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1 **Detection of selection signatures in the genome of a domestic population of anadromous rainbow**

2 **trout (*Oncorhynchus mykiss*)**

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Abstract

Domestication processes and artificial selection are likely to leave signatures that can be detected at a molecular level in farmed rainbow trout (*Oncorhynchus mykiss*). These signatures of selection are genomic regions that contain functional genetic variants that may confer higher fitness to their bearers. We genotyped 749 rainbow trout from a commercial population using a rainbow trout Axiom 57K SNP array panel and identified putative genomic regions under selection using the *pcadapt*, Composite Likelihood Ratio (*CLR*) and Integrated Haplotype Score (*iHS*). After applying quality-control pipelines and statistical analyses, we detected 12, 96 and 16 SNPs putatively under selection, associated with 96, 781 and 115 candidate genes, respectively. Several of these candidate genes were associated with growth, early development, reproduction, behavior and immune system traits. In addition, some of the SNPs were found in relevant biological regions (O4, O5 and O20) associated to autosomal inversions localized in Omy05 and Omy020. These findings could represent a genome-wide map of selection signatures in farmed rainbow trout and could be important in explaining domestication and selection for genetic traits of commercial interest.

1. **Introduction**

The rainbow trout (*Oncorhynchus mykiss* Walbaum 1792) is native to North America and its geographical distribution ranges from Alaska to Mexico [1,2]. The domestication of this anadromous species began in the 1870s in California [1]. Since then, due to its importance for recreational angling and aquaculture, it has been introduced on all continents except Antarctica. It is one of the main species of fish reared in cold freshwater worldwide, particularly in Europe, North America, and Chile. The species production greatly expanded in the 1950s after the development of pelleted feeds [1]. In the early 1970s, AKVAFORSK Inc. began the first genetic improvement program of *O. mykiss* aimed at increasing body growth rate [3,4]. Rainbow trout have reached a high level of domestication (e.g. the entire life cycle is controlled in captivity [5,6]), and there are at least 13 genetic improvement programs [7] including traits such as growth, disease resistance, carcass quality, and age at sexual maturity [1]. The increase in the number of genetic improvement programs for rainbow trout has led to at least 22% of production relying on improved stocks [8]. According to FAO et al. [9], 848.1 thousand tons of rainbow trout were produced in world aquaculture in 2018.

Domestication and genetic improvement programs have produced populations genetically differentiated from the wild varieties from which they derived [10]. Continuous artificial selection has shaped the domestics' genome leaving signatures of selection that are detectable using molecular techniques [11,12]. These candidate regions may be regulated features such as morphology, production performance, reproduction, behavior, adaptation to different environments, and resistance to diseases, among others [13]. Positive selection signatures are genomic regions that contain functional genetic variants that confer higher fitness to their bearers [14], and usually, exhibit (i) increased allele frequencies of favorable

62   adaptive substitutions [15,16], (ii) an increased linkage disequilibrium (LD) that decays with the distance

63   in base pairs from the target of selection [17], and (iii) lower genetic diversity at adjacent sites of a selective

64   sweep than non-selected sites [18]. Vitti et al. [19] divided the methods for detection of selection

65   signatures into three major classes: (a) those that are searching for deviations in allele frequency spectrum

66   (e.g. *Tajima's D*, *Fay & Wu's H, CLR*), (b) those based on extended haplotype homozygosity within

67   populations (e.g. *iHS*, *Rsb, XP-EHH*), and (c) those based on population differentiation (e.g. F_{ST}-based

68   outlier detection and principal component analysis). However, the ability to identify the target of selection

69   depends on many factors, including but not limited to, the number of populations surveyed, temporal scale

70   of the selective event, strength of selection coefficient and type of selection signature [19,20].

71   Consequently, using more than one method to detect targets of selection is often a good option [21], with

72   *pcadapt* [22], *CLR* [23] and *iHS* [24] being two suitable methods to identify recent positive selection.

73

74   Previous studies in salmonids have associated selection signatures to traits such as migration in brown

75   trout (*Salmo trutta*) [25], reproductive ecotypes (i.e. shore or stream spawning) in sockeye salmon

76   (*Oncorhynchus nerka*) [26], ecotypes with different evolutionary thermal adaptation (i.e. populations from

77   deserts and mountains) in redband trout (*Oncorhynchus mykiss gairdneri*) [27], and economically

78   important traits (e.g. growth, early maturation and disease resistance) in Atlantic salmon (*Salmo salar*)

79   [11,28,29] and coho salmon (*Oncorhynchus kisutch*) [30]. Few studies have addressed signatures of

80   selection in rainbow trout (i.e. [31–33]). Martinez et al. [31], using a set of 110 linked expressed sequence

81   tags (EST) and 188 anonymous microsatellites identified selection signatures associated with egg

82   development, spawning time, and life-history variation. Limborg et al. [32], using a panel of 276 SNPs,

83   identified natural selection signatures between anadromous and resident populations at eight candidate

84   loci associated with the adaptive immune response. Weinstein et al. [33], using 57K SNP identified

85   signatures of selection in wild F1 migratory and resident rainbow trout of Southeast Alaska associated

86   with smoltification. All previously mentioned studies focused only on wild populations, leaving a gap in

87   knowledge for the selection history related to rainbow trout domestication.

88

89   The advances in genomics allowed the development of extensive marker panels for agriculture, livestock

90   and aquaculture species. Palti et al. [34] developed a 57K SNP array with SNP distributed across the

91   rainbow trout genome on a scale of one SNP for every ~48,000 bp. Rainbow trout is an excellent model

92   species to identify selection signatures due to its well recognized recent history of domestication, its

93   intense artificial selection record, and its adaptation to different environments. The aim of this study was

94   to identify selection signatures in the genome of one domestic population of rainbow trout. A total of 749

95   individuals of a farmed population were genotyped with a panel of 57K SNP. Selection signatures were

96   searched using two statistical methods: (i) *pcadapt*, (ii) *CLR* and (iii) *iHS*.

97   **2. Materials and Methods**

98

99   *2.1. Sampling*

100   We used 749 rainbow trout from the breeding population belonging to the 2014 year-class of the EFIGEN

101   S.A. (formerly Aguas Claras S.A.) breeding program (Puerto Montt, Chile). These fish were introduced

102   from Denmark in 1998 to Quetroleufu, Chile, by Aguas Claras S.A. [35–37]. Prior to their introduction,

103   there is no further information about this population. Subsequently, this population was implemented to

104   establish a breeding nucleus that has undergone 6 generations of selection for growth (3 generations),

105   carcass quality, and appearance (2 generations) traits [35–37]. In recent years, this strain has been

106   developed to resistance to infectious pancreatic necrosis virus (IPNV) [35,37], sea lice (*Caligus*

107   *rogercresseyi*) [38], and Salmonid rickettsial syndrome (SRS) [36]. Additionally, this anadromous

108   population is characterized by low mortality and late maturation (3rd year) [39]. Bioethical considerations

109   were taken for animal management following regulations of *Comité de Bioética Animal, Facultad de*

110   *Ciencias Veterinarias y Pecuarias, Universidad de Chile, Chile* (certificate Nº17,019-VET-UCH).

111

112   *2.2. Genotyping*

113   Total DNA was obtained from fin-clip samples using the *DNeasy Blood & Tissue* (Qiagen) kit, following

114   the manufacturer´s recommendations. Each sample was genotyped with the commercial rainbow trout

115   Affymetrix® Axiom® 57K SNP panel [34]. The SNP quality control was evaluated using Affymetrix's

116   AXIOM Analysis Suite software with the default settings, removing SNPs that did not match high-quality

117   clustering patterns [35,40]. The SNP array coordinates were updated to the latest version of the rainbow

118   trout genome (GCA_002163495.1 Omyk_1.0) by aligning the 200bp probes of each variant to the

119   Omyd_1.0 genome. Only variants aligned to chromosomes were kept. Furthermore, SNPs that did not

120 pass the following quality control filters were removed using VCFtools v.0.1.15 [41]: (i) call rate < 95%,

121 (ii) SNPs deviated from Hardy-Weinberg Equilibrium after Bonferroni correction (HWE, p-value<1×10^{-6}

122 ^{6}), and (iii) minor allele frequency (MAF) < 0.05. Additionally, we applied a minimum call rate of 90%

123 for individuals. After quality control filtering, 36,538 SNPs and all individuals were kept for further

124 analyses. Finally, we imputed the missing genotypes and phased the haplotypes with Beagle v.3 [42] using

125 default parameters.

126

127 *2.3. Genetic variation and population structure*

128 For the estimation of patterns of genetic variation and population structure, we further removed SNPs that

129 presented correlations between their allele frequencies larger than the basal level of LD found in this

130 population (0.125; described below). Our SNP set was filtered for linkage disequilibrium (LD) using

131 PLINK v1.09 [43] with the option *–indep-pairwise* and using windows of 50 consecutive SNPs, sliding

132 10 SNPs at the time and removing one SNP from each pair when the Pearson's correlation coefficient r^2

133 was 0.125 or higher. Summary statistics of genetic diversity, such as the observed and expected

134 heterozygosity (H_O and H_E) and inbreeding coefficient (F_{IS}), were calculated using PLINK v1.09. To

135 examine the genetic structure, we used a principal component analysis (PCA; calculated in PLINK v1.09

136 and visualized in R). Finally, we implemented PLINK v1.09 to characterize the pairwise linkage

137 disequilibrium (LD) as Pearson's squared correlation coefficient (r^2), where SNP pairs were located into

138 100 bins to calculate the mean values of r^2 for each bin. Additionally, we estimated the historical effective

139 population size (N_e) across generations using SNePv1.1 [44] and an average generation length of three

140 years [45].

141

142 *2.4. Signatures of selection*

143   We used three methods to detect signatures of selection. The first method based on principal component

144   analysis was conducted with the *pcadapt* package v4.3.3 [22]. This method detects outlier markers based

145   on Principal Component Analysis (PCA) while accounting for population structure [22]. This method is

146   robust to admixture and does not assume prior knowledge of population structure [46]. The test statistic

147   used for this method is the Mahalanobis distance (D) where a vector of the *z*-scores is derived for

148   regressing each SNPs with K principal components [22]. To choose the K number of the principal

149   components, we applied Cattell's rule [47]. The *p*-values were obtained from transforming Mahalanobis

150   distance (D) based on the chi-square distribution [47]. To identify the SNPs candidates for selection, we

151   applied the approach of Storey and Tibshirani [48] based on a False Discovery Rate (FDR) at 0.05.

152

153   The second method was the Composite Likelihood Ratio (*CLR*) analysis using the SweeD v3.3.2 software

154   [23]. This intra-population method is based on the skewness in the site-frequency spectrum of the alleles

155   across multiple loci along each chromosome to detect selective scan [49]. *CLR* estimates the ratio of the

156   likelihood of a selective sweep at a given position to the likelihood of a null model [30]. We estimate the

157   *CLR* in each chromosome using the grid size set to 100kb.

158

159   The third method was the standardized Integrated Haplotype Score (*iHS*) [24], which is included in the R

160   package REHH v3.1.2 [50]. This method is based on extended haplotype homozygosity (*EHH*) and

161   corresponds to the probability that two randomly chosen chromosomes carrying the core haplotype are

162   identical by descent [50,51]. The *iHS* compares the *EHH* between alleles within the same population [51].

163   This method requires the information of ancestral allele identification for each SNP. We estimated the

164   ancestral and derived alleles aligning the reference genome of rainbow trout against the *Salmo salar*

165   (GCA_000233375.4) with BLAST using probes of our variants and then applying an in-house script to

166 obtain the ancestral and derived alleles. For SNPs that could not be obtained, the ancestral allele was

167 inferred as the highest allele frequency in the total dataset, as suggested in other studies [52,53].

168

169 Identifying the causal variants of selection is laborious as frequently the markers identified to be under

170 selection are not obvious functional elements (e.g. genes). Therefore, in such cases, it is necessary to look

171 for neighbouring functional elements to the selection target that could explain the signature of selection

172 [16]. Candidate regions for selection were defined as those genomic positions containing SNPs with values

173 of *pcadapt* with an expected FDR $\alpha = 0.05$, scores of *CLR* corresponding to the 99.5th percentile to the

174 distribution and values of *iHS* in the top 0.05% of the distribution. Based on the estimated LD decay in

175 this population, we used a range of up to 250Kb on each side of the candidate SNP to identify candidate

176 genes under selection. The genes intersecting the candidate regions detected by *pcadapt*, *CLR* and *iHS*

177 approaches were considered putative candidates for selection and detected using BEDTools [54].

178

179   3. **Results**

180

181   *3.1. Genetic variation and population structure*

182   We estimated observed and expected heterozygosities of 0.459 and 0.447 and an inbreeding coefficient of

183   -0.026, from a subset of 2,426 SNPs, after pruning SNPs with a LD correlation coefficient (r^2) of 0.125.

184   The genetic structure showed one major clusters based on the principal component analysis (PCA) (Figure

185   1), where the first two eigenvectors explained 10.82% and 8.86% of the variability, respectively.

186

187   The pattern of LD (Figure 2a) showed a quick decay of LD at small distances (less than 25,000 base pairs).

188   Beyond that point (r^2 ~0.22), a steady decrease in LD is observed until reaching a value of ~0.125, which

189   is roughly stable at large genomic distance scales. The average LD (r^2) values in this population was

190   0.1457. The pattern of LD decay within chromosomes was very similar to the overall linkage decay curve,

191   except for chromosomes 5 and 20 that present comparatively higher LD and which also remains high at

192   longer genomic distances, in accordance with the presence of the double inversions in chromosome 5

193   (21.99 and 32.83Mb) and 20 (14Mb) as previously described [55] (Supplementary Figure S1,

194   Supplementary Table S1, Supplementary Material). This population shows a continuously decreasing N_e

195   trend from 1,444 to 86 over the last 1,500 years (Figure 2b).

196

197   *3.2. Signatures of selection*

198

199   Using 36,538 SNPs, we identified several regions harboring evidence of selection signatures by three

200   methods. Besides, we found three relevant regions previously, referred to as regions O4, O5, and O20,

201   that were detected with the *pcadapt*, *CLR*, and *iHS* methods, respectively (Figure 3, Figure 4 and Figure

202   5). Candidate genes related to domestication processes were further labeled as: (G) growth, (E) early

203   development, (R) reproduction, (B) behavior, (I) immune system, and (A) adaptation to culture

204   environment (Supplementary Table S2, Supplementary Material).

205

206   The *pcadapt* approach identified 12 candidate after FDR adjustment at 0.05%. The 12 SNPs are associated

207   with 96 genes localized in Omy04 (11 SNPs) and Omy27 (1 SNP) (Figure 3, Supplementary Table S3,

208   Supplementary Material). The candidate region in Omy04, which be call region O4, consists of two

209   clusters of selection targets, with the first cluster including 9 SNPs with an average distance of ~651Kb,

210   while the second cluster includes only two SNPs separated by ~834Kb. In the Omy27, we found only one

211   SNP that does not appear to have been under selection. Due to the cluster of SNPs under selection in

212   Omy04 (an indicative of a reliable signature of selection) we focused on the markers on that chromosome

213   to search for genes associated with selection signatures. Among these we found genes associated with

214   growth (*Sh3rf1*, *Prkaa2*, *Dab1*, *Plpp3, Dhcr24*, *C1qtnf7*, *Slain2*, *Sgcb*, *Dse*, *Col10a1*, and *Sox8*),

215   reproduction (*Psmb5*, *Cpeb2*, *Spata18*, *Ube2j1*, *Ufl1*, *Hs3st5*, *Rasd1*, *Zar1*, and *Rpl5*), immune system

216   function (*Trim25*, *Rgs1*, *Bach2*, *Tlr13*, *Trim65*, *Trim21*, *Trim39*, and *Palld*), early development (*Gsn*,

217   *Prdm5*, *Rgs2*, *Uchl5* and *Pbx1*) and environmental adaptation (*Gadd45a*) in Omy04. Details of the

218   candidate genes related to domestication are shown in Supplementary Table S2, Supplementary Material.

219

220   The *CLR* methods reveal 96 SNPs over the threshold and associated to 781 genes distributed along the

221   genome, excluding chromosomes Omy13, Omy16, Omy21, and Omy23 (Figure 4, Supplementary Table

222   S4, Supplementary Material). We found a second relevant peak region, called region O5 (Figure 4B),

223   composed of seventeen candidates SNPs, of which a portion of markers overlapped with two adjacent

224   inversions of 22.83 and 32.94 Mb on Omy05 [55]. In O5 region and the other candidates regions, we

225   found several genes previoulsy linked to growth (*Zc3h3*, *Cyld*, *Smad7*, *Arl15*, *Mrap2*, *Col2a1*, *Atp2a1*,

226   *Itga9,* and *Pax9*), reproduction (*Ptges*, *Miga2*, *Kif3b,* and *Mapk10*), immune system (*Calmodulin*, *Dolpp1,*

227   *Gpx7* and *Adcyap1r1*), early development (*Surf1*, *Rpl7a* and *Skiv2l2*), behavior (*Dnmt3a,* and *Dpysl5*) and

228   adaptation to culture environment (*Sema7a* and *Mafa*). Besides, several genes were detected previously

229   in studies of salmonids species (*Isg20l2*, *Vcp*, *Purb*, *Col9a2*, *Pax9*, *Vash1*, *Pomt2*, *Iah1*, *Itgb1bp1*, *Acyp2,*

230   *Ube2g1*, *Foxn3*, *Purb, Tbc1d20, Cyld, Atp2a1*, *Cyld, and Mrap2*). Details of the candidate genes related

231   to domestication are shown in Supplementary Table S2, Supplementary Material.

232

233   The *iHS* analysis revealed 16 SNPs over the 0.05% top values associated with 115 genes localized in the

234   chromosomes 20 (Omy20) (Figure 5, Supplementary Table S5, Supplementary Material), called region

235   O20. The average distance between SNPs in the candidate region O20 corresponds to ~547Kb, which

236   overlapped with an inversion on Omy20 [55]. We found several genes related to growth (*Myof*, *Gdf2*,

237   *Gdf10*, and *Ankrd1*), reproduction (*Htr7*, *Rbp4*, and *Dkk1*), immune system function (*Ch25h* and *Pten*),

238   and early development (*Prkg1*, *P4ha1*, *Pcdh15*, *Noc3l*, *Plce1*, and *Cep55*). Details of the functions of

239   candidate genes associated with domestication are shown in Supplementary Table S2, Supplementary

240   Material.

241

4. Discussion

4.1. Genetic variation and population structure

In this study, we used a 57K SNP panel to analyze the diversity and genetic structure in one domestic population of rainbow trout to detect selection signatures. The genetic diversity found in this farmed population (H_O/H_E= 0.459/0.447) was higher than the levels found in six French domestic strains of rainbow trout, with values of H_O and H_E ranging from 0.36-0.38 and 0.35-0.37, respectively [56]. The genetic diversity values are higher than other domestic salmonids such as Atlantic salmon (H_O=0.27-0.41; H_E=0.24-0.41) [29,57] and coho salmon (H_O=0.37-0.39; H_E=0.36-0.39) [30]. Similarly, the heterozygosities found here were higher than those obtained by Weinstein et al. [33] from two wild experimental crosses (F1) of migratory and resident rainbow trout of Southeast Alaska also genotyped with the 57K SNP array [34], H_O= 0.15-0.18 and H_E= 0.14-0.17, respectively. Gross et al. [58] found higher genetic diversity in domestic rather than wild rainbow trout populations using ten microsatellites. In principle, it is expected that domestic populations that are strongly selected for production traits and are isolated from other populations, should have reduced levels of genetic diversity [59]. Conversely, natural populations should present higher genetic diversity levels, at least in their ancestral distribution range [60]. Therefore, it is possible that the selection has not resulted in a significant decline of diversity despite the continuous decline of Ne, which may be because of a possible hybrid background of this population.

The LD of this domestic population decays relatively rapidly, with LD decreasing by ~50% within the first 100Kb (r^2=0.146), which is in line with LD decay patterns previously described for French rainbow trout lines (r^2=0.23) [56] and other domestic salmonids (Atlantic salmon [61] and coho salmon [30]). The

265   quick decay of LD is consistent with a historical larger effective population size, which can be observed

266   in our results (i.e. ~1,444). However, this N_e has been characterized by a continuous decline over the last

267   1,500 years until reaching the current strain's N_e of 86. These results are consistent with other studies in

268   rainbow trout [56] and Atlantic salmon [61], that show the N_e has been eroded as in most domestic species

269   in their recent history [62]. The minimal N_e to reduce inbreeding to not more than 1% per generation, and

270   thereby maintaining appropriate levels of genetic variation (both neutral and adaptive) in a population on

271   the long term should be at least 50 [63]. While the current N_e of this population is higher than the minimum

272   recommended, it is important to continue to monitor the genetic variation levels, as further selection and

273   genetic improvement may play an important role in affecting levels [56,62,64]. Furthermore, maintaining

274   the current N_e is also necessary to secure a viable genetic background for the future, in line with the

275   Convention on Biological Diversity Aichi target 13 that requires the maintenance of genetic variation and

276   stopping its loss and erosion for all domestic species [65].

277

278   *4.2. Signatures of selection*

279

280   In this study, we applied three different tests to identify selection signatures and studied the effect of

281   domestication and genetic improvement on this rainbow trout population's genome. These methods detect

282   different regions of positive selection in rainbow trout. *CLR* analysis detected the most candidates regions

283   followed by *iHS* and *pcadapt* methods. No overlap was observed among the three methods; yet, *CLR* and

284   *iHS* methods recorded overlapping regions on Omy20, spanning a total of 2.8 Mb that contains 10 shared

285   genes. These patterns of discrepancies between different methods have been observed in previous studies

286   in salmonid species [30]. Besides, we found several genes detected previously in studies about selection

287   signatures in different species, including Atlantic salmon (domestic population: *Isg20l2*, *Vcp*, *Col9a2*,

288   *Pax9*, *Vash1*, *Pomt2*, *Iah1*, *Itgb1bp1*, *Mocs, Trim39* [29]; *Acyp2, Ube2g1, Psmb5, Cpeb2, Palld, Dhcr24,*

289   *C1qtnf7, Slain2, Sgcb, Prdm5* [57]; *Foxn3* [66]; wild population: *Purb and Fbxl5* [67]; domestic-wild

290   populations: *Zip1* [11]); Coho salmon: *Tbc1d20* [30]); *Oreochromis niloticus* (*Trim16* [68]); livestock

291   species (chicken, *Med22* [69], *Ahcyl1* [70]; llama and alcapa, *Pmd8* and *Antxr2* [71]; cattle, *Strip1* [72],

292   *Slc6a117, Hs3st5, Pbx1* [73]*, Tgfbi* [74] and *Dym* [75]) and humans (*Itga9* [76]).

293

294   We found three relevant segments on the genome of functional interest, O4, O5, and O20, localized on

295   the Omy04, Omy05, and Omy20, respectively. In region O4, we found 9 candidate SNPs in Omy04, which

296   overlapped with a paralogous region of the Omy05, which contain two inversions (Figure 3B, dashed red

297   line corresponds to the paralogous regions shared by both chromosomes; Omy05: 58,931,000-86,873,922

298   - Omy04: 13,224,448-40,450,364 [55]). In region O5, we found seventeen candidate SNPs, of which a

299   portion of them (7 SNPs) intersected with two adjacent inversions of 22.83 and 32.94 Mb localized on

300   Omy05 [55] (Figure 4B, dashed blue line corresponds to the probable localization of the two chromosomal

301   inversions). We also identified region O20 in Omy20, which contains 16 SNPs putatively under selection,

302   which overlap with a smaller inversion of 14 Mb that contains multiple rearrangements [55] (Figure 5B,

303   dashed blue line corresponds to the probable localization of the chromosomal inversion).

304

305   Inversion regions are relevant structural variants and play a major role in local adaptation and

306   diversification [77]. They protect inverted sequences from recombination during meiosis, enabling

307   favorable alleles to be maintained over generations by balancing selection [77]. Recently, Pearse et al.

308   [55] described two inversions on Omy05 and Omy20 on Rainbow trout's genome. Omy05 is composed of

309   two adjacent inversions spanning ~55Mb [55], which contains a supergene that mediates sexual conflict

310   over migratory tendencies via sex-dependent dominance reversal. They found genes associated with key

photosensory, circadian rhythm/entrainment, adiposity, and sex-specific effect (gonad/sex steroid). The Omy20 contains a mulptiple small inversion without major description. Homeologous regions for this inversion (Omy05) in Omy01 and Omy12 have previously been associated with migratory phenotypes in northern populations [78,79]. In this study, based on homologous regions between Omy4 and Omy5, we found genes with putative functions associated with domestication that we explain below (*Dab1*, *Prkaa2*, *Plpp3*, *Psmb5*, *Prdm5*, *Sh3rf1*, *Palld*, *Sgcb*, *Gsn*, *Gadd45a*). Here we found that O4, O5, and O20 regions and the other regions harbor candidate genes linked to growth, early development, reproduction, immune system, behavior, and adaptation to the environment (Supplementary Table S2, Supplementary Material). These traits are typically modified in domestic species since they have been direct targets of artificial selection and have been under the effect of inadvertent selection.

Growth has been the principal target in genetic improvement programs in rainbow trout [80]. The population used in this study has been improved for growth for at least three generations. Therefore, findings of genomic regions under selection harbouring genes related to growth were expected. As described in Supplementary Table S2, several genes, including *Cyld, Smad7*, *Atp2a1*, *Dab1*, *Prkaa2*, *Plpp3*, *Mrap2*, *Col2a1, Col10a1*, *Ankrd1*, *Myof*, and *Sox8* have been previously associated with growth-related traits in some teleost fishes, such as *O. mykiss*, *Salmo salar*, *Danio rerio, Sparus aurata* and *Lepisosteus oculatus* [80–87]. In rainbow trout, we found genes putative involve on body weight (*Cyld* [85]*, Dab1*, *Prkaa2*, *Plpp3* [88]), promyogenic role (*Smad7* [86]) and growth trait (*Atp2a1* [80]). In Atlantic salmon, we found genes associated to body weight and jaw deformity (*Mrap2* [81] and *Col2a1*[87]). In addition, we also detected nine genes which have been related to growth in studies performed in livestock species, including chicken (*Dhcr24* [89]; *Slain2* and *Sgcb* [91]), sheep (*C1qtnf7* [92]), pigs (*Arl15* [93]) and cattle (*Gdf10* [94] and *Zn3h3* [95]). We also identified ten candidate genes

16

334   linked with early development in other teleost fish. This trait may influence the growth because the

335   muscles first arise in early embryonic life of teleost fish, unlike other amniotes [96].

336

337   In fish farming, maturation is often delayed by exposing fish to different light regimes to those in natural

338   conditions, affecting the perception of seasonality and circannual rhythms [97]. Additionally, the

339   population used in the present study has been selected for anadromous maturity at three years. In this

340   regard, we expect that genes related to reproductive traits may show evidence of selection. We found

341   sixteen genes involved in **reproduction** under positive selection in this population, of which seven genes

342   (*Rbp4, Mapk10, Zar1*, *Rpl5, Dkk1, Ptges and Kif3b*) are specifically associated with reproduction in

343   teleost fish. The *Rbp4* gene was related to retinoid metabolism in the rainbow trout ovarian follicle, and

344   is expressed in theca and granulosa cells surrounding the oocytes in trout ovaries [98]. The *Mapk10* gene

345   was localized previously in an important chromosomal inversion in Omy05, and it was implicated with

346   circadian rhythm and migratory phenotypes in rainbow trout [55]. *Zar1* gene is a maternal-effect gene

347   crucial for the oocyte-to-embryo turn [99]. In rainbow trout, it might play a role in oocyte/embryo

348   development [100], while in zebrafish, its loss causes early oogenesis arrest and female-to-male sex

349   reversal [101]. *Pteges* gene was linked with gonad differentiation in zebrafish [102]. *Rpl5* gene seems to

350   play a crucial role in the development of ovaries and oogenesis in Nile tilapia [103]. In primitive fish

351   species, the high expression of *Dkk1* has been associated with the gonadal development of sturgeons

352   (*Acipenser ruthenus* [104] and *Scaphirhynchus platorynchus* [105]). In contrast, in zebrafish, the increased

353   expression of *Dkk1* can result in male-biased sex ratios [106]. We also found other groups of candidate

354   genes previously associated with reproduction in other mammals (cattle, *Psmb5* [90,107] and *Ufl1* [108];

355   sheep *Hs3st5* [109]; mouse, *Spata18* [110], *Ube2j1* [111] and *Miga2* [112]) and birds (chicken, *Rasd1*

356   [113]; goose, *Htr7* [114]).

357

358   It is well known that host-pathogen interactions lead to strong selection in the genome of host species

359 [115–117]. In this study, we found several genes that are involved in the immune system and specifically

360 with host-pathogen interaction in a cultured environment. For example, in *Salmo salar*, we found several

361 genes previously associated with response against Amoebic Gill Disease (*Trim39* [118]), hematopoietic

362 necrosis (IHN) virus (*Pten* [119]), sea lice (*Lepeophtheirus salmonis*) (*Calmodulin* [122]) and parasite-

363 driven selection (*Purb and Fbxl5* [67]). In Coho salmon, the *Sh3rf1* gene was associated with disease

364 resistance against *Piscirickettsia salmonis* [123]. *Palld* gene is related to the molecular mechanism against

365 Koi herpesvirus resistance (KHVR) in *Cyprinus carpio* [124]. Finally, *Tlr13* was involved in the immune

366 response against bacteria and viruses in *Acipenser dabryanus* [125]. We suggest that these genes may be

367 involved in traits related to response to diseases in rainbow trout as part of the adaptation to continuous

368 outbreaks of infectious and parasitic diseases in farming conditions. These results may be relevant because

369 the success and sustainability of salmonid aquaculture depend on the control of diseases [126].

370 Development of more resistant fish strains has been one of the primary purposes of research and

371 development in genetic improvement programs of salmonids in Chile and worldwide [127]. Finally, we

372 detected genes associated with the adaptation to the culture environment (*Gadd45a*) and behavior (*Dpysl5*)

373 in rainbow trout. The *Gadd45a* gene is a putative biomarker for cold shock [128] and water quality stress

374 [129]. *Dpysl5* gene has been associated with intergenerational impacts on offspring behavior behind

375 thermal maternal stress [130].

376

377 ***Conclusion***

378 Here we present a genome-wide analysis of the genetic diversity of a Chilean domestic population of

379 steelhead rainbow trout *Oncorhynchus mykiss*. We identified that this lineage presented a historically large

effective population size, which is consistent with a relatively high level of genetic variation and low range of high linkage disequilibrium. However, the current effective population size has reduced to ~86, which in within the range of values recommended by FAO to minimize inbreeding and contribute to the maintenance of the current genetic diversity in captive populations. We also found evidence for selection signatures across the genome of this population. Part of these regions are confined to inversion polymorphisms, facilitating selection to occur within these regions and safekeeping of beneficial alleles from the rest of the recombination landscape across the genome and their loss through other selective processes or genetic drift. Within these inversions and in the rest of the candidates regions detected across the genome of rainbow trout, we found genes mainly associated with growth, reproduction, immune system, behavior and early development; traits which are related to domestication and artificial selection in this species. Lastly, the results presented here provide a background of standing genetic variation and adaptive signals in a farmed rainbow trout population, which provides further knowledge on the effects of domestication and intense directional selection in salmonids. In further research, we suggest including ancestral wild populations of rainbow trout, as a pairwise comparison with their genetic variation may help further elucidating the targert of selection in the domestic strains including details such as which allele was selected for in the domestic lineages. Such analysis would also increase the knowledge about the effect of domestication by exploring the nonparallel and parallel genomic footprints between wild/domestic populations.

399 **Ethics approval and consent to participate**

400 Nile tilapia sampling procedures were approved by the Comité de Bioética Animal from the Facultad de

401 Ciencias Veterinarias y Pecuarias, Universidad de Chile (certificate Nº17,019-VET-UCH).

402

403 **Consent for publication**

404 Not applicable.

405

406 **Availability of data and material**

407 Genotypes from this article have been deposited on FigShare:

408 https://doi.org/10.6084/m9.figshare.7725668.v1.

409

410 **Conflict of Interest Statement**

411 The authors declare that the research was conducted in the absence of any commercial or financial

412 relationships that could be construed as a potential conflict of interest.

413

414 **Funding**

417

418 **Authors' contributions**

419 MIC performed the analysis and wrote the initial version of the manuscript. MEL, DD contributed with

420 analysis, discussion, and writing. GC and RM contributed with data recopilation on functional

421   characterization. JMY, MIC, and MEL conceived, designed the study. MIC, MEL, DGU, CC, POTW, and

422   JMY contributed to discussion and writing. All authors have reviewed and approved the manuscript.

423

429

430   **Appendix A.**

431   **Supplementary Material**

432   Table S1. Values of LD decay in each chromosome.

433   Table S2. Candidate genes under selection on rainbow trout detected by *iHS*, *pcadapt* and *CLR* methods.

434   Table S3. List of all genes detected by *pcadapt* method.

435   Table S4. List of all genes detected by *CLR* method.

436   Table S5. List of all genes detected by *iHS* method.

437

438   FigureS1. LD decay in each chromosome.

439

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854

855 *Figure 1.* Principal component analysis (PCA) of genetic differentiation among 749 individuals of one

856 domestic population of rainbow trout based on 57K SNPs. Each dot represents one individual.

857 *Figure 2.* Results of genetic variations: a) Linkage disequilibrium (r^2) decay over the distance between

858 variants across the genome; b) Historical effective population sizes (N_e) over generations of one domestic

859 population of rainbow trout.

860 *Figure 3.* Results of signatures of selection by the *pcadapt* method in one domestic population of rainbow

861 trout based on 57K SNPs. A) Manhattan plot illustrates the distribution of *pcadapt* scores (-log(*p*-value))

862 across the genome of rainbow trout. Orange spots represent outliers. B) Manhattan plot shows the

863 distribution of *pcadapt* scores (-log(*p*-value)) in region A across chromosome 4; red spots represent

864 outliers and box represent the genes that intersect this region, and colors represent the putative function

865 (blue, reproduction; green, inmmune system; light-magenta, growth, dark-magenta, early development,

866 grey, adaptation to culture enviroment). Dashed blue line represents the approximate ubication of the

867 chromosomal inversion of the Omy20 [55].

868 Figure 4. Results of signatures of selection by the *CLR* method in one domestic population of rainbow

869 trout based on 57K SNPs. A) Manhattan plot illustrates the distribution of *CLR* scores across the genome

870 of rainbow trout. Orange spots represent outliers. B) Manhattan plot shows the distribution of *CLR* scores

871 across chromosome 5; red spots represent outliers; box represents the genes that intersect this region, and

872 colors represent the putative function (blue, reproduction; green, inmmune system; light-magenta, growth,

873 dark-magenta, early development). Dashed blue line represents the approximate localization of the two

874 chromosomal inversions on the Omy05 [55].

875

876   ***Figure 5.*** Results of signatures of selection by the *iHS* method in one domestic population of rainbow

877   trout based on 57K SNPs. A) Manhattan plot illustrates the distribution of *iHS* scores (-log(*p*-value))

878   across the genome of rainbow trout. Orange spots represent outliers. B) Manhattan plot shows the

879   distribution of *iHS* scores (-log(*p*-value)) in region B across chromosome 20; red spots represent outliers;

880   box represents the genes that intersect this region, and colors represent the putative function (blue,

881   reproduction; green, inmmune system; light-magenta, growth, dark-magenta, early development). Dashed

882   red line represents overlapped homeologous region of the Omy04 with Omy05 [55].

883