Early survival in Atlantic salmon is associated with parental genotypes at loci linked to timing of maturation late in life

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Short running title: Parental maturation genotypes influence offspring survival

Author contributions:

Conceptualization: TA, DM, NBM, JMP

Formal analysis: TA

Funding acquisition: TA, NBM, JMP

Lab and Fieldwork: TA, DM, NBM, JMP

Writing: TA, DM, NBM, JMP

Abstract

Genomic regions with large phenotypic effects often contain genes that may have critical roles as early as development, with potentially broad physiological and morphological effects across later life stages. However, the life-stage-specific fitness consequences are rarely explored. In Atlantic salmon (*Salmo salar*), variation in two large effect genomic regions, *six6* and *vgll3*, is linked to both age at maturity (a life-history trait with strong fitness effects) and several physiological and behavioural traits in early life. Here, by analysing offspring DNA samples from an experiment where fertilized eggs from known families of wild Atlantic salmon were planted into natural streams with manipulated nutrient levels, we tested if genetic variation in these loci is associated with survival in early life. We found that higher early life survival was linked to the genotype associated with late maturation in the *vgll3* locus, but with early maturation in the *six6* locus. These effects were significant

only in high-nutrient streams, while we observed no effect in low-nutrient streams. We also showed that the differences in early survival were not explained by additive effects of genes in the offspring generation, but by maternal genotypes in the *six6* locus, and by both parents' genotypes in the *vgll3* locus. These results suggest that indirect genetic effects are significant determinants of early life survival associated with these loci. Our study demonstrates an intriguing case of how large effect loci in the wild might exhibit complex fitness associations across life stages, and indicates that predicting evolutionary dynamics in the wild is likely difficult.

Keywords: age at maturity, parental fitness effect, epigenetics, *vgll3*, *six6*, life-history, genetic correlation, ontogeny

Introduction

Understanding the genetic architecture of fitness has been one of the key aims of evolutionary quantitative genetics. Classical theory suggests that mutations with large adaptive effects may hinder fine scale adaptation (Orr 2000, 2005). Yet, several quantitative trait loci (QTLs) with substantial phenotypic variation have been identified to be associated with fitness in natural systems (Bradshaw and Schemske 2003; Colosimo et al. 2005; Tishkoff et al. 2007; Johnston et al. 2013), indicating that adaptive genetic variation via large effect loci can persist. Adaptation in the wild is a complex process, composed of interactions between many mechanisms, such as context-dependency of fitness landscapes across time and space. Orr (2000) suggests that genetic correlations between fitness components should be selected against. However, Yeaman and Whitlock (2011) predict that under certain migration-selection scenarios, adaptive loci will be selected for to cluster tightly within a genomic region. As such, adaptive genomic regions with large phenotypic effects may contain multiple loci associated with different fitness components, resulting in high genetic correlations among them. How such genetic architecture is tied to physiological processes remains poorly understood. For example, a genomic region with a large phenotypic effect may be centrally located within cellular and developmental networks, and the genetic variation may in turn be linked to broad changes in body plan and/or physiology (Colosimo et al. 2005; Chan et al. 2010; Jimenez-Gomez et al. 2010; Snoek et al. 2012; Weith et al. 2023). Such broad expression of phenotypes is likely to alter fitness via different pathways, perhaps across different tissues or life stages. Yet, little is known of the fitness landscapes of large effect loci across life stages in the wild. Determining the direction of genetic correlations between fitness components and their potential costs across different environmental conditions is crucial to a better understanding of how genetic variation is maintained in populations, and of evolutionary responses to environmental change.

The Atlantic salmon has been emerging as a promising wild model to explore the multitude of fitness effects associated with large effect loci. Wild salmon populations are adapted to their local environments, so that even those in close proximity and lacking barriers to migration can exhibit genetic and phenotypic differences (Taylor 1991; Garcia de Leaniz et al. 2007). At the genetic level, two genomic regions, so-called *vgll3* and *six6* (named after the most predominant genes within the loci, *vestigial-like family member 3* and *SIX homeobox 6*, respectively) exhibit substantial signatures of adaptation within and among populations (Barson et al. 2015; Pritchard et al. 2018). These genomic regions harbour genes encoding e.g., transcription (co)factors, and are expressed as early as embryonic development (Lee et al. 2012; Halperin et al. 2013; Kurko et al. 2020; Moustakas-Verho et al. 2020). Genetic variation in the *vgll3* underpins key life-history traits in Atlantic salmon, such as the age at maturity in wild individuals (Ayllon et al. 2015; Barson et al. 2015) and in captivity (Asheim et al. 2023), the probability of males becoming precociously mature prior to sea migration (Debes et al. 2021), and iteroparity (Aykanat et al. 2019). *Vgll3* is also associated with physiological and behavioural traits in juvenile fish, such as lipid profiles (House et al. 2021), aggression (Bangura et al. 2022) and (sex-specific) smolt migration (Niemela et al. 2022), suggesting that this single QTL can have broad effects across multiple life stages. In addition, maximum metabolic rate and aerobic scope are higher in juvenile salmon with the early than the late genotype in the *vgll3* genomic region, which also exhibits an epistatic interaction with the *six6* genomic region (Prokkola et al. 2022). These genomic regions also show physiological epistasis via the maximal activities of mitochondrial and anaerobic metabolic enzymes in the heart and intestine (Prokkola et al. 2023). Variation in *six6*, in turn, has been associated with stomach content volume during ocean feeding (Aykanat et al. 2020). Similar to *vgll3,* the allele frequencies of the *six6* region are highly correlated with the average age at maturity in wild populations (Barson et al. 2015), and explain variation in age-at-maturity of a domesticated aquaculture strain of Atlantic salmon (Sinclair-Waters et al. 2020), as well as in Pacific salmonids (Waters et al. 2021). Taken together, these studies suggest that genetic variation in these two loci may be linked to differences in resource acquisition and allocation in juvenile salmon, with cascading effects on life-history strategies.

The early life stages of Atlantic salmon are characterized by high rates of mortality, in large part due to intense density-dependent resource competition (Einum et al. 2006; Grossman and Simon 2019). The availability of resources such as food and territorial refuge may strengthen or weaken this competition. The likelihood of an individual surviving to maturation may depend on what resources are available and how capable that individual is at competing for such resources. Considering the associations of *vgll3* and *six6* with resource acquisition and allocation, these loci may interact with variation in stream nutrient levels to predict survival rates of juvenile

salmon, with previous studies showing that the orientation and strength of a given gene-phenotype relationship can vary among environmental contexts (Barrett et al. 2009; Reznick 2016).

In this study we test whether the *vgll3* and *six6* loci are linked to early life survival in Atlantic salmon. We used data from a field experiment in which fertilized eggs from the same wild-origin families were divided among 10 experimental streams, all of which had become oligotrophic in recent years (e.g., Bernthal et al. 2022). Five of these streams were given an experimental supplement to restore nutrient levels (Auer et al. 2018). A previous study using the same field system showed that family-level juvenile survival was influenced by stream nutrient availability in addition to family-level maximum metabolic rate and egg mass (Auer et al. 2018). In this current study, we test for associations between juvenile survival and genetic variation in the two life-history loci, *vgll3* and *six6*. More specifically, we first tested whether differences in survival are due to family-wise genetic effects, i.e., associated with family-level allele frequencies of *vgll3* and *six6*, and second, we tested for direct additive effects of the loci, and parental effects, as occurs when the outcome on offspring survival depends on which parent passed on the allele.

Materials and Methods

The full field protocol is described by Auer et al. (2018). In brief, wild adult Atlantic salmon were trapped on their upstream spawning migration as part of fishery management operations in the River Blackwater (part of the Conon catchment in northern Scotland) in late autumn 2015 and used to generate full-sib crosses by using *in vitro* fertilization. All parental fish had spent one winter at sea (subsequently confirmed by scale reading) to avoid major differences in egg (and hence initial offspring) size, which could affect among-family differences in early life survival. Egg mass was estimated for all families using a subset of eggs. Parents were weighed (to nearest 10 g) and measured for fork length (to nearest 5 mm), and a fin clip was taken for DNA analyses, i.e., for the parental assignment of each of the recaptured offspring (see below). Condition factor was calculated using a modified version of Fulton's condition factor, $CF = 100 \times Weight / (Length)^m$, where *m* is the slope coefficient of the linear regression between log(weight) (response variable) and log(length), as the covariate (Bolger and Connolly 1989). This formula corrects for the residual relationship between length (or weight) and condition factor, hence condition factor can be modelled independently from the length of individuals.

Eggs were initially reared as family-specific groups and were overwintered in a local hatchery until the eyed stage of development, when a subsample of eggs from each of 29 full-sib families were transferred to the aquarium facilities at the University of Glasgow to be reared under standardized conditions. Meanwhile,

another subsample of 100 eggs from each of the same 29 families were planted at the same density in each of 10 streams (in the River Conon catchment) in February/early March 2016, thus equalling 2,900 eggs per stream. There was no natural spawning of Atlantic salmon in these streams due to the presence of downstream dams that prevented the upstream migration of spawning fish. All ten streams were oligotrophic at the start of the experiment. Half of these streams were then experimentally supplemented with nutrient pellets at the time of egg planting, thereby simulating the decay of parental carcasses (referred to as the high nutrient streams, Auer et al. 2018), whereas nutrient levels in the other five streams were unaltered (referred to as the low nutrient streams). Previous ecological analyses of data from this experiment have shown that these nutrient additions led to significant increases in macroinvertebrate densities, and consequently faster growth of the young salmon (details in Auer et al. 2018; McLennan et al. 2019).

The maximum metabolic rate (MMR) and standard metabolic rate (SMR) of 10 individuals from each family were measured using continuous flow-through respirometry in late June 2016, using the offspring that had been reared under common garden conditions (Auer et al. 2018) following protocols from (Auer et al. 2015). Standardized triple-pass electrofishing surveys were conducted in each of the experimental streams in July 2016, when the fish were approximately three months post-first-feeding (Auer et al. 2018), to calculate-family level rates of growth and survival. A small sample of adipose fin tissue was taken from the recaptured individuals to allow parental (and thus family) assignment (Auer et al. 2018). In the present study, we used these same DNA samples of the parental fish and of the offspring that survived in the streams to genotype individuals at the *vgll3* and *six6* loci, using the kompetitive allele specific PCR (KASP) method, as described in Prokkola et al. (2022). Throughout the paper, we refer to the alleles associated with early and late maturation as E and L, respectively (for example, $vgll3^{E}$, $vgll3^{L}$). Consequently, EE and LL will be used for fish that are homozygous for E and L alleles and EL for heterozygotes, respectively (for example, $vgll3^{EE}$, $vgll3^{LL}$, $vgll3^{EL}$). Out of 1246 juveniles that were collected and genotyped, the genotyping success was 96.3% and 97.5% for *six6* and *vgll3* genotypes, respectively. Three individuals were scored with improbable genotypes (one for *six6*, and two for *vgll3* loci) which did not conform to the Mendelian expectations based on parental genotypes. The genotype of one of these individuals was excluded which could have not been inferred, while the genotypes of two individuals were corrected to the genotype value that was invariable within the full-sib family.

Family-wise early life survival in relation to life-history genotype

We performed a generalized linear mixed model to quantify survival among full-sib families within the high and low nutrient streams in relation to their genotype. We measured local survival as the number of individuals recaptured from the 100 eggs per family that were planted in each stream. While emigration is possible,

juvenile salmon are predominantly sedentary in their first year of life, with limited movement and a high rate of mortality (Saunders and Gee 1964), suggesting that the local recapture rate can be mostly attributable to survival rather than emigration. Models were run using the *glmmTMB* package in R version 4.2.2 (Brooks et al. 2022; R Core Team 2021) and fitted using a negative binomial error structure with quadratic parameterization of mean in relation to variance (the *negbin2* family structure in the *glmmTMB* function).

The full model structure is as follows:

$$Y = \mu + SMR_{family} + MMR_{family} + \text{egg mass}_{mother} + vgll3 + six6 + vgll3{:}six6 + \varepsilon_{family} + \varepsilon_{stream} + \varepsilon_{error}$$

Whereby Y is the number of surviving individuals per family and stream, μ is the intercept, and *vgll3* and *six6* are the family-wise expected genotype frequency in these genomic regions, and *vgll3:six6* indicating the interaction term between *vgll3* and *six6*. In addition, the model included SMR_{family}, MMR_{family}, and egg $mass_{mother}$ which are family-wise mean values for maximum metabolic rate (MMR) and standard metabolic rate (SMR), and mean egg mass per mother, respectively. These physiological indices were added as covariates, since Auer et al. (2018) showed that family-wise local survival was positively related to family-wise MMR and egg mass in the low nutrient streams, and marginally positively related to SMR in the high nutrient streams.

Genotypes were modelled additively (i.e., EE, EL, and LL alleles were coded as 0, 0.5, and 1, respectively) with no dominance effects, to avoid model over-parameterization. Family-wise expected genotype frequencies were calculated based on parental genotypes and segregation of alleles according to the Mendelian inheritance principles. For example, in a family where the parents' genotypes are EE (0) and EL (0.5), the family-wise expected genotype frequency is 0.25, with 50% probability of offspring to be EE and 50% probability to be EL (see Supplementary Table 1 for parental genotype information). Family and stream were included in the model as random terms to account for non-independence among individuals of a given family or in each stream.

We performed a semi-automated model evaluation, using the *dredge* function in the *MuMin* package (version 1.47.1, Barton 2022) in R, by which we evaluated all possible fixed effect structures reduced from the full model, and ranked their fit according to the AICc value (a version of Akaike information criterion that corrects for small sample size), in which models within ΔAICc < 2 to the best model considered equally parsimonious. In a few instances, where convergence have not been archived, models were re-run using *glmer.nb* in *lme4* package (version 1.1.27.1, Bates et al. 2015), which provides nearly identical parameter estimates and AICc values. The model fits were checked using the *DHARMa* package (version 0.4.6, Hartig 2022). Marginal means for genotype effects and their confidence intervals were calculated using the *emmeans* package (version, 1.8.5, Lenth 2023), whereby the values of continuous covariates were fixed at the mean value, and the value of the

181 non-focal locus' genotype was fixed at 0.5 (i.e. the EL genotype). We performed separate analyses for low- and
182 high- nutrient streams to avoid overly complex model structures, since those two environments have been
183 shown to have different associations with physiological indices (Auer et al. 2018).

184 **Partitioning additive and parental genetic effects**

185 Given that the genotype effects for both *vgll3* and *six6* were significant in high nutrient streams (see Results
186 below), we then employed individual level analyses to decompose the genetic variation to its additive (direct
187 genetic effects) and parental genetic effects (indirect genetic effects), and further, to assess the contributions
188 of each parent's effects (i.e. maternal vs paternal, or both). Teasing out additive vs. parental genetic effects
189 requires individual level survival data from the offspring, but we obviously did not have the genotype data for
190 the missing (dead or emigrated) progeny. Therefore, the genotype of the missing progeny was inferred in
191 accordance with Mendelian segregation of the parental genotypes, and after accounting for the known
192 genotypes of the recaptured (surviving) individuals. As an example, suppose that for a family with parental
193 $vgll3^{EE}$ and $vgll3^{EL}$ genotypes, nine offspring out of initial 100 implanted eggs survived in a particular stream,
194 with seven of them being $vgll3^{EE}$ and two of them being $vgll3^{EL}$ genotype. In this case, and in accordance to
195 Mendelian segregation laws, we can estimate that N=43 and N=48 offspring are missing (dead or emigrated)
196 for the $vgll3^{EE}$ and $vgll3^{EL}$ genotype groups, respectively. A small subset of recaptured individuals with no
197 genotype data (3.7% and 2.5% of the recaptured individuals for *six6* and *vgll3*, respectively) were randomly
198 imputed a genotype based on Mendelian segregation of parental genotypes. The dataset contained 29000 data
199 points (100 offspring per 29 family and 10 streams), of which N=1246 consisted of recaptured individuals.

200 We then built and compared the fit of binomial models with different parametrization of parental effects. All
201 these models included family-wise SMR as a covariate (since this was significant in the high nutrient streams in
202 the family-wise model – see Results), and the additive effects of the genotypes, but they differed in the
203 parametrization of the parental effects, whereby each model contained a different combination of parental
204 effects for *six6* and *vgll3* genotypes. As such, the general models structure could be written as follows:

205 $$Y = \mu + SMR_{family} + vgll3_{add.} + six6_{add.} + vgll3_{parent/mother/father} + six6_{parent/mother/father} + \varepsilon_{family} + \varepsilon_{stream} + \varepsilon_{error}$$

206 whereby, Y is a Boolean response variable for local survival (with missing and recaptured individuals scored as 0
207 and 1, respectively), SMR_{family} is the family-wise mean SMR value, $vgll3_{add.}$ and $six6_{add.}$ are the additive genetic
208 effects, and $vgll3_{parent/mother/father}$ and $six6_{parent/mother/father}$ are different combinations of parental effects
209 associated with *six6* and *vgll3* loci. In total nine different parental genotype combinations were tested in nine
210 models, whereby the parental covariates included in the models are as follows: (1) $vgll3_{parent} + six6_{parent}$, (2)

211 *vgll3*$_{parent}$ + *six6*$_{mother}$, (3) *vgll3*$_{parent}$ + *six6*$_{father}$, (4) *vgll3*$_{mother}$ + *six6*$_{parent}$, (5) *vgll3*$_{mother}$ + *six6*$_{mother}$, (6) *vgll3*$_{mother}$ +
212 *six6*$_{father}$, (7) *vgll3*$_{father}$ + *six6*$_{parent}$, (8) *vgll3*$_{father}$ + *six6*$_{mother}$, (9) *vgll3*$_{father}$ + *six6*$_{father}$. Family and stream were
213 included in the models as random terms. The fit of the models containing different combinations of parental
214 genotypes were then compared according to the AICc criteria, in which models within ΔAICc < 2 to the best
215 model were considered equally parsimonious.

216 To account for uncertainty of genotype distributions associated with sampling variation, we also performed
217 random sampling of genotypes, in which genotypes of missing individuals were randomly drawn from expected
218 genotype probabilities, in accordance with Mendelian segregation of the parental genotypes. In this case, we
219 simulated the genotypes of 100 offspring per family/stream (i.e. the initial number of individuals released per
220 family to each stream) and assigned genotypes for missing individuals after excluding the genotypes of
221 recaptured (surviving) individuals from the simulated set. A small subset of recaptured individuals with no
222 genotype data (3.7% and 2.5% of the recaptured individuals for *six6* and *vgll3*, respectively) were also randomly
223 imputed a genotype based on Mendelian segregation of parental genotypes. The random data sampling was
224 repeated 1000 times.

225

226 Results

227 The observed local survival per family was dependent on genotype in high but not low nutrient streams (see
228 also the observed family-wise data in Supplementary Figure 1). In the low nutrient streams all parsimonious
229 models (models within ΔAICc = 2 of the best model) contained egg mass and MMR as covariates, a result that is
230 consistent with Auer et al. (2018). While the *vgll3* effect was present in the best model, it was insignificant, and
231 the parameter was not present in all parsimonious models (Figure 1, Supplementary Table 2). In the high
232 nutrient streams, all parsimonious models contained *six6* and SMR as covariates. In the best model, a higher
233 SMR (p = 0.018) and *six6*^{E} allele (p = 0.025) were significantly and positively associated with local survival, while
234 there was a marginal negative association with the *vgll3*^{E} allele (p = 0.049). Allelic substitution from *vgll3*^{E} to
235 *vgll3*^{L} increased the odds of survival 1.67 times (SE = 0.432, p = 0.049), whereby the marginal survival
236 probability associated with *vgll3*^{EE} was 3.16% (95% CI 2.46 -4.05), compared to 5.28% (95% CI 3.47 – 8.02) for
237 *vgll3*^{EL} (Figure 1). Allelic substitution effect from *six6*^{E} to *six6*^{L} was in opposite direction, decreasing the odds of
238 survival 1.49 times (SE = 0.118, p = 0.025), whereby the marginal survival probability associated with *six6*^{EE} was
239 7.85% (95% CI 4.94 -12.46), compared to 5.28% (95% CI 3.47 – 8.02) for *six6*^{EL} (Figure 1). Models were
240 substantially more parsimonious when both genotype and physiological indices (SMR, MMR and egg mass)

241 were included as covariates compared to the models that included only genotypes. However, family-wise SMR,
242 MMR and egg mass were not significantly associated with either genomic region (Supplementary Table 3),
243 suggesting an independent effect of genotypes and physiological traits on local survival rates.

244 For the high nutrient streams, we then used an individual-based, binomial model to partition the significant
245 family-wise genotype effects into additive effects and different combinations of parental genetic effects. A
246 model with only additive genetic terms had substantially lower fit compared to models that additionally
247 parametrized parental genotypes as covariates (Figure 2). Among different combinations of parental genetic
248 effects, the best model included parental *vgll3* and maternal *six6* genetic effects (Figure 2). This model was
249 superior to the second-best model with an AICc differential 2.08 (SE=0.25, Figure 2). An allelic substitution from
250 $vgll3^{E}$ to $vgll3^{L}$ in parental genotype increased the odds of survival by 1.98 times (SE = 0.60, p = 0.023), whereby
251 the marginal survival probability associated with parental genotype $vgll3^{EE}$ was 2.44% (95% CI 1.71 -3.46),
252 compared to 4.72% (95% CI 3.09 – 7.15) for $vgll3^{EL}$ (Figure 3, Table 1). Likewise, an allelic substitution from $six6^{E}$
253 to $six6^{L}$ associated with maternal genotype decreased the odds of survival by 1.58 times (SE = 0.10, p = 0.003),
254 whereby the marginal survival probability associated with $six6^{EE}$ maternal genotype was 7.25% (95% CI 4.69 -
255 11.07), compared to 4.72 % (95% CI 3.09 – 7.15) for $six6^{EL}$ (Figure 3). The additive (direct) *E* to *L* allelic
256 substitutions was insignificant both for *vgll3* (p = 0.51) and *six6* loci (p = 0.36, Figure 3, Table 1). The individual-
257 based analyses were robust to sampling variation associated with imputing the missing genotypes, since similar
258 effect sizes were obtained across 1000 simulated datasets (Supplementary Figure 2). The results were also
259 robust to some families being invariant in *vgll3* and *six6* genotypes, which may result in lower power for
260 quantifying the additive genetic variance compared to the parental genetic effects. As such, when the analyses
261 included only families which harboured genetic variation in these loci (21 and 14 families for *vgll3* and *six6*,
262 respectively, see Supplementary Table 3), the effect sizes and associated *p-values* were similar to those
263 obtained from the full dataset, and parental genetic effect sizes were substantially higher than the additive
264 genetic effects (Supplementary Table 4).

265 In salmonids, the maternal genotype might be more important to offspring survival than the paternal
266 genotype, since mothers also determine the egg size and composition that influences offspring viability
267 (Fleming 1996). To test the if maternal body size drives the association between local survival and the maternal
268 genetic effects (in *six6* locus), maternal body size traits (i.e. length, weight and condition factor) were added
269 separately to the most parsimonious models explaining the maternal genotype effects on offspring local
270 survival in the high nutrient streams. None of the maternal size traits had a significant effect on survival and did
271 not improve the model fit, with or without the *six6* maternal effects present in the models (Supplementary

Table 5). This suggests that maternal size is not driving the association between offspring survival and maternal *six6* genotypes, although it should be noted that variation in maternal size within the sample was constrained as a result of only using females that had spent a single winter at sea. On the other hand, a maternal *six6* genotype had strong associations with her size and condition (Supplementary Table 6), with the late genotype being associated with larger size and higher body condition. This indicates that a genetic correlation exists between parental size and early offspring survival via *six6*, but the association between *six6* and offspring survival could be mediated by a different process than female body size.

Discussion

Understanding the genetic architecture of adaptation is crucial for predicting how populations respond to changing environmental conditions at contemporary time scales. Genomic regions with large phenotypic effects may begin to shape phenotypes at early developmental stages, changing the fitness landscape via multiple pathways (Colosimo et al. 2005). This study has demonstrated that the loci that are associated with maturation timing in Atlantic salmon can also affect early life survival, but in a manner that interacts with nutrient levels and the availability of food in the streams that they inhabit. Intriguingly, this effect did not operate via additive genetic effects associated with offspring own genotype, but via a maternal effect in *six6* loci, and via parental effects in *vgll3*.

Age at maturity is an important trait that can influence fitness and is likely maintained in the population via balancing selection (Barson et al. 2015). Our results suggest that the viability selection acting on *vgll3* and *six6* loci in early juvenile stages will likely alter the age-structure, hence the dynamics of the evolutionary response in the population. As such, the rate of evolutionary response in age at maturity may be attributed, in part, to ecological processes operating very early in life. On the other hand, while our results indicate that a genetic correlation between early- and late-life fitness components exists, it does not reveal the possible physiological basis or how the observed correlation between fitness components contributes to the complexity of adaptation (Orr 2000). For example, it is unclear if the direction of selection associated with early- and late-life fitness components are aligned (i.e., synergistic pleiotropy) or inflicts a cost to the life-history adaptations (i.e., constraining selection via trade-offs, Orr 2000; Rennison and Peichel 2022; Thorholludottir et al. 2023). A recent study showed that a rapid evolutionary response towards earlier maturation (i.e., younger age structure) in the *vgll3* locus was partly driven by the abundance of salmon prey species in the ocean (Czorlich et al. 2022). If, for example, the selection in early stages favours for the opposite *vgll3* allele (i.e., late), as out

302 results in the high nutrient streams suggests, one might predict a larger evolutionary costs to age-at-maturity
303 evolution at the *vgll3* loci, i.e. via slower evolutionary response to changing environment (and larger genetic
304 load to population, Orr 2000). Yet, we find that the genetic effects on survival are dependent on nutrient levels,
305 and there is a context dependency in the correlated selection with age at maturity, suggesting that the cost of
306 correlation between fitness components might be population/condition dependent. Finally, the survival effects
307 associated with *six6* and *vgll3* loci are in opposite directions to each other with respect to their effect on
308 maturation timing: While the *vgll3*^{L} allele (the allele linked to later age at maturity) appears to be associated
309 with higher offspring survival, it is the early maturation allele (*six6*^{E}) that positively influences offspring survival
310 in the *six6* region, necessitate to account for both loci effect when formulating predictions. All these highlight
311 the complexity of evolutionary responses that are related to predicting the evolutionary dynamics of
312 maturation age in Atlantic salmon.

313 The indirect genetic effect on viability selection via parental genotypes might have theoretical implications for
314 evolutionary processes (e.g. Rausher 1992; Räsänen and Kruuk 2007). In the classical sense, indirect genetic
315 effects via parental genetic variation have been considered as a component of environmental effects, and are
316 thought to help maintain genetic diversity i.e. by reducing the narrow sense heritability with increasing
317 environmental variance, Wolf et al. 1998). However, in our context, the indirect genetic effects of parents are
318 also correlated with the offspring' life-history and thereby fitness of the offspring via the direct effect of
319 genotypes on age at maturity (Wolf et al. 1998). Therefore, selection on offspring survival would alter the
320 phenotypic variation of life-history traits, resulting in deviating from the optimal trait variation maintained
321 under balancing selection (Turelli and Barton 2004). Yet, theoretical predictions accounting for this complexity
322 have not been explored explicitly (e.g., Oomen et al. 2020).

323 Our results highlight that the effect of viability selection on these genomic regions is dependent on the
324 environment, as it appears to only operate under conditions of high nutrient availability. Both loci are linked to
325 a number of different physiological and behavioural traits that mediate energy homeostasis (Mobley et al.
326 2021). However, we did not find a direct link between these genomic regions and SMR or MMR (measured at
327 the family level), thereby suggesting that metabolic rates are not underlying mechanisms for mediating the
328 effects of *vgll3*/*six6* loci on early survival. Earlier studies have shown a broad range of effects on physiological
329 and behavioural traits linked to genetic variation in *vgll3* locus, such as MMR (Prokkola et al. 2022), lipid
330 profiles (House et al. 2021), and aggressive behaviour (Bangura et al. 2022), and that the *six6* genomic region
331 can be broadly expressed during embryonic developmental (Moustakas-Verho et al. 2020). The effect of these

332 on fitness is likely to be context-dependent, supporting our conclusions, although the exact mechanisms are
333 yet to be elucidated.

334 The higher local survival of juvenile fish with the early maturation genotype at the *six6* locus was explained
335 solely by the maternal genotype. Indirect genetic effects associated with the maternal environment (i.e.,
336 maternal effects) are commonly observed in salmonids and in other organisms (e.g., Mousseau and Fox 1998;
337 Heath et al. 1999; Aykanat et al. 2012). However, because salmonids lack parental provisioning in their early
338 life, these effects are mostly limited to egg size and/or composition, which in turn can be influenced by the size
339 of the mother (Munoz et al. 2014). Our results showed that in the high nutrient streams, family-level egg mass
340 was neither correlated with survival (Supplementary Table 3), nor with variation in the *six6* maternal genotype
341 (Supplementary Table 2), thereby ruling out a genetic effect of egg mass via *six6*. Similarly, we found that
342 maternal size did not explain the correlation between a mother's *six6* genotype and the survival of her
343 offspring, despite the observed correlation between maternal size and *six6* (Supplementary Table 6). A
344 plausible mechanism explaining our results is that that variation in *six6* alters early life survival via changes in
345 egg composition. In oviparous species, the composition of eggs, such as hormone levels, albumin and fat
346 content, may mediate the phenotype and behaviour of the offspring, and subsequently their fitness (Williams
347 1994; Thorn and Morbey 2019; Widowski et al. 2022). In Chinook salmon, carotenoid composition in the eggs
348 has been shown to be associated with early life survival (Tyndale et al. 2008). Therefore, despite the apparent
349 absence of a link between the *six6* region and family-level egg mass, we cannot rule out potential effects on
350 offspring survival via changes in egg composition. Future studies could test such a hypothesis in a common
351 garden cross design, by quantifying potential markers associated with egg composition, and their effect on the
352 survival of their full sibs. Alternatively, but less parsimoniously, epigenetic mechanisms may be associated with
353 a mothers' *six6* genotype, whereby the maternal *six6* locus controls the epigenetic signature of the offspring
354 genome and thus influences early life developmental pathways (see, Wolf and Wade 2009; Lawson et al. 2013;
355 Venney et al. 2021). *Six6* and other candidate genes located in the same genomic region (i.e., *six1* and *six4*) are
356 known transcription factors, and *six6* expression has been documented in Atlantic salmon in early development
357 (Moustakas-Verho et al. 2020). It is therefore plausible that a mother's *six6* genotype may play a role in the
358 regulation of her offspring's genome.

359 The effect of a parent's *vgll3* genotype on offspring early life survival was not solely limited to the maternal
360 contribution. A plausible mechanism that is consistent with the observed results is that the genomes inherited
361 from parents are already modified via epigenetic mechanisms, such as via DNA methylation (Lawson et al.
362 2013). In salmonids, epigenetic effects via DNA methylation have been widely documented, for example,

363 between hatchery and wild origin fish associated with both parents of origin (Smith and Kornfield 2002; Le
364 Luyer et al. 2017; Koch et al. 2022), with implications for evolutionary genetics and conservation efforts (Smith
365 and Kornfield 2002; Le Luyer et al. 2017; Koch et al. 2022). Thus, our results are consistent with a hypothesis
366 whereby variation in epigenetic signals could result in differences in gene expression during early development,
367 subsequently altering offspring survival. Such a hypothesis may be tested by designing cross-breeding
368 experiments, where offspring epigenetic signals, such as genome wide methylation patterns, could be
369 examined among crosses from parents with different genotypes, and in relation to offspring phenotype and
370 survival. Alternatively, histone modification is another plausible mechanism that might generate parental
371 genotype-specific modification of chromatin structure, and subsequent survival differences between families
372 (Koch et al. 2022).

373 Even though we have shown that the same genomic regions can account for variance in different fitness
374 components, it is unclear whether covariation between fitness components is causally linked to a single genetic
375 mutation (true pleiotropy), or takes place as a result of physically linked loci acting on different fitness
376 components. While molecular evidence suggests that both *vgll3* and *six6* regulate multiple functions across
377 multiple life stages (Mobley et al. 2021), implying pleiotropy, genetic linkage within the genomic regions cannot
378 be ruled out. There is accumulating evidence to suggest that co-adapted gene complexes are common in wild
379 species (Thompson and Jiggins 2014; Li et al. 2022; Matschiner et al. 2022). Moreover, theoretical models have
380 predicted the evolution of genetic architecture with fewer, larger, and more tightly linked divergent alleles in
381 species that exhibits marked local adaptation between migratory populations (Yeaman and Whitlock 2011). In
382 keeping with this model, Atlantic salmon exhibit local adaptation across closely situated populations with both
383 *six6* and *vgll3* genomic regions harbouring substantial signals of divergence, even between adjacent
384 populations (e.g. Barson et al. 2015; Pritchard et al. 2018). Therefore, it is plausible that the genetic
385 correlations of fitness components via the *six6* and *vgll3* genomic regions might be explained by independent
386 loci with tight linkage within these genomic regions. Such genetic architecture may be instrumental in
387 maintaining the genetic variation and local adaptation of populations amidst high gene flow, although explicit
388 mathematical models and empirical tests of this hypothesis is still lacking.

389 In this study, we provide a rare example of how indirect genetic effects from loci influencing adult age at
390 maturity and adaptive divergence shape the early-life survival of offspring. This indicates a complex genetic
391 architecture associated with large effect loci (Oomen et al. 2020), and highlights the challenges associated with
392 predicting evolutionary dynamics of Atlantic salmon in a changing world. Our study also calls for a better

understanding of the ecological role and evolutionary consequences of epigenetic inheritance (Koch et al. 2022).

Data accessibility

The compiled datasets and R-codes to reproduce the results are available from the dryad repository https://doi.org/10.5061/dryad.866t1g1xk.

Acknowledgements

We thank the Cromarty Firth Fishery Trust (in particular the late Simon McKelvey), Sonya Auer and our field team for assistance in fieldwork, and Leena Laaksonen and the MES Lab in the University of Helsinki for help with the KASP assays. Funding came from the European Research Council (Advanced Grants 322784 and 834653 to NBM), and from the Academy of Finland (353388 and 325964 to TA, 348965 to JMP).

References

Asheim, E. R., P. V. Debes, A. House, P. Liljestrom, P. T. Niemela, J. P. Siren, J. Erkinaro, and C. R. Primmer. 2023. Atlantic salmon (*Salmo salar*) age at maturity is strongly affected by temperature, population and age-at-maturity genotype. *Conserv. Physiol.* 11:coac086.

Auer, S. K., G. J. Anderson, S. McKelvey, R. D. Bassar, D. McLennan, J. D. Armstrong, K. H. Nislow, H. K. Downie, L. McKelvey, T. A. J. Morgan, K. Salin, D. L. Orrell, A. Gauthey, T. C. Reid, and N. B. Metcalfe. 2018. Nutrients from salmon parents alter selection pressures on their offspring. *Ecol. Lett.* 21:287-295.

Auer, S. K., K. Salin, A. M. Rudolf, G. J. Anderson, N. B. Metcalfe, and W. Hopkins. 2015. The optimal combination of standard metabolic rate and aerobic scope for somatic growth depends on food availability. *Funct. Ecol.* 29:479-486.

Aykanat, T., C. A. Bryden, and D. D. Heath. 2012. Sex-biased genetic component distribution among populations: additive genetic and maternal contributions to phenotypic differences among populations of Chinook salmon. *J. Evol. Biol.* 25:682-690.

Aykanat, T., M. Ozerov, J. P. Vaha, P. Orell, E. Niemela, J. Erkinaro, and C. R. Primmer. 2019. Co-inheritance of sea age at maturity and iteroparity in the Atlantic salmon *vgll3* genomic region. *J. Evol. Biol.* 32:343-355.

Aykanat, T., M. Rasmussen, M. Ozerov, E. Niemela, L. Paulin, J. P. Vaha, K. Hindar, V. Wennevik, T. Pedersen, M. A. Svenning, and C. R. Primmer. 2020. Life-history genomic regions explain differences in Atlantic salmon marine diet specialization. *J. Anim. Ecol.* 89:2677-2691.

Ayllon, F., E. Kjaerner-Semb, T. Furmanek, V. Wennevik, M. F. Solberg, G. Dahle, G. L. Taranger, K. A. Glover, M. S. Almen, C. J. Rubin, R. B. Edvardsen, and A. Wargelius. 2015. The *vgll3* Locus Controls Age at Maturity in Wild and Domesticated Atlantic Salmon (*Salmo salar L.)* Males. *PLoS Genet.* 11:e1005628.

Bangura, P. B., K. Tiira, P. T. Niemela, J. Erkinaro, P. Liljestrom, A. Toikkanen, and C. R. Primmer. 2022. Linking vgll3 genotype and aggressive behaviour in juvenile Atlantic salmon (*Salmo salar*). *J. Fish Biol.* 100:1264-1271.

Barrett, R. D., S. M. Rogers, and D. Schluter. 2009. Environment specific pleiotropy facilitates divergence at the Ectodysplasin locus in threespine stickleback. *Evolution* 63:2831-2837.

Barson, N. J., T. Aykanat, K. Hindar, M. Baranski, G. H. Bolstad, P. Fiske, C. Jacq, A. J. Jensen, S. E. Johnston, S. Karlsson, M. Kent, T. Moen, E. Niemela, T. Nome, T. F. Naesje, P. Orell, A. Romakkaniemi, H. Saegrov, K. Urdal, J. Erkinaro, S. Lien, and C. R. Primmer. 2015. Sex-dependent dominance at a single locus maintains variation in age at maturity in salmon. *Nature* 528:405-408.

Bartoń K (2022). MuMIn: Multi-Model Inference. R package version 1.47.1.

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *J. of Stat. Soft.*, 67(1).

Bernthal, F. R., J. D. Armstrong, K. H. Nislow, and N. B. Metcalfe. 2022. Nutrient limitation in Atlantic salmon rivers and streams: Causes, consequences, and management strategies. *Aquat. Conserv.* 32:1073-1091.

Bolger, T. and P. L. Connolly. 1989. The selection of suitable indices for the measurement and analysis of fish condition. *J. Fish Biol.* 34:171-182.

Bradshaw, H. D. and D. W. Schemske. 2003. Allele substitution at a flower colour locus produces a pollinator shift in monkeyflowers. *Nature* 426:176-178.

Chan, Y. F., M. E. Marks, F. C. Jones, G. Villarreal, Jr., M. D. Shapiro, S. D. Brady, A. M. Southwick, D. M. Absher, J. Grimwood, J. Schmutz, R. M. Myers, D. Petrov, B. Jonsson, D. Schluter, M. A. Bell, and D. M. Kingsley. 2010. Adaptive evolution of pelvic reduction in sticklebacks by recurrent deletion of a *Pitx1* enhancer. *Science* 327:302-305.

Colosimo, P. F., K. E. Hosemann, S. Balabhadra, G. Villarreal, Jr., M. Dickson, J. Grimwood, J. Schmutz, R. M. Myers, D. Schluter, and D. M. Kingsley. 2005. Widespread parallel evolution in sticklebacks by repeated fixation of Ectodysplasin alleles. *Science* 307:1928-1933.

Czorlich, Y., T. Aykanat, J. Erkinaro, P. Orell, and C. R. Primmer. 2022. Rapid evolution in salmon life history induced by direct and indirect effects of fishing. *Science* 376:420-423.

Debes, P. V., N. Piavchenko, A. Ruokolainen, O. Ovaskainen, J. E. Moustakas-Verho, N. Parre, T. Aykanat, J. Erkinaro, and C. R. Primmer. 2021. Polygenic and major-locus contributions to sexual maturation timing in Atlantic salmon. *Mol. Ecol.* 30:4505-4519.

Einum, S., Sundt-Hansen, L., & H. Nislow, K. (2006). The partitioning of density-dependent dispersal, growth and survival throughout ontogeny in a highly fecund organism. *Oikos*, 113(3), 489-496.

Fleming, I. A. 1996. Reproductive strategies of Atlantic salmon: ecology and evolution. *Rev. Fish Biol. Fish.* 6:379-416.

Garcia de Leaniz, C., I. A. Fleming, S. Einum, E. Verspoor, W. C. Jordan, S. Consuegra, N. Aubin-Horth, D. Lajus, B. H. Letcher, A. F. Youngson, J. H. Webb, L. A. Vollestad, B. Villanueva, A. Ferguson, and T. P. Quinn. 2007. A critical review of adaptive genetic variation in Atlantic salmon: implications for conservation. *Biol. Rev. Camb. Philos. Soc.* 82:173-211.

Grossman, G. D., & Simon, T. N. (2019). Density-dependent effects on salmonid populations: A review. *Ecol. Fresh. Fish*, 29(3), 400-418.

Halperin, D. S., C. Pan, A. J. Lusis, and P. Tontonoz. 2013. Vestigial-like 3 is an inhibitor of adipocyte differentiation. *J. Lipid Res.* 54:473-481.

Hartig F (2022). DHARMa: Residual Diagnostics for Hierarchical (Multi-Level / Mixed) Regression Models. R package version 0.4.6.

472 Heath, D. D., C. W. Fox, and J. W. Heath. 1999. Maternal effects on offspring size: Variation through early
473 development of chinook salmon. *Evolution* 53:1605-1611.
474 House, A. H., P. V. Debes, J. Kurko, J. Erkinaro, R. Kakela, and C. R. Primmer. 2021. Sex-specific lipid profiles in
475 the muscle of Atlantic salmon juveniles. *Comp. Biochem. Phys. Gen. & Prot.* 38.
476 Jimenez-Gomez, J. M., A. D. Wallace, and J. N. Maloof. 2010. Network analysis identifies *ELF3* as a QTL for the
477 shade avoidance response in Arabidopsis. *PLoS Genet.* 6:e1001100.
478 Johnston, S. E., J. Gratten, C. Berenos, J. G. Pilkington, T. H. Clutton-Brock, J. M. Pemberton, and J. Slate. 2013.
479 Life history trade-offs at a single locus maintain sexually selected genetic variation. *Nature* 502:93-95.
480 Koch, I. J., H. M. Nuetzel, and S. R. Narum. 2022. Epigenetic effects associated with salmonid supplementation
481 and domestication. *Environ. Biol. Fishes* 106:1093-1111.
482 Kurko, J., P. V. Debes, A. H. House, T. Aykanat, J. Erkinaro, and C. R. Primmer. 2020. Transcription Profiles of
483 Age-at-Maturity-Associated Genes Suggest Cell Fate Commitment Regulation as a Key Factor in the
484 Atlantic Salmon Maturation Process. *G3-Genes Genom. Genet.* 10:235-246.
485 Lawson, H. A., J. M. Cheverud, and J. B. Wolf. 2013. Genomic imprinting and parent-of-origin effects on
486 complex traits. *Nat. Rev. Genet.* 14:609-617.
487 Le Luyer, J., M. Laporte, T. D. Beacham, K. H. Kaukinen, R. E. Withler, J. S. Leong, E. B. Rondeau, B. F. Koop, and
488 L. Bernatchez. 2017. Parallel epigenetic modifications induced by hatchery rearing in a Pacific salmon.
489 *Proc Natl Acad Sci U S A*.
490 Lee, B., K. Rizzoti, D. S. Kwon, S. Y. Kim, S. Oh, D. J. Epstein, Y. Son, J. Yoon, K. Baek, and Y. Jeong. 2012. Direct
491 transcriptional regulation of *Six6* is controlled by *SoxB1* binding to a remote forebrain enhancer. *Dev.*
492 *Biol.* 366:393-403.
493 Lenth R (2023). emmeans: Estimated Marginal Means, aka Least-Squares Means. R package version 1.8.5.
494 Li, Q., D. Lindtke, C. Rodriguez-Ramirez, R. Kakioka, H. Takahashi, A. Toyoda, J. Kitano, R. L. Ehrlich, J. Chang
495 Mell, and S. Yeaman. 2022. Local Adaptation and the Evolution of Genome Architecture in Threespine
496 Stickleback. *Genom. Biol. Evol.* 14.
497 Matschiner, M., J. M. I. Barth, O. K. Torresen, B. Star, H. T. Baalsrud, M. S. O. Brieuc, C. Pampoulie, I. Bradbury,
498 K. S. Jakobsen, and S. Jentoft. 2022. Supergene origin and maintenance in Atlantic cod. *Nat. Ecol. Evol.*
499 6:469-481.
500 McLennan, D., Auer, S. K., Anderson, G. J., Reid, T. C., Bassar, R. D., Stewart, D. C., . . . Metcalfe, N. B. (2019).
501 Simulating nutrient release from parental carcasses increases the growth, biomass and genetic
502 diversity of juvenile Atlantic salmon. *J. App. Ecol.,* 56(8), 1937-1947.
503 Mobley, K. B., T. Aykanat, Y. Czorlich, A. House, J. Kurko, A. Miettinen, J. Moustakas-Verho, A. Salgado, M.
504 Sinclair-Waters, J. P. Verta, and C. R. Primmer. 2021. Maturation in Atlantic salmon (*Salmo salar,*
505 *Salmonidae*): a synthesis of ecological, genetic, and molecular processes. *Rev. Fish Biol. Fish.* 31:523-
506 571.
507 Mollie E. Brooks, Kasper Kristensen, Koen J. van Benthem, Arni Magnusson, Casper W. Berg, Anders Nielsen,
508 Hans J. Skaug, Martin Maechler and Benjamin M. Bolker (2017). glmmTMB Balances Speed and
509 Flexibility Among Packages for Zero-inflated Generalized Linear Mixed Modeling. *The R Journal*, 9(2),
510 378-400.
511 Mousseau, T. A. and C. Fox. 1998. Maternal Effects As Adaptations. Oxford University Press.
512 Moustakas-Verho, J. E., J. Kurko, A. H. House, J. Erkinaro, P. Debes, and C. R. Primmer. 2020. Developmental
513 expression patterns of *six6*: A gene linked with spawning ecotypes in Atlantic salmon. *Gene. Expr. Patt.*
514 38:119149.
515 Munoz, N. J., K. Anttila, Z. Chen, J. W. Heath, A. P. Farrell, and B. D. Neff. 2014. Indirect genetic effects underlie
516 oxygen-limited thermal tolerance within a coastal population of chinook salmon. *Proc. Roy. Soc. B-Biol.*
517 *Sci.* 281:20141082.

Niemela, P. T., I. Klemme, A. Karvonen, P. Hyvarinen, P. V. Debes, J. Erkinaro, M. Sinclair-Waters, V. L. Pritchard, L. S. Harkonen, and C. R. Primmer. 2022. Life-history genotype explains variation in migration activity in Atlantic salmon (Salmo salar). *Proc. Roy. Soc. B-Biol. Sci.* 289:20220851.

Oomen, R. A., A. Kuparinen, and J. A. Hutchings. 2020. Consequences of single-locus and tightly linked genomic architectures for evolutionary responses to environmental change. *J. Hered.* 111:319-332.

Orr, H. A. 2000. Adaptation and the cost of complexity. *Evolution* 54:13-20.

Orr, H. A. 2005. The genetic theory of adaptation: a brief history. *Nat. Rev. Genet.* 6:119-127.

Pritchard, V. L., H. Makinen, J. P. Vaha, J. Erkinaro, P. Orell, and C. R. Primmer. 2018. Genomic signatures of fine-scale local selection in Atlantic salmon suggest involvement of sexual maturation, energy homeostasis and immune defence-related genes. *Mol. Ecol.* 27:2560-2575.

Prokkola, J. M., E. R. Asheim, S. Morozov, P. Bangura, J. Erkinaro, A. Ruokolainen, C. R. Primmer, and T. Aykanat. 2022. Genetic coupling of life-history and aerobic performance in Atlantic salmon. *Proc. Roy. Soc. B-Biol. Sci.* 289:20212500.

Prokkola, J. M., K. K. Chew, K. Anttila, K. S. Maamela, A. Yildiz, E. R. Åsheim, C. R. Primmer, and T. Aykanat. 2024. Tissue-specific metabolic enzyme levels covary with whole-animal metabolic rates and life-history loci via epistatic effects. *Phil. T. Roy. Soc. B. 379.*

R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

Räsänen, K. and L. E. B. Kruuk. 2007. Maternal effects and evolution at ecological time-scales. *Funct. Ecol.* 21:408-421.

Rausher, M. D. 1992. The Measurement of Selection on Quantitative Traits: Biases Due to Environmental Covariances between Traits and Fitness. *Evolution* 46.

Rennison, D. J. and C. L. Peichel. 2022. Pleiotropy facilitates parallel adaptation in sticklebacks. *Mol. Ecol.* 31:1476-1486.

Reznick, D. 2016. Hard and Soft Selection Revisited: How Evolution by Natural Selection Works in the Real World. *J. Hered.* 107:3-14.

Saunders, R. L. and J. H. Gee. 1964. Movements of Young Atlantic Salmon in a Small Stream. *J. Fish. Res. Board Can.* 21:27-36.

Sinclair-Waters, M., J. Odegard, S. A. Korsvoll, T. Moen, S. Lien, C. R. Primmer, and N. J. Barson. 2020. Beyond large-effect loci: large-scale GWAS reveals a mixed large-effect and polygenic architecture for age at maturity of Atlantic salmon. *Genet. Sel. Evol.* 52:9.

Smith, P. F. and I. Kornfield. 2002. Phylogeography of Lake Malawi cichlids of the genus Pseudotropheus: significance of allopatric colour variation. *Proc. Roy. Soc. B-Biol. Sci.* 269:2495-2502.

Snoek, L. B., I. R. Terpstra, R. Dekter, G. Van den Ackerveken, and A. J. Peeters. 2012. Genetical Genomics Reveals Large Scale Genotype-By-Environment Interactions in *Arabidopsis thaliana*. *Front. Genet.* 3:317.

Taylor, E. B. 1991. A Review of Local Adaptation in Salmonidae, with Particular Reference to Pacific and Atlantic Salmon. *Aquaculture* 98:185-207.

Thompson, M. J. and C. D. Jiggins. 2014. Supergenes and their role in evolution. *Heredity (Edinb)* 113:1-8.

Thorholludottir, D. A. V., V. Nolte, and C. Schlotterer. 2023. Temperature-driven gene expression evolution in natural and laboratory populations highlights the crucial role of correlated fitness effects for polygenic adaptation. *Evolution* 77:2081-2089.

Thorn, M. W. and Y. E. Morbey. 2019. Survival under the Gravel: the Effects of Egg Size and Parental Identity on the In Situ Hatching Success of Chinook Salmon. *Trans. Am. Fish. Soc.* 148:991-1003.

Tishkoff, S. A., F. A. Reed, A. Ranciaro, B. F. Voight, C. C. Babbitt, J. S. Silverman, K. Powell, H. M. Mortensen, J. B. Hirbo, M. Osman, M. Ibrahim, S. A. Omar, G. Lema, T. B. Nyambo, J. Ghori, S. Bumpstead, J. K. Pritchard, G. A. Wray, and P. Deloukas. 2007. Convergent adaptation of human lactase persistence in Africa and Europe. *Nat. Genet.* 39:31-40.

566 Turelli, M., & Barton, N. H. (2004). Polygenic Variation Maintained by Balancing Selection: Pleiotropy, Sex-
567 Dependent Allelic Effects and G × E Interactions. *Genetics*, 166(2), 1053-1079.
568 doi:10.1093/genetics/166.2.1053
569 Tyndale, S. T., R. J. Letcher, J. W. Heath, and D. D. Heath. 2008. Why are salmon eggs red? Egg carotenoids and
570 early life survival of Chinook salmon (*Oncorhynchus tshawytscha*). *Evol. Ecol. Res.* 10:1187-1199.
571 Venney, C. J., K. W. Wellband, and D. D. Heath. 2021. Rearing environment affects the genetic architecture and
572 plasticity of DNA methylation in Chinook salmon. *Heredity (Edinb)* 126:38-49.
573 Waters, C. D., A. Clemento, T. Aykanat, J. C. Garza, K. A. Naish, S. Narum, and C. R. Primmer. 2021.
574 Heterogeneous genetic basis of age at maturity in salmonid fishes. *Mol. Ecol.* 30:1435-1456.
575 Weith, M., J. Grossbach, M. Clement-Ziza, L. Gillet, M. Rodriguez-Lopez, S. Marguerat, C. T. Workman, P. Picotti,
576 J. Bahler, R. Aebersold, and A. Beyer. 2023. Genetic effects on molecular network states explain
577 complex traits. *Mol. Syst. Biol.* 19:e11493.
578 Widowski, T. M., L. Cooley, S. Hendriksen, and M. Peixoto. 2022. Maternal age and maternal environment
579 affect egg composition, yolk testosterone, offspring growth and behaviour in laying hens. *Sci. Rep.*
580 12:1828.
581 Williams, T. D. 1994. Intraspecific variation in egg size and egg composition in birds: effects on offspring fitness.
582 *Biol. Rev. Camb. Philos. Soc.* 69:35-59.
583 Wolf, J. B., E. D. Brodie Iii, J. M. Cheverud, A. J. Moore, and M. J. Wade. 1998. Evolutionary consequences of
584 indirect genetic effects. *Trends Ecol. Evol.* 13:64-69.
585 Wolf, J. B. and M. J. Wade. 2009. What are maternal effects (and what are they not)? *Phil. T. Roy. Soc. B.*
586 364:1107-1115.
587 Yeaman, S. and M. C. Whitlock. 2011. The genetic architecture of adaptation under migration-selection
588 balance. *Evolution* 65:1897-1911.
589

590 Tables and Figures

591 **Table 1:** Estimated coefficients (fixed effects) and variance (random effects) for individual based binomial
592 model with local survival as the response variable. The coefficients are from the best-fitted model across
593 different parametrization of the parental genetic effects in the high nutrient environment.

Fixed effects	Estimate	Std. Error	*z* value	*p* value
(Intercept)	-5.959	1.156	-5.154	<0.0001
Family SMR	16.142	6.945	2.324	0.0201
vgll3 additive	-0.141	0.213	-0.662	0.5080
six6 additive	0.145	0.159	0.911	0.3625
vgll3 parental	1.368	0.602	2.274	0.0230
six6 maternal	-0.914	0.305	-3.002	0.0027
Random effects	Variance			
Family origin	0.1543			
Stream	0.0047			

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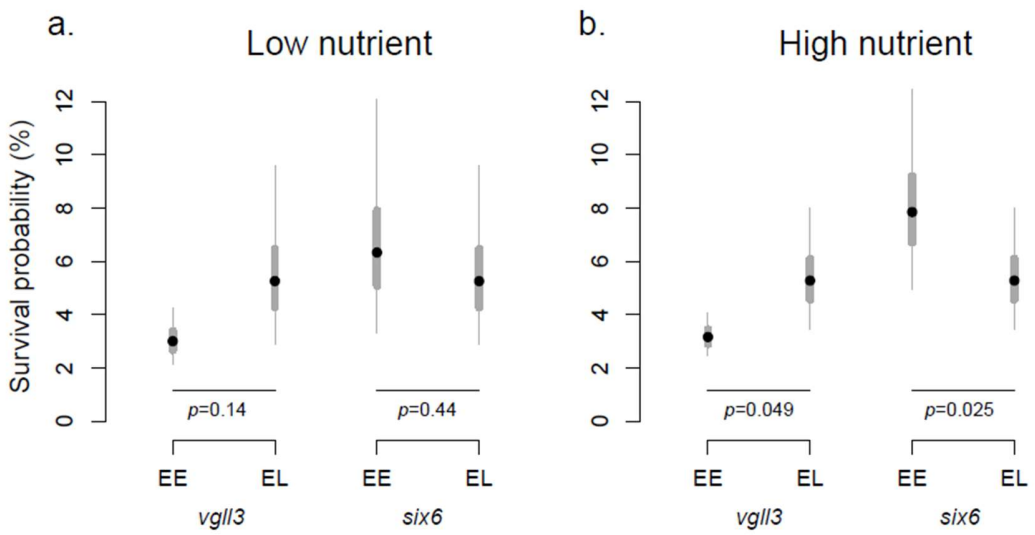

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598 **Figure 1:** Marginal means for probability of survival of offspring in relation to family-wise *vgll3* and *six6*
599 genotypes for (a) low, and (b) high nutrient streams. Data are plotted for the homozygote early (EE) and
600 heterozygote (EL) genotypes (no homozygote-LL families were present for either locus). The estimated values
601 are from the most parsimonious models including both *vgll3* and *six6* effects, which is the best fitting model for
602 the high nutrient streams and the fourth best model for the low nutrient streams (see M&M and
603 Supplementary Table 2 for details). Thin and thick grey bars indicate 50% and 95% confidence intervals,
604 respectively.

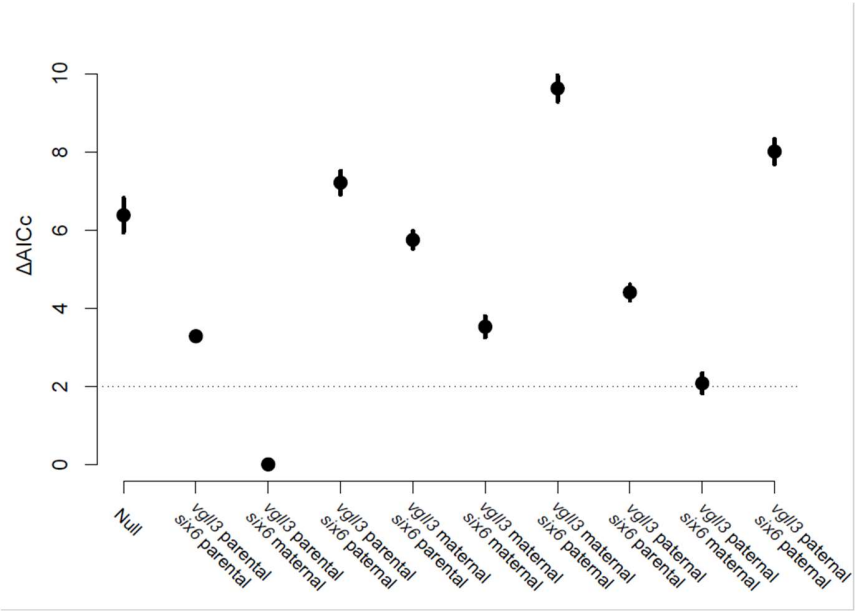

Figure 2: The likelihood differences among individual-based models with different parametrization of the parental genetic effects that explains survival in the high nutrient environment. ΔAICc = 0 indicates a best fitted model. All models contained SMR and additive *vgll3* and *six6* genetic effects as covariates. Y-axis indicates the ΔAICc to the best model, and the dashed line indicates ΔAIC = 2. Error bars represents one standard error of ΔAICc across 1000 models using 1000 data that simulated the genotypes of dead/emigrated individuals (see Materials and Methods for details).

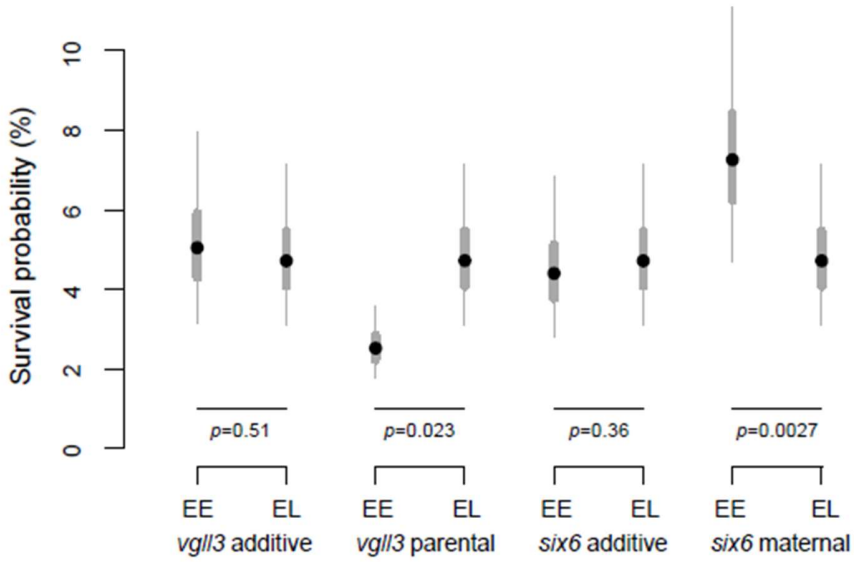

Figure 3: Marginal offspring survival probability of the genetic effects for the best-fit parental genetic structure model in the high nutrient streams. Thin and thick grey bars indicate 50% and 95% confidence intervals, respectively. Data are plotted for the homozygote early (EE) and heterozygote (EL) genotypes (no homozygous-LL families were present for either locus).