
748 Aquac. Res. 33, 987-993. <https://doi.org/10.1046/j.1365-2109.2002.00751.x>

749 Grove, D.J., 1994. Chromatophores, in: Nilsson, S., Holmgren, S. (Eds.), Comparative Physiology and
750 Evolution of the Autonomic Nervous System. Harwood Academic Publishers, Switzerland, pp. 331-
751 352.

752 Guillot, R., Ceinos, R.M., Cal, R., Rotllant, J., Cerda-Reverter, J.M., 2012. Transient ectopic
753 overexpression of agouti-signalling protein 1 (asip1) induces pigment anomalies in flatfish. PLoS One
754 7. <https://doi.org/10.1371/journal.pone.0048526>

755 Guillot, R., Muriach, B., Rocha, A., Rotllant, J., Kelsh, R.N., Cerdá-Reverter, J.M., 2016. Thyroid
756 hormones regulate zebrafish melanogenesis in a gender-specific manner. PloS one, 11.
757 <https://doi.org/10.1371/journal.pone.0166152>

758 Güroy, B., Şahin, İ., Mantoğlu, S., Kayalı, S., 2012. *Spirulina* as a natural carotenoid source on growth,
759 pigmentation and reproductive performance of yellow tail cichlid *Pseudotropheus acei*. Aquac. Int.
760 20, 869-878. <https://doi.org/10.1007/s10499-012-9512-x>

761 Hamre, K., Opstad, I., Espe, M., Solbakken, J., Hemre, G.I., Pittman, K., 2002. Nutrient composition and
762 metamorphosis success of Atlantic halibut (*Hippoglossus hippoglossus*, L.) larvae fed natural
763 zooplankton or *Artemia*. Aquac. Nutr. 8, 139-148. <https://doi.org/10.1046/j.1365-2095.2002.00201.x>

764 Hamre, K., Moren, M., Solbakken, J., Opstad, I., Pittman, K., 2005. The impact of nutrition on
765 metamorphosis in Atlantic halibut (*Hippoglossus hippoglossus* L.). Aquaculture 250, 555-565.
766 <https://doi.org/10.1016/j.aquaculture.2005.01.016>

767 Hamre, K., Holen, E., Moren, M., 2007. Pigmentation and eye migration in Atlantic halibut
768 (*Hippoglossus hippoglossus* L.) larvae: new findings and hypotheses. Aquac. Nutr. 13, 65-80.
769 <https://doi.org/10.1111/j.1365-2095.2007.00467.x>

770 Han, D., Xie, S., Lei, W., Zhu, X., Yang, Y., 2005. Effect of light intensity on growth, survival and skin
771 color of juvenile Chinese longsnout catfish (*Leiocassis longirostris* Günther). Aquaculture 248, 299-
772 306. <https://doi.org/10.1016/j.aquaculture.2005.03.016>

773 Harpaz, S., Padowicz, D., 2007. Color enhancement in the ornamental dwarf cichlid *Microgeophagus*
774 *ramirezi* by addition of plant carotenoids to the fish diet. *Isr. J. Aquacult. Bamid.* 59, 195–200.

775 Heath, P.L., Moore, C.G., 1997. Rearing dover sole larvae on *Tisbe* and *Artemia* diets. *Aquac. Int.* 5, 29-
776 39. <https://doi.org/10.1007/BF02764785>

777 Höglund, E., Balm, P.H., Winberg, S., 2000. Skin darkening, a potential social signal in subordinate
778 arctic charr (*Salvelinus alpinus*): the regulatory role of brain monoamines and pro-opiomelanocortin-
779 derived peptides. *J. Exp. Biol.* 203, 1711-1721.

780 Höglund, E., Balm, P.H., Winberg, S., 2002. Behavioural and neuroendocrine effects of environmental
781 background colour and social interaction in Arctic charr (*Salvelinus alpinus*). *J. Exp. Biol.* 205, 2535-
782 2543.

783 Iga, T., Matsuno, A., 1992. A novel leucophore in the darkbanded rockfish, *Sebastes inermis* I.
784 ultrastructure. (Physiology) Proceedings of the Sixty-Third Annual Meeting of the Zoological Society
785 of Japan. *Zoolog. Sci.* 9, 1226.

786 Inui, Y., Miwa, S., 2012. Metamorphosis of flatfish (Pleuronectiformes), in: Dufour, S., Rousseau, K.,
787 Kapoor, B.G. (Eds.), *Metamorphosis in Fish*. CRC Press, Boca Raton, pp. 107–153.

788 Ishibashi, Y., Kurata, M., Izumi, T., Okada, T., 2013. Effects of tank wall pattern on survival, bone injury
789 rate, and stress response of juvenile Pacific bluefin tuna, *Thunnus orientalis*. *Aquac. Eng.* 56:13-17.
790 <https://doi.org/10.1016/j.aquaeng.2013.03.004>.

791 Itoh, K., Washio, Y., Fujinami, Y., Shimizu, D., Uji, S., Yokoi, H., Suzuki, T., 2012. Continuous
792 illumination through larval development suppresses dopamine synthesis in the suprachiasmatic
793 nucleus, causing activation of α -MSH synthesis in the pituitary and abnormal metamorphic skin
794 pigmentation in flounder. *Gen. Comp. Endocrinol.* 176, 215-221.
795 <https://doi.org/10.1016/j.ygcen.2012.01.017>

796 Janz, D.M., Weber, L.P., 2000. Endocrine system, in: Ostrander, G.K. (Ed.), *The Laboratory Fish*.
797 Academic Press, pp. 415-439. <https://doi.org/10.1016/B978-012529650-2/50031-7>

798 Jentoft, S., ØXnevad, S., Aastveit, A.H., Andersen, Ø., 2006. Effects of tank wall color and up-welling
799 water flow on growth and survival of Eurasian perch larvae (*Perca fluviatilis*). J. World Aquac. Soc.
800 37, 313-317. <https://doi.org/10.1111/j.1749-7345.2006.00042.x>

801 Kalinowski, C.T., Izquierdo, M.S., Schuchardt, D., Robaina, L.E., 2007. Dietary supplementation time
802 with shrimp shell meal on red porgy (*Pagrus pagrus*) skin colour and carotenoid concentration.
803 Aquaculture 272, 451-457. <https://doi.org/10.1016/j.aquaculture.2007.06.008>

804 Kanazawa, A., 1993. Nutritional mechanisms involved in the occurrence of abnormal pigmentation in
805 hatchery-reared flatfish. J. World Aquacult. Soc. 24, 162-166. <https://doi.org/10.1111/j.1749-7345.1993.tb00005.x>

806

807 Kaneko, T., 1996. Cell biology of somatolactin. Int. Rev. Cytol. 169, 1-24. [https://doi.org/10.1016/S0074-7696\(08\)61983-X](https://doi.org/10.1016/S0074-7696(08)61983-X)

808

809 Karakatsouli, N., Papoutsoglou, S.E., Manolossos, G., 2007. Combined effects of rearing density and tank
810 colour on the growth and welfare of juvenile white sea bream *Diplodus sargus* L. in a recirculating
811 water system. Aquac. Res. 38, 1152-1160. <https://doi.org/10.1111/j.1365-2109.2007.01780.x>

812 Kasai, A., Oshima, N., 2006. Light-sensitive motile iridophores and visual pigments in the neon tetra,
813 *Paracheirodon innesi*. Zoolog. Sci. 23, 815-819. <https://doi.org/10.2108/zsj.23.815>

814 Kasukawa, H., Oshima, N., Fujii, R., 1986. Control of chromatophore movements in dermal chromatic
815 units of blue damselfish--II. The motile iridophore. Comp. Biochem. Physiol. C 83, 1-7.
816 [https://doi.org/10.1016/0742-8413\(86\)90003-4](https://doi.org/10.1016/0742-8413(86)90003-4)

817 Kawauchi, H., Baker, B.I., 2004. Melanin-concentrating hormone signaling systems in fish. Peptides 25,
818 1577-1584. <https://doi.org/10.1016/j.peptides.2004.03.025>

819 Kawauchi, H., Sower, S.A., Moriyama, S., 2009. The neuroendocrine regulation of prolactin and
820 somatolactin secretion in fish. Fish Physiol. 28, 197-234. [https://doi.org/10.1016/S1546-5098\(09\)28005-8](https://doi.org/10.1016/S1546-5098(09)28005-8)

821

822 Khan, U.W., Øverli, Ø., Hinkle, P.M., Pasha, F.A., Johansen, I.B., Berget, I., Silva, P.I.M., Kittilsen, S.,
823 Höglund, E., Omholt, S.W., Våge, D.I., 2016. A novel role for pigment genes in the stress response in
824 rainbow trout (*Oncorhynchus mykiss*). *Sci. Rep.* 6, 1-11. <https://doi.org/10.1038/srep28969>

825 Kimura, T., Nagao, Y., Hashimoto, H., Yamamoto-Shiraishi, Y.I., Yamamoto, S., Yabe, T., Takada, S.,
826 Kinoshita, M., Kuroiwa, A., Naruse, K., 2014. Leucophores are similar to xanthophores in their
827 specification and differentiation processes in medaka. *Proc. Natl. Acad. Sci.* 111, 7343-7348.
828 <https://doi.org/10.1073/pnas.1311254111>

829 Kitta, K., Makino, M., Oshima, N., Bern, H.A., 1993. Effects of prolactins on the chromatophores of the
830 tilapia, *Oreochromis niloticus*. *Gen. Comp. Endocrinol.*, 92, 355-365.
831 <https://doi.org/10.1006/gcen.1993.1173>

832 Kobayashi, Y., Chiba, H., Mizusawa, K., Suzuki, N., Cerdá-Reverter, J.M., Takahashi, A., 2011.
833 Pigment-dispersing activities and cortisol-releasing activities of melanocortins and their receptors in
834 xanthophores and head kidneys of the goldfish *Carassius auratus*. *Gen. Comp. Endocrinol.*, 173, 438-
835 446. <https://doi.org/10.1016/j.ygcen.2011.06.019>

836 Kobayashi, Y., Mizusawa, K., Saito, Y., Takahashi, A., 2012. Melanocortin systems on pigment
837 dispersion in fish chromatophores. *Front. Endocrinol.* 3, 9. <https://doi.org/10.3389/fendo.2012.00009>

838 Kobayashi, Y., Hamamoto, A., Takahashi, A., Saito, Y., 2016. Dimerization of melanocortin receptor 1
839 (MC1R) and MC5R creates a ligand-dependent signal modulation: Potential participation in
840 physiological color change in the flounder. *Gen. Comp. Endocrinol.* 230, 103-109.
841 <https://doi.org/10.1016/j.ygcen.2016.04.008>

842 Kolios P., Kiritsis S., Katribusas N., 1997. Larval-rearing and growout of the red porgy (*Pagrus pagrus*)
843 in the Riopesca hatchery (Greece). *Hydrobiologia* 358,321-325.
844 <https://doi.org/10.1023/A:1003132903785>

845 Korzan, W.J., Fernald, R.D., 2007. Territorial male color predicts agonistic behavior of conspecifics in a
846 color polymorphic species. *Behav. Ecol.* 18, 318-323. <https://doi.org/10.1093/beheco/arl093>

847 Korzan, W.J., Robison, R.R., Zhao, S., Fernald, R.D., 2008. Color change as a potential behavioral
848 strategy. *Horm. Behav.* 54, 463-470. <https://doi.org/10.1016/j.yhbeh.2008.05.006>

849 Lamers, A.E., Balm, P.H.M., Haenen, H.E.M.G., Jenks, B.G., Bonga, S.W., 1991. Regulation of
850 differential release of α -melanocyte-stimulating hormone forms from the pituitary of a teleost fish,
851 *Oreochromis mossambicus*. J. Endocrinol. 129, 179-187. <https://doi.org/10.1677/joe.0.1290179>

852 Le Douarin, N.M., Dupin, E., 2003. Multipotentiality of the neural crest. Curr. Opin. Genet. Dev. 13, 529-
853 536. <https://doi.org/10.1016/j.gde.2003.08.002>

854 Leclercq, E., Taylor, J.F., Migaud, H., 2010. Morphological skin colour changes in teleosts. Fish Fish. 11,
855 159-193. <https://doi.org/10.1111/j.1467-2979.2009.00346.x>

856 Lerner, A., Neidhöfer, S., Torsten, M., 2017. The Gut Microbiome Feelings of the Brain: A Perspective
857 for Non-Microbiologists. Microorganisms 5, 66. <https://doi.org/10.3390/microorganisms5040066>

858 Ligon, R.A., McCartney, K.L., 2016. Biochemical regulation of pigment motility in vertebrate
859 chromatophores: a review of physiological color change mechanisms. Curr. Zool. 62, 237-252.
860 <https://doi.org/10.1093/cz/zow051>

861 Lim, K.C., Yusoff, F.M., Shariff, M., Kamarudin, M.S., 2018. Astaxanthin as feed supplement in aquatic
862 animals. Rev. Aquacult. 10, 738-773. <https://doi.org/10.1111/raq.12200>

863 Lin, M.Q., Ushio, H., Ohshima, T., Yamanaka, H., Koizumi, C., 1998. Skin color control of the red sea
864 bream (*Pagrus major*). LWT-Food Sci. Tech. 31, 27-32. <https://doi.org/10.1006/fstl.1997.0280>

865 López, A.V., Müller, M.I., Radonic, M., Bambill, G.A., Boccanfuso, J.J., 2009. Larval culture technique
866 and quality control in juveniles of flounder *Paralichthys orbignyanus* (Valenciennes, 1839) in
867 Argentina. Span. J. Agric. Res. 7, 75-82. <https://doi.org/10.5424/sjar/2009071-400>

868 Lund, I., Steinfeldt, S.J., Banta, G., Hansen, B.W., 2008. The influence of dietary concentrations of
869 arachidonic acid and eicosapentaenoic acid at various stages of larval ontogeny on eye migration,
870 pigmentation and prostaglandin content of common sole larvae (*Solea solea* L.). Aquaculture 276,
871 143-153. <https://doi.org/10.1016/j.aquaculture.2008.01.004>

872 Lund, I., Steinfeldt, S.J., Hansen, B.W., 2010. Influence of dietary arachidonic acid combined with light
873 intensity and tank colour on pigmentation of common sole (*Solea solea* L.) larvae. Aquaculture 308,
874 159-165. <https://doi.org/10.1016/j.aquaculture.2010.08.004>

875 Lyon, V.E., Baker, B.I., 1993. The effect of photoperiod on plasma levels of melanin-concentrating
876 hormone in the trout. *J. Neuroendocrinol.* 5, 493-499. [https://doi.org/10.1111/j.1365-](https://doi.org/10.1111/j.1365-2826.1993.tb00513.x)
877 [2826.1993.tb00513.x](https://doi.org/10.1111/j.1365-2826.1993.tb00513.x)

878 Lythgoe, J.N., Shand, J., 1983. Diel colour changes in the neon tetra *Paracheirodon innesi*. *Environ. Biol.*
879 *Fishes* 8, 249-254. <https://doi.org/10.1007/BF00001090>

880 Martinez-Cardenas, L., Purser, G.J., 2011. Effect of temperature on growth and survival in cultured early
881 juvenile pot-bellied seahorses, *Hippocampus abdominalis*. *J. World Aquac. Soc.* 42, 854-862.
882 <https://doi.org/10.1111/j.1749-7345.2011.00526.x>

883 Matsuda, N., Yamamoto, I., Masuda, R., Tagawa, M., 2018. Cortisol promotes staining-type
884 hypermelanosis in juvenile Japanese flounder. *Aquaculture*, 497, 147-154.
885 <https://doi.org/10.1016/j.aquaculture.2018.07.055>

886 Matsui, S., Tanabe, T., Furuichi, M., Yoshimatsu, T., Kitajima, C., 1992. Reduction of black lines in the
887 muscle of cultured red sea bream and improvement of the body color. *Nippon Suisan Gakkaishi*, 58,
888 1459-1464. <https://doi.org/10.2331/suisan.58.1459>

889 McMenamin, S.K., Bain, E.J., McCann, A.E., Patterson, L.B., Eom, D.S., Waller, Z.P., Hamill, J.C.,
890 Kuhlman, J.A., Eisen, J.S., Parichy, D.M., 2014. Thyroid hormone-dependent adult pigment cell
891 lineage and pattern in zebrafish. *Science*, 345, 1358-1361. <https://doi.org/10.1126/science.1256251>

892 McNulty, J.C., Jackson, P.J., Thompson, D.A., Chai, B., Gantz, I., Barsh, G.S., Dawson, P.E., Millhauser,
893 G.L., 2005. Structures of the agouti signaling protein. *J. Mol. Biol.* 346, 1059-1070.
894 <https://doi.org/10.1016/j.jmb.2004.12.030>

895 Menter, D.G., Obika, M., Tchen, T.T., Taylor, J.D., 1979. Leucophores and iridophores of *Fundulus*
896 *heteroclitus*: biophysical and ultrastructural properties. *J. Morphol.* 160, 103-119.
897 <https://doi.org/10.1002/jmor.1051600107>

898 Merighe, G.K.F., Pereira-da-Silva, E.M., Negrão, J.A., Ribeiro, S., 2004. Effect of background color on
899 the social stress of Nile tilapia (*Oreochromis niloticus*). *Revista Brasileira de Zootecnia*, 33, 828-837.
900 <https://doi.org/10.1590/S1516-35982004000400002>

901 Miwa, S., Yamano, K., 1999. Retinoic acid stimulates development of adult-type chromatophores in the
902 flounder. J. Exp. Zool. 284, 317-324. [https://doi.org/10.1002/\(SICI\)1097-](https://doi.org/10.1002/(SICI)1097-010X(19990801)284:3<317::AID-JEZ9>3.0.CO;2-B)
903 [010X\(19990801\)284:3<317::AID-JEZ9>3.0.CO;2-B](https://doi.org/10.1002/(SICI)1097-010X(19990801)284:3<317::AID-JEZ9>3.0.CO;2-B)

904 Mizusawa, K., Saito, Y., Wang, Z., Kobayashi, Y., Matsuda, K., Takahashi, A., 2009. Molecular cloning
905 and expression of two melanin-concentrating hormone receptors in goldfish. Peptides 30, 1990-1996.
906 <https://doi.org/10.1016/j.peptides.2009.04.010>

907 Mizusawa, K., Kobayashi, Y., Sunuma, T., Asahida, T., Saito, Y., Takahashi, A., 2011. Inhibiting roles of
908 melanin-concentrating hormone for skin pigment dispersion in barfin flounder, *Verasper moseri*. Gen.
909 Comp. Endocrinol. 171, 75-81. <https://doi.org/10.1016/j.ygcen.2010.12.008>

910 Mizusawa, K., Kobayashi, Y., Yamanome, T., Saito, Y., Takahashi, A., 2013. Interrelation between
911 melanocyte-stimulating hormone and melanin-concentrating hormone in physiological body color
912 change: roles emerging from barfin flounder *Verasper moseri*. Gen. Comp. Endocrinol. 181, 229–234.
913 <https://doi.org/10.1016/j.ygcen.2012.09.026>

914 Moren, M., Waagbø, R., Hamre, K., 2011. Micronutrients. Larval fish nutrition, 117-149.
915 <https://doi.org/10.1002/9780470959862.ch4>

916 Næss, T., Lie, Ø., 1998. A sensitive period during first feeding for the determination of pigmentation
917 pattern in Atlantic halibut, *Hippoglossus hippoglossus* L., juveniles: the role of diet. Aquac. Res. 29,
918 925-934. <https://doi.org/10.1046/j.1365-2109.1998.29120925.x>

919 Nagao, Y., Takada, H., Miyadai, M., Adachi, T., Seki, R., Kamei, Y., Hara, I., Taniguchi, Y., Naruse, K.,
920 Hibi, M., Kelsh, R.N., Hashimoto, H., 2018. Distinct interactions of Sox5 and Sox10 in fate
921 specification of pigment cells in medaka and zebrafish. PLoS Genet. 14, e1007260.
922 <https://doi.org/10.1371/journal.pgen.1007260>

923 Nagaishi, H., Oshima, N., 1989. Neural control of motile activity of light-sensitive iridophores in the
924 neon tetra. Pigment Cell Res. 2, 485-492. <https://doi.org/10.1111/j.1600-0749.1989.tb00243.x>

925 Nakamasu, A., Takahashi, G., Kanbe, A., Kondo, S., 2009. Interactions between zebrafish pigment cells
926 responsible for the generation of Turing patterns. *Proc. Natl. Acad. Sci.* 106, 8429-8434.
927 <https://doi.org/10.1073/pnas.0808622106>

928 Nakamura, M., Seikai, T., Aritaki, M., Masuda, R., Masaru, T., Tagawa, M., 2010. Dual appearance of
929 xanthophores, and ontogenetic changes in other pigment cells during early development of Japanese
930 flounder *Paralichthys olivaceus*. *Fish Sci* 76, 243–250. <https://doi.org/10.1007/s12562-009-0209-7>

931 Nguyen, N., Sugimoto, M., Zhu, Y., 2006. Production and purification of recombinant somatolactin β and
932 its effects on melanosome aggregation in zebrafish. *Gen. Comp. Endocrinol.* 145, 182-187.
933 <https://doi.org/10.1016/j.yggen.2005.09.015>

934 Nüsslein-Volhard, C., Singh, A.P., 2017. How fish color their skin: a paradigm for development and
935 evolution of adult patterns: multipotency, plasticity, and cell competition regulate proliferation and
936 spreading of pigment cells in zebrafish coloration. *BioEssays*, 39, 1600231.
937 <https://doi.org/10.1002/bies.201600231>

938 O'Connor, K.I., Metcalfe, N.B., Taylor, A.C., 1999. Does darkening signal submission in territorial
939 contests between juvenile Atlantic salmon, *Salmo salar*?. *Anim. Behav.* 58, 1269-1276.
940 <https://doi.org/10.1006/anbe.1999.1260>

941 Orihuela, L., Montes, M., Linares, J., Castro, A., Carrera, L., Lazo, J.P., 2018. Effect of Two Novel
942 Experimental Microdiet Types on Growth, Survival, and Pigmentation during the Weaning Period of
943 the Fine Flounder, *Paralichthys adspersus*, Larvae. *J. World Aquacult. Soc.* 49, 770-779.
944 <https://doi.org/10.1111/jwas.12526>

945 Oshima, N., Kasukawa, H., Fujii, R., Wilkes, B.C., Hruby, V.J., Hadley, M.E., 1986. Action of melanin-
946 concentrating hormone (MCH) on teleost chromatophores. *Gen. Comp. Endocrinol.* 64, 381-388.
947 [https://doi.org/10.1016/0016-6480\(86\)90072-9](https://doi.org/10.1016/0016-6480(86)90072-9)

948 Oshima, N., Kasukawa, H., Fujii, R., 1989. Control of chromatophore movements in the blue-green
949 damselfish, *Chromisviridis*. *Comp. Biochem. Physiol. C Pharmacol.* 93, 239-
950 245. [https://doi.org/10.1016/0742-8413\(89\)90227-2](https://doi.org/10.1016/0742-8413(89)90227-2)

951 Oshima, N., Makino, M., Iwamuro, S., Bern, H.A., 1996. Pigment dispersion by prolactin in cultured
952 xanthophores and erythrophores of some fish species. *J. Exp. Zool.* 275, 45-52.
953 [https://doi.org/10.1002/\(SICI\)1097-010X\(19960501\)275:1<45::AID-JEZ7>3.0.CO;2-A](https://doi.org/10.1002/(SICI)1097-010X(19960501)275:1<45::AID-JEZ7>3.0.CO;2-A)

954 Oshima, N., Goto, M., 2000. Prolactin signaling in erythrophores and xanthophores of teleost fish.
955 *Pigment Cell Res.* 13, 35-40. <https://doi.org/10.1034/j.1600-0749.13.s8.8.x>

956 Oshima, N., 2001. Direct reception of light by chromatophores of lower vertebrates. *Pigment Cell Res.*
957 14, 312-319. <https://doi.org/10.1034/j.1600-0749.2001.140502.x>

958 Otsuki, Y., Okuda, Y., Naruse, K., Saya, H., 2020. Identification of kit-ligand a as the Gene Responsible
959 for the Medaka Pigment Cell Mutant few melanophore. *G3 (Bethesda)* 10, 311-319.
960 <https://doi.org/10.1534/g3.119.400561>

961 Øverli, Ø., Harris, C.A., Winberg, S., 1999. Short-term effects of fights for social dominance and the
962 establishment of dominant-subordinate relationships on brain monoamines and cortisol in rainbow
963 trout. *Brain Behav. Evol.* 54, 263-275. <https://doi.org/10.1159/000006627>

964 Pandolfi, M., Cánepa, M., Ravaglia, M., Maggese, M., Paz, D., Vissio, P., 2003. Melanin-concentrating
965 hormone system in the brain and skin of the cichlid fish *Cichlasoma dimerus*: anatomical localization,
966 ontogeny and distribution in comparison to α -melanocyte-stimulating hormone-expressing cells. *Cell*
967 *Tissue Res.* 311, 61-69. <https://doi.org/10.1007/s00441-002-0654-4>

968 Parichy, D.M., Spiewak, J.E., 2015. Origins of adult pigmentation: diversity in pigment stem cell lineages
969 and implications for pattern evolution. *Pigment Cell Melanoma Res.* 28, 31-50.
970 <https://doi.org/10.1111/pcmr.12332>

971 Pérez Sirkin, D.I., Cánepa, M.M., Fossati, M., Fernandino, J.I., Delgadin, T., Canosa, L.F., Somoza,
972 G.M., Vissio, P.G., 2012. Melanin concentrating hormone (MCH) is involved in the regulation of
973 growth hormone in *Cichlasoma dimerus* (Cichlidae, Teleostei). *Gen. Comp. Endocrinol.* 176, 102-
974 111. <https://doi.org/10.1016/j.ygcen.2012.01.002>

975 Pinto, P.I.S., Guerreiro, C.C., Costa, R.A., Martinez-Blanch, J.F., Carballo, C., Codoñer, F.M.,
976 Manchado, M., Power, D.M., 2019. Understanding pseudo-albinism in sole (*Solea senegalensis*): a

977 transcriptomics and metagenomics approach. Sci Rep 9, 13604. <https://doi.org/10.1038/s41598-019->
978 [49501-6](https://doi.org/10.1038/s41598-019-49501-6)

979 Pittman, K., Yúfera, M., Pavlidis, M., Geffen, A.J., Koven, W., Ribeiro, L., Zambonino-Infante, J.L.,
980 Tandler, A., 2013. Fantastically plastic: fish larvae equipped for a new world. Rev. Aquac. 5, S224-
981 S267. <https://doi.org/10.1111/raq.12034>

982 Ponce-Palafox, J.T., Arredondo-Figueroa, J.L., Vernon-Carter, E.J., 2004. Pigmentación de la tilapia
983 (*Oreochromis niloticus*) con carotenoides de flor de cempasúchil (*Tagetes erecta*) en comparación con
984 la astaxantina. Rev. Mex. Ing. Quim. 3(2), 219-225. <https://www.redalyc.org/pdf/620/62030207.pdf>

985 Price, A.C., Weadick, C.J., Shim, J., Rodd, F.H., 2008. Pigments, patterns, and fish behavior. Zebrafish 5,
986 297-307. <https://doi.org/10.1089/zeb.2008.0551>

987 Reitan, K.I., Rainuzzo, J.R., Olsen, Y., 1994. Influence of lipid composition of live feed on growth,
988 survival and pigmentation of turbot larvae. Aquac. Int. 2, 33-48. <https://doi.org/10.1007/BF00118531>

989 Ribeiro, A.R., Gonçalves, A., Barbeiro, M., Bandarra, N., Nunes, M.L., Carvalho, M.L., Silva, J.,
990 Navalho, J., Dinis, M.T., Silva, T., Dias, J., 2017. *Phaeodactylum tricornutum* in finishing diets for
991 gilthead seabream: effects on skin pigmentation, sensory properties and nutritional value. J. Appl.
992 Phycol. 29, 1945-1956. <https://doi.org/10.1007/s10811-017-1125-3>

993 Rønnestad, I., Yúfera, M., Ueberschär, B., Ribeiro, L., Sæle, Ø., Boglione, C., 2013. Feeding behaviour
994 and digestive physiology in larval fish: current knowledge, and gaps and bottlenecks in research. Rev.
995 Aquacult. 5, S59-S98. <https://doi.org/10.1111/raq.12010>

996 Rotllant, J., Tort, L., Montero, D., Pavlidis, M., Martinez, M., Bonga, S.W., Balm, P.H.M., 2003.
997 Background colour influence on the stress response in cultured red porgy *Pagrus pagrus*. Aquaculture
998 223, 129-139. [https://doi.org/10.1016/S0044-8486\(03\)00157-1](https://doi.org/10.1016/S0044-8486(03)00157-1)

999 Ruane, N.M., Makridis, P., Balm, P.H.M., Dinis, M.T., 2005. Skin darkness is related to cortisol, but not
1000 MSH, content in post-larval *Solea senegalensis*. J. Fish Biol. 67, 577-581.
1001 <https://doi.org/10.1111/j.0022-1112.2005.00747.x>

- 1002 Sage, M., 1970. Control of prolactin release and its role in color change in the teleost *Gillichthys*
1003 *mirabilis*. J. Exp. Zool. 173, 121-127. <https://doi.org/10.1002/jez.1401730109>
- 1004 Sánchez, E., Rubio, V.C., Cerdá-Reverter, J.M., 2010. Molecular and pharmacological characterization of
1005 the melanocortin type 1 receptor in the sea bass. Gen. Comp. Endocrinol. 165, 163-169.
1006 <https://doi.org/10.1016/j.ygcen.2009.06.008>
- 1007 Santos, T.G., Schorer, M., dos Santos, J.C., Pelli, A., Pedreira, M.M., 2019. The light intensity in growth,
1008 behavior and skin pigmentation of juvenile catfish *Lophiosilurus alexandri* (Steindachner). Lat. Am.
1009 J. Aquat. Res. 47, 416-422. <http://dx.doi.org/10.3856/vol47-issue3-fulltext-3>
- 1010 Sato, M., Ishikura, R., Oshima, N., 2004. Direct effects of visible and UVA light on pigment migration in
1011 erythrophores of Nile tilapia. Pigment Cell Res. 17, 519-524. [https://doi.org/10.1111/j.1600-](https://doi.org/10.1111/j.1600-0749.2004.00178.x)
1012 [0749.2004.00178.x](https://doi.org/10.1111/j.1600-0749.2004.00178.x)
- 1013 Saunders, L.M., Mishra, A.K., Aman, A.J., Lewis, V.M., Toomey, M.B., Packer, J.S., Qiu, X., McFaline-
1014 Figueroa, J.L., Corbo, J.C., Trapnell, C., Parichy, D.M., 2019. Thyroid hormone regulates distinct
1015 paths to maturation in pigment cell lineages. Elife, 8. <https://doi.org/10.7554/elife.45181>.
- 1016 Schartl, M., Larue, L., Goda, M., Bosenberg, M.W., Hashimoto, H., Kelsh, R.N., 2016. What is a
1017 vertebrate pigment cell?. Pigment Cell Melanoma Res. 29, 8-14. <https://doi.org/10.1111/pcmr.12409>
- 1018 Seikai, T., 1985. Reduction in occurrence frequency of albinism in juvenile flounder *Paralichthys*
1019 *olivaceus* hatchery-reared on wild zooplankton. Bull. Japan. Soc. Sci. Fish, 51, 1261-1267.
1020 <https://doi.org/10.2331/suisan.51.1261>
- 1021 Seikai, T., Matsumoto, J., Shimosaki, M., Oikawa, A., Akiyama, T., 1987. An association of
1022 melanophores appearing at metamorphosis as vehicles of asymmetric skin color formation with
1023 pigment anomalies developed under hatchery conditions in the Japanese flounder, *Paralichthys*
1024 *olivaceus*. Pigment Cell Res. 1, 143-151. <https://doi.org/10.1111/j.1600-0749.1987.tb00405.x>
- 1025 Shahidi, F., Brown, J.A., 1998. Carotenoid pigments in seafoods and aquaculture. Crit. Rev. Food Sci.
1026 Nutr. 38, 1-67. <https://doi.org/10.1080/10408699891274165>
- 1027 Shields, R.J., Bell, J.G., Luiz, F.S., Gara, B., Bromage, N.R., Sargent, J.R., 1999. Natural copepods are
1028 superior to enriched *Artemia* nauplii as feed for halibut larvae (*Hippoglossus hippoglossus*) in terms

1029 of survival, pigmentation and retinal morphology: relation to dietary essential fatty acids. *J. Nutr.* 129,
1030 1186-1194. <https://doi.org/10.1093/jn/129.6.1186>

1031 Sinha, A., Asimi, O.A., 2007. China rose (*Hibiscus rosasinensis*) petals: a potent natural carotenoid
1032 source for goldfish (*Carassius auratus* L.). *Aquac. Res.* 38, 1123-1128.
1033 <https://doi.org/10.1111/j.1365-2109.2007.01767.x>

1034 Sköld, H.N., Amundsen, T., Svensson, P.A., Mayer, I., Bjelvenmark, J., Forsgren, E., 2008. Hormonal
1035 regulation of female nuptial coloration in a fish. *Horm. Behav.* 54, 549-556.
1036 <https://doi.org/10.1016/j.yhbeh.2008.05.018>

1037 Sköld, H.N., Aspengren, S., Cheney, K.L., Wallin, M., 2016. Fish chromatophores—from molecular
1038 motors to animal behavior. In *International Review of Cell and Molecular Biology* (Vol. 321, pp. 171-
1039 219). Academic Press. <https://doi.org/10.1016/bs.ircmb.2015.09.005>

1040 Sneddon, L.U., Wolfenden, D.C., Thomson, J.S., 2016. Stress Management and Welfare, in: Schreck,
1041 C.B., Tort, L., Farrell, A.P., Brauner C.J. (Eds.), *Fish Physiology: Biology of Stress in Fish*. Academic
1042 Press, San Diego, pp. 463-539. <https://doi.org/10.1016/B978-0-12-802728-8.00012-6>

1043 Steingrímsson, E., Copeland, N.G., Jenkins, N.A., 2004. Melanocytes and the microphthalmia
1044 transcription factor network. *Annu. Rev. Genet.*, 38, 365-411.
1045 <https://doi.org/10.1146/annurev.genet.38.072902.092717>

1046 Strand, Å., Alanärä, A., Staffan, F., Magnhagen, C., 2007. Effects of tank colour and light intensity on
1047 feed intake, growth rate and energy expenditure of juvenile Eurasian perch, *Perca fluviatilis* L.
1048 *Aquaculture*, 272, 312-318. <https://doi.org/10.1016/j.aquaculture.2007.08.052>

1049 Sugimoto, M., 1993. Morphological color changes in the medaka, *Oryzias latipes*, after prolonged
1050 background adaptation. I: changes in the population and morphology of melanophores. *Comp.*
1051 *Biochem. Physiol. Comp. Physiol.* 104, 513-518. [https://doi.org/10.1016/0300-9629\(93\)90457-F](https://doi.org/10.1016/0300-9629(93)90457-F)

1052 Sugimoto, M., Uchida, N., Hatayama, M., 2000. Apoptosis in skin pigment cells of the medaka, *Oryzias*
1053 *latipes* (Teleostei), during long-term chromatic adaptation: the role of sympathetic innervation. *Cell*
1054 *Tissue Res.* 301, 205-216. <https://doi.org/10.1007/s004410000226>

- 1055 Sugimoto, M., 2002. Morphological color changes in fish: regulation of pigment cell density and
1056 morphology. *Microsc. Res. Tech.* 58, 496-503. <https://doi.org/10.1002/jemt.10168>
- 1057 Szisch, V., Van derSalm, A.L., Bonga, S.W., Pavlidis, M., 2002. Physiological colour changes in the red
1058 porgy, *Pagrus pagrus*, following adaptation to blue lighting spectrum. *Fish Physiol. Biochem.* 27, 1-8.
1059 <https://doi.org/10.1023/B:FISH.0000021719.65318.5a>
- 1060 Takahashi, A., Tsuchiya, K., Yamanome, T., Amano, M., Yasuda, A., Yamamori, K., Kawauchi, H.,
1061 2004. Possible involvement of melanin-concentrating hormone in food intake in a teleost fish, barfin
1062 flounder. *Peptides* 25, 1613-1622. <https://doi.org/10.1016/j.peptides.2004.02.022>
- 1063 Takahashi, A., Kawauchi, H., 2006. Evolution of melanocortin systems in fish. *Gen. Comp. Endocrinol.*
1064 148, 85-94. <https://doi.org/10.1016/j.ygcen.2005.09.020>
- 1065 Takahashi, A., Mizusawa, K., & Amano, M. (2014). Multifunctional roles of melanocyte-stimulating
1066 hormone and melanin-concentrating hormone in fish: evolution from classical body color change.
1067 TERRAPUB. <https://doi.org/10.5047/absm.2014.00701.0001>
- 1068 Tejera, N., Cejas, J.R., Rodríguez, C., Jerez, S., Pérez, J.A., Felipe, B.C., Lorenzo, A., 2010.
1069 Pigmentation, carotenoids, lipid peroxides and lipid composition of red porgy (*Pagrus pagrus*) skin
1070 reared under open-cage conditions. *Aquac. Res.* 41, 1043-1053. [https://doi.org/10.1111/j.1365-](https://doi.org/10.1111/j.1365-2109.2009.02388.x)
1071 [2109.2009.02388.x](https://doi.org/10.1111/j.1365-2109.2009.02388.x)
- 1072 Theveneau, E., Mayor, R., 2012. Neural crest delamination and migration: from epithelium-to-
1073 mesenchyme transition to collective cell migration. *Dev. Biol.* 366, 34-54.
1074 <https://doi.org/10.1016/j.ydbio.2011.12.041>
- 1075 Uren Webster, T.M., Rodriguez-Barreto, D., Consuegra, S., Garcia de Leaniz, C., 2020. Cortisol-related
1076 signatures of stress in the fish microbiome. *Front. Microbiol.* 11, 1621.
1077 <https://doi.org/10.3389/fmicb.2020.01621>
- 1078 Valente, L.M., Araújo, M., Batista, S., Peixoto, M.J., Sousa-Pinto, I., Brotas, V., Cunha, L.M., Rema, P.,
1079 2016. Carotenoid deposition, flesh quality and immunological response of Nile tilapia fed increasing
1080 levels of IMTA-cultivated *Ulva* spp. *J. Appl. Phycol.* 28, 691-701. [https://doi.org/10.1007/s10811-](https://doi.org/10.1007/s10811-015-0590-9)
1081 [015-0590-9](https://doi.org/10.1007/s10811-015-0590-9)

- 1082 Van der Salm, A.L., Pavlidis, M., Flik, G., Bonga, S.W., 2004. Differential release of α -melanophore
1083 stimulating hormone isoforms by the pituitary gland of red porgy, *Pagrus pagrus*. Gen. Comp.
1084 Endocrinol., 135, 126-133. <https://doi.org/10.1016/j.yggen.2003.09.002>
- 1085 Van der Salm, A.L., Spanings, F.A.T., Gresnigt, R., Bonga, S.W., Flik, G., 2005. Background adaptation
1086 and water acidification affect pigmentation and stress physiology of tilapia, *Oreochromis*
1087 *mossambicus*. Gen. Comp. Endocrinol., 144, 51-59. <https://doi.org/10.1016/j.yggen.2005.04.017>
- 1088 Venizelos, A., Benetti, D.D., 1999. Pigment abnormalities in flatfish. Aquaculture, 176, 181-188.
1089 [https://doi.org/10.1016/S0044-8486\(99\)00060-5](https://doi.org/10.1016/S0044-8486(99)00060-5)
- 1090 Vieiras Rodrigues, R., Freitas, L.S., Robaldo, R.B., Sampaio, L.A., 2012. Crescimento e sobrevivência de
1091 juvenis do linguado *Paralichthys orbignyanus*: efeitos do enriquecimento da Artemia SP. Com N-3
1092 HUFA. Atlântica (Rio Grande), 34, 121-127. <https://doi.org/10.5088/atlantica.v34i2.3120>
- 1093 Villalta, M., Estévez, A. Bransden, M.P., 2005. Arachidonic acid enriched live prey induces albinism in
1094 Senegal sole (*Solea senegalensis*) larvae. Aquaculture 245, 193– 209.
1095 <https://doi.org/10.1016/j.aquaculture.2004.11.035>
- 1096 Vizcaíno-Ochoa, V., Lazo, J.P., Barón-Sevilla, B., Drawbridge, M.A., 2010. The effect of dietary
1097 docosahexaenoic acid (DHA) on growth, survival and pigmentation of California halibut *Paralichthys*
1098 *californicus* larvae (Ayres, 1810). Aquaculture 302(3-4), 228-234.
1099 <https://doi.org/10.1016/j.aquaculture.2010.02.022>
- 1100 Volkoff, H., 2016. The Neuroendocrine Regulation of Food Intake in Fish: A Review of Current
1101 Knowledge. Front. Neurosci. 10: 540. <https://doi.org/10.3389/fnins.2016.0054>
- 1102 Wang, C.A., Xu, Q., Li, J., Wang, L., Zhao, Z., Du, X., Luo, L., Yin, J., 2017. Effects of tank colour on
1103 growth and survival of taimen *Hucho taimen* (Pallas, 1773) larvae. Aquac. Int. 25, 437-446.
1104 <https://doi.org/10.1007/s10499-016-0041-x>
- 1105 Wang, L.M., Bu, H.Y., Song, F.B., Zhu, W.B., Fu, J.J., Dong, Z.J., 2019. Characterization and functional
1106 analysis of slc7a11 gene, involved in skin color differentiation in the red tilapia. Comp. Biochem.
1107 Phys. A, 236, 110529. <https://doi.org/10.1016/j.cbpa.2019.110529>

- 1108 Walpita, C.N., Van der Geyten, S., Rurangwa, E., Darras, V.M., 2007. The effect of 3,5,3'-
1109 triiodothyronine supplementation on zebrafish (*Danio rerio*) embryonic development and expression
1110 of iodothyronine deiodinases and thyroid hormone receptors. *Gen. Comp. Endocrinol.* 152, 206-214.
1111 <https://doi.org/10.1016/j.ygcen.2007.02.020>
- 1112 Walpita, C.N., Crawford, A.D., Janssens, E.D., Van der Geyten, S., Darras V.M., 2009. Type 2
1113 iodothyronine deiodinase is essential for thyroid hormone-dependent embryonic development and
1114 pigmentation in zebrafish. *Endocrinology* 150, 530-539. <https://doi.org/10.1210/en.2008-0457>
- 1115 Wendelaar Bonga, S.E., 1997. The stress response in fish. *Physiol. Rev.* 77, 591-625.
1116 <https://doi.org/10.1152/physrev.1997.77.3.591>
- 1117 Wilcox, J.A., Tracy, P.L., Marcus, N.H., 2006. Improving live feeds: effect of a mixed diet of copepod
1118 nauplii (*Acartia tonsa*) and rotifers on the survival and growth of first-feeding larvae of the southern
1119 flounder, *Paralichthys lethostigma*. *J. World Aquacult. Soc.* 37, 113-120.
1120 <https://doi.org/10.1111/j.1749-7345.2006.00014.x>
- 1121 Winberg, S., Lepage, O., 1998. Elevation of brain 5-HT activity, POMC expression, and plasma cortisol
1122 in socially subordinate rainbow trout. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 274, R645-R654.
1123 <https://doi.org/10.1152/ajpregu.1998.274.3.R645>
- 1124 Yamada, T., Okauchi, M., Araki, K., 2010. Origin of adult-type pigment cells forming the asymmetric
1125 pigment pattern, in Japanese flounder (*Paralichthys olivaceus*). *Dev. Dyn.* 239, 3147-3162.
1126 <https://doi.org/10.1002/dvdy.22440>
- 1127 Yamada, T., Donai, H., Okauchi, M., Tagawa, M., Araki, K., 2011. Induction of ambicoloration by
1128 exogenous cortisol during metamorphosis of spotted halibut *Verasper variegatus*. *Comp. Biochem.*
1129 *Physiol. Biochem. Mol. Biol.* 160, 174-180. <https://doi.org/10.1016/j.cbpb.2011.08.004>
- 1130 Yamanome, T., Amano, M., Takahashi, A., 2005. White background reduces the occurrence of staining,
1131 activates melanin-concentrating hormone and promotes somatic growth in barfin flounder.
1132 *Aquaculture* 244, 323-329. <https://doi.org/10.1016/j.aquaculture.2004.11.020>

- 1133 Yamanome, T., Chiba, H., Takahashi, A., 2007. Melanocyte-stimulating hormone facilitates
1134 hypermelanosis on the non-eyed side of the barfin flounder, a pleuronectiform fish. *Aquaculture* 270,
1135 505-511. <https://doi.org/10.1016/j.aquaculture.2007.05.037>
- 1136 Yamanome, T., Mizusawa, K., Hasegawa, E.I., Takahashi, A., 2009. Green light stimulates somatic
1137 growth in the barfin flounder *Verasper moseri*. *J. Exp. Zool. A Ecol. Genet. Physiol.* 311, 73-79.
1138 <https://doi.org/10.1002/jez.497>
- 1139 Yoo, J.H., Takeuchi, T., Tagawa, M., Seikai, T., 2000. Effect of thyroid hormones on the stage-specific
1140 pigmentation of the Japanese flounder *Paralichthys olivaceus*. *Zoolog. Sci.*, 17, 1101-1106.
1141 <https://doi.org/10.2108/zsj.17.1101>
- 1142 Zhu, Y., Thomas, P., 1996. Elevations of somatolactin in plasma and pituitaries and increased a-MSH cell
1143 activity in red drum exposed to black background and decreased illumination. *Gen. Comp.*
1144 *Endocrinol.* 101, 21-31. [https://doi.org/10.1016/s0016-6480\(96\)90191-4](https://doi.org/10.1016/s0016-6480(96)90191-4)
- 1145 Zhu, Y., Thomas, P., 1997. Effects of somatolactin on melanosome aggregation in the melanophores of
1146 red drum (*Sciaenops ocellatus*) scales. *Gen. Comp. Endocrinol.*, 105, 127-133.
1147 <https://doi.org/10.1006/gcen.1996.6810>
- 1148 Zhu, Y., Thomas, P., 1998. Effects of light on plasma somatolactin levels in red drum (*Sciaenops*
1149 *ocellatus*). *Gen. Comp. Endocrinol.* 111, 76-82. <https://doi.org/10.1006/gcen.1998.7092>
- 1150 Zhu, Y., Yoshiura, Y., Kikuchi, K., Aida, K., Thomas, P., 1999. Cloning and phylogenetic relationship of
1151 red drum somatolactin cDNA and effects of light on pituitary somatolactin mRNA expression. *Gen.*
1152 *Comp. Endocrinol.* 113, 69-79. <https://doi.org/10.1006/gcen.1998.7180>
- 1153

1154 **Table 1.** Summary of the hormonal skin color regulation in fish. In this table we only
1155 focus on their role in pigmentation; therefore, some general characteristics of each
1156 hormone are omitted.

1157 **Mch:** Kawauchi and Baker, 2004¹; Amano and Takahashi, 2009²; Pandolfi et al., 2003³;
1158 Mizusawa et al., 2009⁴; Takahashi et al., 2004⁵; Yamanome et al., 2007⁶; Oshima et al.,
1159 1986⁷; Mizusawa et al., 2011⁸; Kasukawa et al., 1986⁹; Baker et al., 1986¹⁰; Yamanome
1160 et al., 2005¹¹. **Msh:** Cal et al., 2017¹²; Takahashi and Kawauchi, 2006¹³; Lamers et al.,
1161 1991¹⁴; Arends et al., 2000¹⁵; Kobayashi et al., 2012¹⁶; Sánchez et al., 2010¹⁷;
1162 Kobayashi et al., 2016¹⁸; Dijkstra et al., 2017¹⁹; Fujii and Miyashita, 1982²⁰; Kobayashi
1163 et al., 2011²¹; Ligon and McCartney, 2016²²; Sugimoto, 2002²³. **Sl:** Kaneko, 1996²⁴;
1164 Fukada et al., 2005²⁵; Chang and Wong, 2009²⁶; Cánepa et al., 2012²⁷; Fukamachi and
1165 Meyer, 2007²⁸; Zhu et al., 1999²⁹; Nguyen et al., 2006³⁰; Fukamachi et al., 2004³¹,
1166 2009³². **Asip:** Cerdá-Reverter et al., 2005³³; Guillot et al., 2012³⁴; Ceinos et al., 2015³⁵;
1167 Cal et al., 2019³⁶; McNulty et al., 2005³⁷. **Cortisol:** Wendelaar Bonga, 1997³⁸; Khan et
1168 al., 2016³⁹; Ruane et al., 2005⁴⁰; Yamada et al., 2011⁴¹; Matsuda et al., 2018⁴². **Prl:**
1169 Kawauchi et al., 2009⁴³; Freeman et al., 2000⁴⁴; Kitta et al., 1993⁴⁵; Oshima and Goto,
1170 2000⁴⁶; Oshima et al., 1996⁴⁷; Sage, 1970⁴⁸; Sköld et al., 2008⁴⁹. **Mt:** Falcon et al.,
1171 2011⁵⁰, 2010⁵¹; Fujii, 2000⁵²; Fujii and Oshima, 1994⁵³; Nagaishi and Oshima, 1989⁵⁴;
1172 Oshima et al., 1989⁵⁵. **Th:** Janz, 2000⁵⁶ Blanton et al., 2007⁵⁷; Bernier et al., 2009⁵⁸;
1173 Walpita et al., 2009⁵⁹, 2007⁶⁰; Saunders et al., 2019⁶¹; Guillot et al., 2016⁶²; Yoo et al.,
1174 2000⁶³; McMenamin et al., 2014⁶⁴.

1175

1176 **Figure 1.** Endocrine and nervous factors involved in physiological and morphological
1177 color changes. This figure summarized the physiological (left) and morphological
1178 (right) hormone effects over different chromatophores presented in Table 1. Besides,
1179 local synthesis (as it was described for Asip and Mch) and factors delivered through the
1180 bloodstream are shown. Note that most studies focus on the regulation of melanophores
1181 while there is scarce information about other pigmentary cell's regulation. Arrows
1182 indicate stimulation and T-lines indicate inhibition. Mch: melanin-concentrating
1183 hormone; Msh; melanophore-stimulating hormone; Sl: somatolactin; Prl: prolactin; Mt:
1184 melatonin; Th: thyroid hormone; Asip: agouti signaling protein; CA: catecholamines;
1185 NA: noradrenaline.

Hormone/peptide	Synthesis (place and/or gene)	Mode of action	Receptors	Overall effect	Physiological changes in chromatophores	Morphological changes in chromatophores
Melanin-concentrating hormone (Mch)	-NLT, some neurons project to the hypophysis and bloodstream ^{1,2} -Skin neuromast ³	endocrine paracrine	Type 1 G-protein coupled receptors. Two subtypes: Mch-r1 and Mch-r2 ^{2,4}	Skin paling ^{5,6}	-Aggregation of melanosomes in several fish species ^{5,6} erythrosomes in swordtail ⁷ and xanthosomes in medaka ⁸ -Dispersion of light-scattering organelles of leucophores in medaka ⁷ - No effect over iridophores in blue damselfish ^{7,9}	- Prevents melanin synthesis ^{10,11} -Prevent melanophore differentiation ¹¹
Melanophore-stimulating hormone (Msh)	-melanotropes of the <i>pars intermedia</i> ¹² -Skin ¹⁶ -In teleost: α -Msh and β -Msh isoforms ¹³	-endocrine -paracrine - α -Msh: des-, mono- (dominant), and di-acetylated ^{14,15}	Seven transmembrane-domain-G-protein-coupled family/rhodopsin class family A-13. Subtypes: Mc1R and Mc5R ^{12,16-18}	Skin darkening ¹² and/or promotes yellow coloration ¹⁹	- Dispersion of melanosomes (epidermis and dermis) ²⁰ and xanthosomes in <i>A. burtoni</i> ^{16,19,21} -Promotes platelet aggregation in motile iridophores ²²	- Stimulate melanin synthesis ²³ -Acts as a melanophore differentiation factor ²³
Somatolactin (Sl)	-somatolactotropes of the <i>pars intermedia</i> ²⁴	-endocrine	Proposed: type I cytokine receptor: growth hormone (Gh) receptor type 1 (GhR1) ²⁵⁻²⁸	Skin darkening ^{27,29-30}	-Dispersion of melanosomes in red drum ²⁹ and zebrafish ³⁰	-Promotes proliferation of melanophores in <i>C. dimerus</i> ²⁷ , and it is involved in the proliferation and morphogenesis of certain chromatophores in medaka ³¹⁻³²
Agouti signaling protein (Asip)	-skin ^{12,33-36}	-paracrine	Antagonist of Mc1R ^{33,37}	Determines dorso-ventral pigment pattern ^{12,33-36} Involved in skin paling?	- Aggregation of melanosomes in medaka ³³	-Inhibits melanogenesis ³⁶ and modulates chromatoblast fate: decreasing melanophores n° in different species of flatfish ^{33,34} , and also decreasing xanthophores and increasing iridophores n° in zebrafish ³⁶
Cortisol	- Interrenal cells of the head kidneys ³⁸	-endocrine	Direct or indirect effect? Proposed to act through <i>asip</i> in	Skin darkening or paling depending on species ³⁹⁻⁴²		

Prolactin (Prl)	-lactotropes of the <i>rostral pars distalis</i> ⁴³	-endocrine	rainbow trout ³⁹ Cytokine/hematopoietin superfamily. Long and Short isoforms of Prlr ⁴⁴	Promotes red and yellow skin coloration ⁴⁵⁻⁴⁸	-Weak aggregating effect on melanophores ^{45,46} . -Dispersion of xanthosomes in Nile tilapia and the rose bitterling ⁴⁶ , and of erythrocytes in Nile tilapia, swordtails and paradise gobies ⁴⁷ . Similar effects in two-spotted gobies and the mudsucker ^{48,49}
Melatonin (Mt)	-Pineal gland ⁵⁰	-endocrine	Seven transmembrane-domain-G-protein-coupled family: Mt1 Mt2 and Mel1c ⁵¹	Skin paling and transparency ^{49,52}	-Aggregation of melanosomes ⁵² and erythrocytes ^{49,53} . -Dispersion of erythrocytes and xanthosomes ⁴⁹ . -Increase between platelets spacing in iridophores ^{54,55} .
Thyroid hormones (Th)	-Thyroid follicles, local conversion to T3 ⁵⁶⁻⁵⁸	-endocrine	transcription factors from the family of type-2 nuclear receptors: α and β TR ⁵⁸	Skin paling ⁵⁹⁻⁶²	-Prevent melanin synthesis ^{59,60} -Change the balance of melanophore stem cell proliferation/ differentiation in zebrafish ^{61,62} and Japanese flounder ⁶³ - Decrease melanophore and increase xanthophore number <i>Danio albolineatus</i> ⁶⁴

