



REVIEW



Beyond hybridization: the genetic impacts of non-reproductive ecological interactions of salmon aquaculture on wild populations

I. R. Bradbury^{1,*}, I. Burgetz², M. W. Coulson², E. Verspoor³, J. Gilbey⁴, S. J. Lehnert¹, T. Kess¹, T. F. Cross⁵, A. Vasemägi^{6,7}, M. F. Solberg⁸, I. A. Fleming⁹, P. McGinnity⁵

¹Fisheries and Oceans Canada, Northwest Atlantic Fisheries Centre, 80 E White Hills Rd, St. John's, Newfoundland, A1C 5X1, Canada

²Fisheries and Oceans Canada, 200 Kent Street Ottawa, Ontario, K1A 0E6, Canada

³Rivers and Lochs Institute, University of the Highlands and Islands, Inverness, IV3 5SQ, UK

⁴Marine Scotland Science, Freshwater Fisheries Laboratory, Pitlochry, Scotland PH16 5LB, UK

⁵School of Biological, Earth and Environmental Sciences, University College, Cork, T12 YN60, Ireland

⁶Chair of Aquaculture, Institute of Veterinary Medicine and Animal Sciences, Estonian University of Life Sciences, 51014 Tartu, Estonia

⁷Department of Aquatic Resources, Institute of Freshwater Research, Swedish University of Agricultural Sciences, 17893 Drottningholm, Sweden

⁸Population Genetics Research Group, Institute of Marine Research, 5817 Bergen, Norway

⁹Memorial University of Newfoundland, Department of Ocean Sciences, St. John's, Newfoundland, A1C 5S7, Canada

ABSTRACT: Cultured Atlantic salmon *Salmo salar* are of international socioeconomic value, and the process of domestication has resulted in significant behavioural, morphological, and allelic differences from wild populations. Substantial evidence indicates that direct genetic interactions or interbreeding between wild and escaped farmed Atlantic salmon occurs, genetically altering wild salmon and reducing population viability. However, genetic interactions may also occur through ecological mechanisms (e.g. disease, parasites, predation, competition), both in conjunction with and in the absence of interbreeding. Here we examine existing evidence for ecological and non-reproductive genetic interactions between domestic Atlantic salmon and wild populations and the potential use of genetic and genomic tools to resolve these impacts. Our review identified examples of genetic changes resulting from ecological processes, predominately through pathogen or parasite transmission. In addition, many examples were identified where aquaculture activities have either altered the selective landscape experienced by wild populations or resulted in reductions in population abundance, both of which are consistent with the widespread occurrence of indirect genetic changes. We further identify opportunities for genetic or genomic methods to quantify these impacts, though careful experimental design and pre-impact comparisons are often needed to accurately attribute genetic change to aquaculture activities. Our review indicates that ecological and non-reproductive genetic interactions are important, and further study is urgently needed to support an integrated understanding of aquaculture–ecosystem interactions, their implications for ecosystem stability, and the development of potential mitigation and management strategies.

KEY WORDS: Atlantic salmon · Aquaculture · Management · Genetic

1. INTRODUCTION

Atlantic salmon *Salmo salar* aquaculture is of international socioeconomic importance, and the process

of domestication has resulted in significant phenotypic (i.e. physiological, Handeland et al. 2003; behavioural, Fleming et al. 1996; morphological, Fleming et al. 1994); and genetic (Cross & King 1983, Karlsson et al.

*Corresponding author: ibradbur@me.com

2011, Wringe et al. 2019) differences from wild populations. Escape events from Atlantic salmon net pen aquaculture are a regular occurrence (Keyser et al. 2018), and the number of escapees can equate to an appreciable fraction of, or exceed, wild Atlantic salmon census size (Morris et al. 2008, Skilbrei et al. 2015, Wringe et al. 2018). There is substantial evidence that direct genetic interactions, defined as interbreeding, occurs between wild Atlantic salmon and escaped domestic individuals (Karlsson et al. 2016, Glover et al. 2017, Wringe et al. 2018) and can genetically alter wild salmon and reduce population viability (McGinnity et al. 2003, Bourret et al. 2011, Glover et al. 2013, Bolstad et al. 2017, Bradbury et al. 2020). Both in Canada and Norway, recent evidence suggests hybridization may be extensive following escape events (Karlsson et al. 2016, Wringe et al. 2018) and accounts for a substantial proportion of production in smaller rivers (Sylvester et al. 2018b). Accordingly, escaped farmed salmon and direct genetic interactions have been identified as a major threat to the persistence and stability of wild Atlantic salmon across the North Atlantic (Forseth et al. 2017, Bradbury et al. 2020).

However, genetic impacts may also occur, either in concert with or in the absence of hybridization (Verspoor et al. 2015), due to ecological interactions such as competition, predation, and disease or parasite transfer. These non-reproductive genetic changes in wild populations can result from ecological changes that either alter the selective landscape experienced by native fish, and thus change allele frequencies of loci linked to fitness, and/or reduce population abundance, resulting in a loss of genetic diversity (Fig. 1). As these effects do not involve hybridization, they can arise whether domestic animals escape or remain in containment and impact wild populations of any native species. Although practices to limit reproductive genetic interactions with wild Atlantic salmon have been implemented in many areas through the use of sterilization (Verspoor et al. 2015), exotic species, and improved containment strategies (Diserud et al. 2019), these efforts do not prevent non-reproductive genetic effects. In other species such as brown trout *Salmo trutta* or Pacific salmon species (*Oncorhynchus* spp.)

where hybridization with escapees is not common or possible, ecologically induced genetic interactions with Atlantic salmon aquaculture remain an ongoing concern (e.g. Coughlan et al. 2006, Ford & Myers 2008). Moreover, given recent trends in industry expansion (e.g. DFO 2016, 2018) and growing concerns regarding the amplification of pests and pathogens such as sea lice through net pen aquaculture (e.g. Vollset et al. 2016, Karbowski et al. 2019), the potential for both ecological and non-reproductive genetic interactions is likely to increase. Nonetheless, despite the potentially broad reaching and significant impacts of non-reproductive genetic interactions on wild Atlantic salmon and other species, the evidence for their presence and our ability to quantify their magnitude has been limited to date (Verspoor et al. 2015).

The goal of this review is to highlight evidence pertaining to the potential for ecological and associated non-reproductive genetic impacts of Atlantic salmon aquaculture on wild populations. Specifically, our

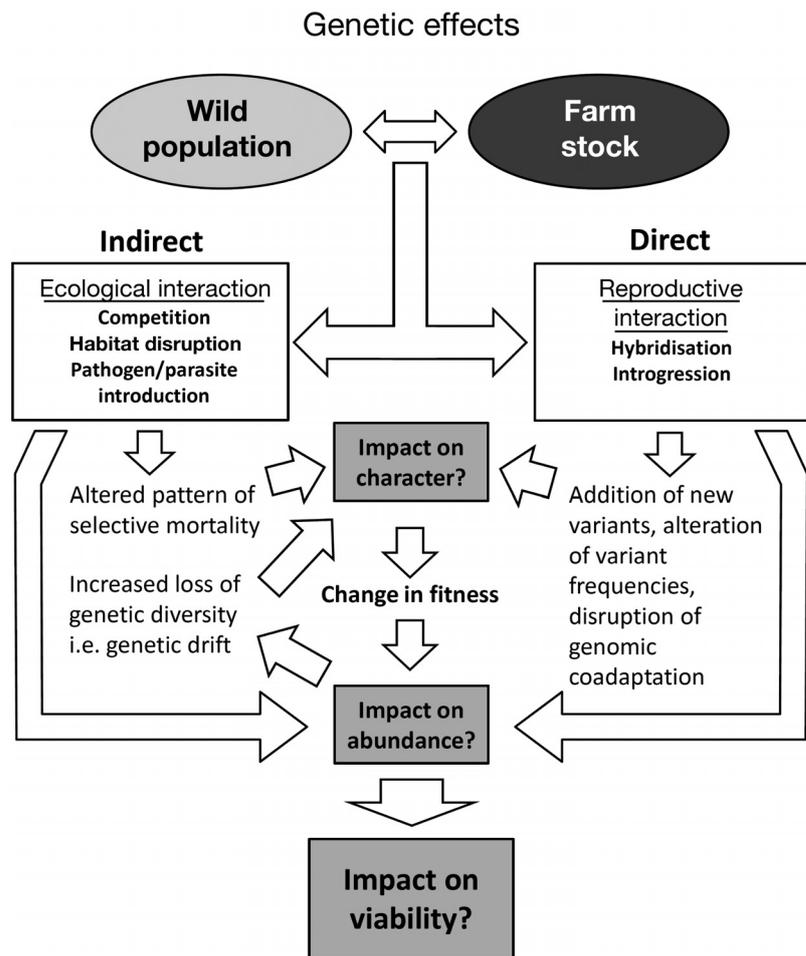


Fig. 1. Schematic of reproductive and non-reproductive genetic interactions between wild and domestic Atlantic salmon *Salmo salar*

objectives are to (1) review examples of genetic changes in wild populations resulting from ecological interactions, or likely more common, evidence for changes in population abundance or the environment experienced by wild populations; and (2) discuss the opportunity recent advances in population genomic approaches present for the assessment of these genetic impacts. Through our review, we highlight opportunities for the further study of non-reproductive genetic impacts of Atlantic salmon aquaculture on wild populations. We directly build on previous reviews and empirical studies focusing on hybridization and introgression (e.g. Karlsson et al. 2016, Glover et al. 2017, Bradbury et al. 2020) and on risk assessments considering both reproductive and non-reproductive effects (e.g. Verspoor et al. 2015). Ultimately, we suggest that ecological and subsequent non-reproductive genetic impacts are likely ubiquitous wherever salmon farming occurs, and that further research is urgently required to better understand the magnitude of these interactions and provide advice regarding impact management and mitigation.

2. EVIDENCE FOR ECOLOGICAL AND NON-REPRODUCTIVE GENETIC IMPACTS

Atlantic salmon net pen aquaculture represents a substantial change to the natural environment and thus the adaptive landscape experienced by wild individuals (Garcia de Leaniz et al. 2007). As such, it can alter the stability and future evolutionary trajectories of wild populations. Furthermore, it might be expected that adjustments to a new adaptive landscape will result in reductions in productivity through increased maladaptation predicted by theoretical demographic-evolutionary models (Bürger & Lynch 1995, Gomulkiewicz & Holt 1995, Kirkpatrick & Barton 1997). Existing studies address genetic changes in naïve populations through disease and parasite transmission, the potential for recovery of disease or parasite resistance through natural selection, observations on genetic changes in co-occurring congener species, and impacts of the farming of non-native species or subspecies. Examples of the latter are the farming of European origin salmon on both the east and west coasts of North America as well as in western South America or Australia. Below we review the literature related to non-reproductive genetic interactions associated with disease and parasite transfer, increased predation pressure, and finally, increased competition (see Table 1). In each case, we first high-

light examples of genetic change resulting from these interactions and then set out evidence of demographic decline or the potential for selection consistent with significant genetic impacts. In practice, it can be difficult to distinguish the impacts of reproductive and non-reproductive genetic interactions in examples related to wild Atlantic salmon. As such, here we focus on instances where mechanisms have been identified which are clearly non-reproductive in nature.

2.1. Ecological and non-reproductive genetic changes through disease transmission

Ecological and genetic interactions via disease transmission may result in both alterations to the selective landscape potentially impacting immune associated genetic variation as well as reductions in overall genetic diversity due to demographic decline. To date, few studies have examined the presence of genetic changes due to disease transfer (Table 1A). However, de Eyto et al. (2007, 2011) present evidence of genetic impacts due to novel disease exposure associated with aquaculture activities. In these studies, the progeny of Atlantic salmon from a river without previous exposure to aquaculture were transferred to a river with a long history of associated farming and captive breeding that was expected to have acquired novel micro- and macro-parasitic communities. This experimental design enabled the exposure of animals to novel disease challenges associated with escapes or inadvertent or deliberate introductions. Comparison of observed and expected genotype frequencies at a marker locus for the MHC class II alpha gene and control neutral microsatellite loci of parr and migrant Atlantic salmon stages in the wild demonstrated that genetic change had occurred, and that selection was likely a result of disease-mediated natural selection, rather than any demographic event.

A substantial and growing body of research supports the hypothesis that wild salmon populations are adapted to local pathogen communities both in space and time (Dionne et al. 2007, Tonteri et al. 2010, Consuegra et al. 2011, Kjærner-Semb et al. 2016, Pritchard et al. 2018, Zueva et al. 2018). This suggests a genetic basis for differences in population immunity and that the introduction of new pathogens into susceptible populations could both impose novel selection pressures and reduce genetic diversity through demographic decline. The possibility that pathogen transfer from domestic to wild salmon could drive genetic change in wild populations is supported by

Table 1. Summary of studies presenting evidence for or consistent with the potential for ecological and non-reproductive genetic interactions among Atlantic salmon *Salmo salar* aquaculture and wild salmonid populations. N/A: not applicable

Interaction	Primary observation	Evidence (direct or supportive)	Selection / demographic	Species impacted	Reference
(A) Disease transfer					
Common garden experiment (naïve non-local wild population introduced into different river system as eggs)	Evidence of allele frequency change at major histocompatibility (MH) genes during first 6 months in introduced population; no change in local population)	Supportive	Selection	Atlantic salmon <i>S. salar</i>	de Eyto et al. (2007)
Common garden experiment (naïve non-local wild population introduced into different river as eggs)	Evidence of different allele frequency change at major histocompatibility (MH) genes in introduced population from 6 months to 18 months; no change in local population)	Supportive	Selection	Atlantic salmon <i>S. salar</i>	de Eyto et al. (2011)
Genetic survey of natural populations (not associated with aquaculture)	Evidence of clinal geographical response in major histocompatibility (MH) genes in response to water temperature variation)	Supportive	Selection	Atlantic salmon <i>S. salar</i>	Dionne et al. (2007)
Genetic survey of natural populations potentially sensitive and tolerant of <i>Gyrodactylus salaris</i>	Evidence of clinal geographical response in major histocompatibility (MH) & other immune relevant genes in response to water temperature variation)	Supportive (possible direct link to <i>G. salaris</i> parasite)	Selection	Atlantic salmon <i>S. salar</i>	Tonteri et al. (2010)
Genetic survey of natural populations in areas with and without aquaculture activity	Evidence of spatial allele variation at major histocompatibility (MH) genes	Supportive (possible direct link to viral pathogens)	Selection	Atlantic salmon <i>S. salar</i>	Consuegra et al. (2011)
Genetic survey of natural populations in region of significant aquaculture activity	Evidence of SNP variation associated with selective sweeps of immune response genes	Supportive (source of selective agent unknown)	Selection	Atlantic salmon <i>S. salar</i>	Kjærner-Semb et al. (2016)
Genetic survey of natural populations within single large river complex (not associated with aquaculture)	Evidence of SNP variation associated with major histocompatibility (MH) genes	Supportive	Selection	Atlantic salmon <i>S. salar</i>	Pritchard et al. (2018)
Disease screening of escaped farmed Atlantic salmon in a wild river	Virus infected escaped farmed salmon entering rivers near cage sites	Supportive	Both	Atlantic salmon <i>S. salar</i>	Madhuh et al. (2015)
Disease screening of returning wild Atlantic salmon in Norway at 6 sites	Evidence for the infection of wild salmon from escaped farmed salmon at marine feeding areas	Supportive	Both	Atlantic salmon <i>S. salar</i>	Madhuh et al. (2018)
Genetic screening of PRV in wild and farmed Atlantic salmon	Evidence for long distance transmission of PRV likely associated with aquaculture industry	Supportive	Both	Atlantic salmon <i>S. salar</i>	Garseth et al. (2013)

Table continued on next page

Table 1 (continued)

Interaction	Primary observation	Evidence (direct or supportive)	Selection / demographic	Species impacted	Reference
Review of studies documenting furunculosis prevalence in Norway from 1964–1992	Evidence for the transfer of furunculosis from fish farms to wild salmonids in Norway	Supportive	Demographic	Various salmonids	Johnsen & Jensen (1994)
Genetic screening of ISAV variants in wild and farmed salmon in Norway	Evidence for the horizontal transmission of ISAV variants seen in farmed salmon to wild populations	Supportive	Both	Atlantic salmon <i>S. salar</i>	Nylund et al. (2019)
(B) Parasite transfer Statistical modeling of the effect on return rates of sea lice levels (low/med/high) over a 26 year period for ISW Erriff salmon	Wild salmon returns were strongly reduced (>50%) following years with high lice levels during smolt out-migration (farms located at the mouth of the estuary)	Supportive	Both	Atlantic salmon <i>S. salar</i>	Shepherd & Gargan (2017)
Tag/recapture experiment of prophylactically treated smolts exposed to different farm-origin sea lice pressure	Recapture rate of untreated adult salmon following exposure to high sea lice density was 0.03% compared to treated salmon (1.86%)	Direct	Both	Atlantic salmon <i>S. salar</i>	Bøhn et al. (2020)
Association between sea lice counts on farmed Atlantic salmon and wild out-migrating chum salmon	Significant positive association between the sea lice abundance on farms and the likelihood that juvenile chum salmon would be infested. Increased abundance of lice on farms was not significantly associated with the levels of infestation observed on juvenile chum salmon	Supportive	Both	Chum salmon <i>Oncorhynchus keta</i>	Nekouei et al. (2018)
Experimental sea lice infection of wild brown trout post-smolts and examinations of marine migratory behavior	Experimental sea lice infection associated with increased mortality, and decreased migration distance, and marine residency	Supportive	Both	Sea trout <i>S. trutta</i>	Serra-Linares et al. (2020)
Review paper: integrating laboratory and field observational studies of lice on out-migrating <i>S. salar</i> and <i>S. trutta</i>	Sea lice loads on out-migrating sea trout in areas with aquaculture commonly exceed threshold levels that are known to induce physiological compromise or mortality in laboratory experiments	Supportive	Both	Sea trout <i>S. trutta</i>	Thorstad & Finstad (2018)
Review paper: integrating laboratory and field observational studies of lice on out-migrating <i>S. salar</i> and <i>S. trutta</i>	Premature migratory return	Direct	Demographic	Sea trout <i>S. trutta</i>	Thorstad & Finstad (2018)

Table continued on next page

Table 1 (continued)

Interaction	Primary observation	Evidence (direct or supportive)	Selection / demographic	Species impacted	Reference
Review paper: integrating laboratory and field observational studies of lice on out-migrating <i>S. salar</i> and <i>S. trutta</i>	Summary of meta-analysis and tagged treated smolt survival to returning adults experiment	Supportive	Both	Atlantic salmon <i>S. salar</i>	Thorstad & Finstad (2018)
Sea lice abundance on out-migrating pink salmon and chum salmon differences pre- and post-exposure to Atlantic salmon farms	Quantitative estimate of transmission rates from farm to out-migrating pink and chum salmon, including subsequent transmission dynamics of lice within the wild population	Supportive	Demographic	Pink salmon <i>O. gorbuscha</i> and chum salmon <i>O. keta</i>	Krkošek et al. (2005)
Hierarchical model of stock-recruit dynamics of coho salmon with differential sea lice infestation	Coho salmon population productivity in an area of intensive salmon aquaculture was depressed approximately sevenfold during a period of salmon louse infestations compared to unexposed populations.	Supportive	Demographic	Coho salmon <i>O. kisutch</i>	Connors et al. (2010)
Modeling effect of sea lice infections on population abundance of pink salmon	Pink salmon populations exposed to salmon farms; mortality rate caused by sea lice was estimated to range from 16 to 97%	Supportive	Demographic	Pink salmon <i>O. gorbuscha</i>	Krkošek et al. (2007)
Analysis of spawner-recruit data and sea lice abundance on farms	Sea lice counts on fish farms were negatively associated with adult returns of 2 species of Pacific salmon	Supportive	Demographic	Pink salmon <i>O. gorbuscha</i> and Coho salmon <i>O. kisutch</i>	Krkošek et al. (2011a)
Screening of pyrethroid resistance genotype in <i>Lepeophtheirus salmonis</i> over time	Widespread changes in the frequency of genotype associated with pyrethroid resistance in sea lice across the North Atlantic	Direct	Selection	Salmon louse <i>Lepeophtheirus salmonis</i>	Børretzen Fjørtoft et al. (2020)
<i>G. salaris</i> infection associated with wild salmon population decline	Wild stocks decreased in size by an average of 85% and smolt numbers decreased by as much as 98% following introduction of <i>G. salaris</i> into Norway	Supportive	Demographic	Atlantic salmon <i>S. salar</i>	Denholm et al. (2016)
Genomic basis of resistance to <i>G. salaris</i>	Identified 3 genomic regions associated with adaptation to parasite resistance in wild salmon	Supportive	N/A	Atlantic salmon <i>S. salar</i>	Zueva et al. (2014)
Genomic basis of resistance to <i>G. salaris</i>	Identified 57 candidate genes potentially under positive selection associated with <i>G. salaris</i> resistance and enriched for lymph node development, focal adhesion genes and anti-viral responses	Supportive	N/A	Atlantic salmon <i>S. salar</i>	Zueva et al. (2018)

Table continued on next page

Table 1 (continued)

Interaction	Primary observation	Evidence (direct or supportive)	Selection / demographic	Species impacted	Reference
Growth and survival of sea lice infected Arctic Charr	Infection intensity correlated positively with mortality and negatively with growth in experimental trials	Supportive	Both	Arctic charr <i>Salvelinus alpinus</i>	Fjelldal et al. (2019)
(C) Predation					
Increased predation on wild species	Increased avian predation on wild salmon and brown trout following the release of captive bred smolts	Supportive	Demographic / selective?	Brown trout <i>S. trutta</i>	Kennedy & Greer (1988)
Predation on released farmed escapes	High levels of predation on released farmed Atlantic salmon near cage sites	Supportive	Demographic / selective?	Atlantic salmon <i>S. salar</i>	Hamoutene et al. (2018)
(D) Competition					
Competition between wild and farmed juvenile Atlantic salmon in freshwater	30% reduction in wild population productivity in the presence of farmed fish	Supportive	Demographic	Atlantic salmon <i>S. salar</i>	Fleming et al. (2000)
Competition between wild and farmed juvenile Atlantic salmon in freshwater	Overlap in diet among types of crosses demonstrates competition	Supportive	Demographic	Atlantic salmon <i>S. salar</i>	Skaala et al. (2012)
Metabolic rate and survival of farmed Atlantic salmon offspring	Presence of wild-farmed hybrids reduced survival of wild individuals	Supportive	Demographic	Atlantic salmon <i>S. salar</i>	Robertsen et al. (2019)

several recent findings documenting the potential for exposure and supporting pathogen transfer as mechanisms for genetic impacts (Table 1A). First, Madhun et al. (2015) report the detection of virus infected escaped farmed salmon entering rivers near cage sites, suggesting clear evidence of exposure of freshwater rearing juvenile salmon populations to aquaculture associated pathogens. Second, Madhun et al. (2018) also document the presence of piscine orthoreovirus (PRV) in returning wild adult Atlantic salmon in Norway, and that the frequency of infection increased with body size and displayed no geographic signal, suggesting infection was occurring between escapees and wild salmon at marine feeding areas. Nylund et al. (2019) report that infectious salmon anemia virus (ISAV) variants in farmed salmon are increasing in prevalence in the wild consistent with horizontal transmission from farmed salmon to wild populations. Similarly, Garseth et al. (2013) examine pathogen transfer between wild and farmed salmon using analysis of protein coding sequences in PRV in Norway and suggest occurrence in the wild is due to long distance transmission likely associated with the aquaculture industry. Finally, several studies have documented the spread of furunculosis, a septicemic bacterial disease, from fish farms to wild salmonids in Norwegian rivers (Johnsen & Jensen 1994). Taken together, these findings indicate that ecologically induced genetic impacts on wild salmon populations associated with disease transmission from aquaculture populations are highly likely. However, both the magnitude of new selection pressures and demographic impacts are uncertain and likely case specific.

Diseases, introduced or increased in incidence by salmon aquaculture activities, could also have an impact on co-occurring wild species such as anadromous brown trout, as implied by the steep decline in anadromous trout numbers in many Irish, Scottish, and Nor-

wegian rivers since the late 1980s, which may be linked to sea lice infestations (see Section 2.2) associated with marine salmonid farming. A study by Coughlan et al. (2006) in some Irish rivers suggested that salmon farming and ocean ranching could indirectly affect, most likely mediated by disease, the genetics of cohabiting anadromous brown trout by reducing variability at major histocompatibility class I genes. A significant decline in allelic richness and gene diversity at the Satr-UBA marker locus, observed since aquaculture started, which may indicate a selective response, was not reflected by similar reductions at neutral loci. Subsequent recovery of variability at the Satr-UBA marker, seen among later samples, may reflect an increased contribution by resident brown trout to the remaining anadromous population. Similarly, Miller et al. (2011) link genomic profiles consistent with viral infection with increased likelihood of mortality prior to spawning in Fraser River sockeye salmon *Oncorhynchus nerka*. Morton et al. (2017) document piscine orthoreovirus (PRV) in 95% of farmed Atlantic salmon in British Columbia, Canada, and infection rates in wild Pacific salmon of 37–45% near salmon farms, and of 5% at sites distant to farms suggesting PRV transfer is occurring from salmon farms to wild salmon populations.

2.2. Ecological and non-reproductive genetic effects through parasites

Like disease transfer, the introduction of novel parasites could both impose new selection pressures and drive demographic decline. Although no examples of genetic change attributable to parasite transfer from salmon aquaculture were identified, substantial research has demonstrated the (1) transfer of parasites from aquaculture salmon to wild populations, (2) significant demographic impacts resulting, and (3) a genetic basis to resistance, all of which support the presence of genetic change occurring as a result. Examples to date have most notably been via infections of sea lice or the monogenetic trematode *Gyrodactylus salaris* (Table 1B). Declines in wild stocks attributed to sea lice outbreaks in farm-intensive areas have been documented in Ireland, Scotland and Norway. Thorstad & Finstad (2018) reviewed the literature related to sea lice impacts on wild stocks documenting 12–29% fewer returning adult spawners due to lice-induced mortality from fish farms. In one of the most extreme cases documented to date, Shephard & Gargan (2017) suggested that one-sea-winter (1SW) salmon returns on the River Erriff were

more than 50% lower in years following high lice levels on nearby farms. This increased mortality was in addition to decreased returns due to poorer marine survival. Similarly, Bøhn et al. (2020) tagged and released Atlantic salmon smolts both with a prophylactic treatment against lice and without such treatment, and recaptured survivors returning to freshwater after spending 1–4 yr at sea. They report that the mortality of untreated smolts was as much as 50 times higher compared to treated smolts during sea lice outbreaks. It is worth noting that these estimates of lice-induced mortality among Atlantic salmon should be considered as minimum estimates for species such as anadromous brown trout, whose marine migrations are more coastal, thus increasing their exposure to net pen sites (Thorstad & Finstad 2018). Recent work by Serra-Llinares et al. (2020) reports increased mortality, reduced marine migrations, and reduced marine residency in brown trout experimentally infested with sea lice, consistent with significant demographic impacts of sea lice infection in brown trout. Similarly, for migratory Arctic char *Salvelinus alpinus* exposed to elevated sea lice burden due to fish farming activity (Bjørn et al. 2001), the negative impact on growth and survival may potentially lead to selection against anadromy (Fjellidal et al. 2019).

In addition to potential impacts on Atlantic salmonids, evidence also exists that the transfer of sea lice from farmed Atlantic salmon to Pacific salmon species occurs (e.g. Nekouei et al. 2018), again consistent with the potential non-reproductive genetic interactions. For example, out-migrating juvenile pink salmon *O. gorbuscha* and chum salmon *O. keta*, are estimated to experience 4 times greater sea lice infection pressure near Atlantic salmon farms compared to background infection levels (Krkošek et al. 2005), and in juvenile sockeye salmon *O. nerka*, infection rates were elevated after migration past these salmon farms (Krkošek et al. 2005, Price et al. 2011). For Coho salmon *O. kisutch*, ecological interactions with infected species, as well directly with Atlantic salmon farms, can result in higher infection levels (Connors et al. 2010). These lice infections in Pacific salmon species have also been associated with population declines. Krkošek et al. (2007) found that sea lice infestation from Atlantic salmon farms on out-migrating pink salmon smolts have led to declines in wild populations in the Broughton Archipelago, with forecasting models suggesting that local extinction was imminent. For these pink salmon populations exposed to salmon farms, mortality rate caused by sea lice was estimated to range from 16 to 97% (Krkošek et al. 2007), and population declines were also ob-

served in Coho salmon populations (Connors et al. 2010). Krkošek et al. (2011a) demonstrated that sea lice abundance on fish farms in British Columbia, Canada, were negatively associated with nearby returns of both pink salmon and Coho salmon. Furthermore, changes in parasite management on salmon farms have been shown to help reduce infection rates on wild salmon (Peacock et al. 2013), supporting this linkage and suggesting mitigation might be possible.

Given evidence of significant sea lice associated demographic declines, it seems likely that sea lice-induced mortality could drive reductions in genetic diversity. However, a large body of research suggests resistance to sea lice may have a genetic basis and be heritable (Tsai et al. 2016, Correa et al. 2017, Robledo et al. 2019), making it highly likely that wild populations would change in response to new selection pressures. In support of this hypothesis, Børretzen Fjørtoft et al. (2020) documented large-scale genetic changes in sea lice in response to chemotherapeutant usage across the North Atlantic. They observed significant temporal changes in wild sea lice populations in the frequency of a genotype associated with pyrethroid resistance due to strong selection pressure associated with its usage in Atlantic salmon aquaculture. Similarly, Dionne et al. (2009) reported significant changes in myxozoan resistance associated MHC alleles in Atlantic salmon, most likely linked with an infection-related mortality event, further supporting the potential for parasite-associated genetic impacts in wild populations.

The first appearance of *G. salaris* in Norway has been linked to the introduction of Atlantic salmon from Baltic catchments, resulting in high levels of mortality among wild populations (Johnsen & Jensen 1991). Admittedly, the spread of *G. salaris* in the wild does not seem primarily linked to salmon aquaculture. Instead, the transfer of individuals associated with stocking activities seems to have played a dominant role in transmission. Nonetheless, it is included here, as it clearly illustrates the potential for the introduction of non-native individuals to transfer parasites to local populations, the potential for subsequent significant demographic impacts, and a genetic basis to parasite resistance. In *G. salaris* infections, very high rates of mortality in naïve wild populations strongly supports the potential for significant demographic decline, losses of genetic diversity, and parasite driven selection, as has been recently concluded (Karlsson et al. 2020). For example, following several independent introductions of *G. salaris* into Norway, exposed wild populations decreased in abundance by an average of 85%, and smolt numbers decreased by as much as

98% (Denholm et al. 2016). Several studies suggest a genetic basis to *G. salaris* resistance among wild salmon populations in Europe. Gilbey et al. (2006) identified 10 genomic regions associated with heterogeneity in both innate and acquired resistance using crosses of resistant Baltic and susceptible Atlantic populations. Zueva et al. (2014) compared Baltic and Atlantic Atlantic salmon populations characterized by different levels of resistance to *G. salaris* and identified 3 genomic regions potentially experiencing parasite-associated adaptation in the wild. More recently, Zueva et al. (2018) compared salmon populations from northern Europe classified as extremely susceptible or resistant to *G. salaris*. They identify 57 candidate genes potentially under resistance-associated selection and this set of loci was shown to be enriched for genes associated with both innate and acquired immunity. These findings suggest that ecological and non-reproductive genetic impacts on wild populations associated with parasite transmission, such as sea lice from aquaculture installations, are highly likely, both because of the potential for substantial mortality to occur through exposure and for it to be selective through a clear genetic basis to population differences in resistance.

2.3. Ecological and non-reproductive genetic effects through predation

Increased predation associated with salmon aquaculture activities could result in both declines in abundance and selective mortality. Although direct estimates are lacking, some evidence exists to support the possibility of such a link, most likely through predators being attracted to aquaculture activities (Table 1C). Aquaculture sites have been shown to attract wild fish, invertebrates, marine mammals, and birds, likely due to the addition of food, and the farmed salmon themselves (see review in Callier et al. 2018), and the end result may be increased predation on wild individuals in the vicinity. Although it is possible that escapees could distract predators and reduce predation on wild populations through predator swamping, there is no evidence to date to support this. In fact, Kennedy & Greer (1988) reported heavy predation on hatchery smolts and wild Atlantic salmon and brown trout from the river Bush in Northern Ireland by the great cormorant *Phalacrocorax carbo*. This suggested a link between the release of captive bred smolts (a proxy for farm escapes), the attraction of increased numbers of these predatory birds to the river, and increased predation on the

river's wild Atlantic salmon and brown trout. Similarly, Hamoutene et al. (2018) conducted experimental releases and tracking of aquaculture Atlantic salmon near cage sites in southern Newfoundland, Canada. They found that most released fish were not detected beyond a few weeks of release, with temperature and movement data supporting predation as a cause. Increased predation of wild salmon smolts or adults near sea cages could therefore drive demographic decline or potentially act as a selective agent if predators cued on size, behaviour, or other traits. Moreover, rates of predation may be higher for individuals already experiencing infections, such as sea lice (see Section 2.2). Krkošek et al. (2011b) reported experimental evidence that predators selectively consuming infected prey which could simultaneously impose predation associated impacts and amplify disease or parasite associated selection and mortality.

2.4. Ecological and non-reproductive genetic effects through competitive interactions

Ecological and non-reproductive genetic effects have also been suggested via evidence for competitive interactions among farm and wild salmon. These competitive effects could be the result of ecological interactions among wild, farm escaped and hybrid offspring involving differences in behaviour among cross types such as in aggression, dominance, risk proneness, feeding/foraging activity. And as such, competition associated with these behavioral differences may influence survival and the selective environments experienced by wild fish. Given the clear overlap in habitat use-, and evidence for density dependence, these seem most likely to take place in freshwater during the juvenile stage (Table 1D). This has been illustrated by the work of Fleming et al. (2000), who released sexually mature farm and wild Atlantic salmon into the River Imsa in Norway. Despite the farm fish achieving less than one-third of the breeding success compared to wild fish, there was evidence of resource competition and competitive displacement, as the productivity of the wild fish was depressed by more than 30%. Fleming et al. (2000) concluded that invasions of farm fish have the potential for impacting wild population productivity both via changes to locally adaptive traits as well as reductions in genetic diversity. Skaala et al. (2012) documented similar effects in another natural system in Norway. These authors compared the performance of farm, wild, and hybrid Atlantic salmon and suggested that overlap in diets and competitions can impact

wild productivity, which could reduce genetic variation in wild populations. Supporting this hypothesis, Robertsen et al. (2019) demonstrated that the presence of farmed–wild hybrids reduced the survival of wild half-sibs under semi-natural conditions. There is also clear evidence that escaped farmed salmon can compete for spawning habitats and may superimpose redds on top of those of wild Atlantic salmon (Webb et al. 1991, 1993a,b, Fleming et al. 1996). Such superimposition of redds could affect both spawning time and location of wild fish, as well as the growth and survival of wild offspring. Overall, it seems highly probable that increased competition can result in changes to the selective landscape experienced by wild individuals and in reductions in population size.

3. QUANTIFYING GENETIC EFFECTS OF NON-REPRODUCTIVE ECOLOGICAL INTERACTIONS

The studies reviewed above demonstrate strong potential for non-reproductive genetic interactions to occur in wild populations. However, quantifying these interactions between wild populations and domestic strains remains a major challenge, particularly when hybridization is occurring (i.e. direct genetic interactions). Dramatic increases in DNA sequencing capacity over the last decade present new opportunities for the use of genomic tools to quantify the impacts of net pen aquaculture on wild populations. Non-reproductive genetic interactions represent a special, more complex challenge, and the utility of genetic and genomic tools to resolve these genetic interactions will depend on the route and genomic scale of impact. That said, a large body of literature has been produced in recent years on the use of genetic/genomic tools to quantify both adaptive diversity and neutral diversity and effective population size or changes therein. As such, a clear opportunity exists to apply genetic and genomic methods to quantify these impacts.

3.1. Detecting changes in adaptive diversity

In the context of impacts due to changes in the selective landscape driven by ecological change, genomic change could be associated with a single gene, or many genes (i.e. polygenic). Genetic and genomic tools are increasingly being used to quantify the magnitude of natural selection in the wild (Vitti et al. 2013) and many approaches have been developed (Table 2A). One of the best approaches to quantify

Table 2. Summary of available genetic and genomic methods to evaluate non-reproductive genetic interactions

Method	Comparison	Statistics/tests	Reference
(A) Changes in adaptive diversity			
Time-series analysis	Changes in allele frequency Changes in allele frequency	Empirical likelihood ratio test (ELR) Frequency increment test (FIT)	Feder et al. (2014) Feder et al. (2014)
Temporal comparisons, pre- vs. post-impact	Changes in allele frequencies	Principal component analysis, outlier detection, genetic differentiation (F_{ST})	Bitter et al. (2019)
Temporal comparisons, pre- vs. post-impact	Changes in allele frequencies in response to size-selection gradients	% polymorphism, nucleotide diversity, & allele frequency shifts (controls vs. experimental samples)	Therkildsen et al. (2019)
Domestic ancestry estimation under different stocking intensities	Relationship between domestic ancestry and recombination rate at different genomic scales		Leitwein et al. (2019)
Outlier detection	Locus-specific comparison of posterior probabilities of models with and without selection	F_{ST} coefficient & and Bayes factor scores	Foll & Gaggiotti (2008)
Outlier detection	Tests of neutrality based on principal components analysis	Mahalanobis distance	Luu et al. (2017)
Impacted vs. non-impacted	Signatures of selection that covary with environmental stressor (e.g. pollution)	F_{ST} , population branch statistic, differences in nucleotide diversity along 20-kilobase sliding window	Oziolor et al. (2019)
Impacted vs. non-impacted	Signatures of selection associated with environmental stressor	F_{ST} outlier (FDIST2)	Dayan et al. (2019)
Genome-wide association studies	Polygenic associations with population decline involving genomic regions related to metabolism, developmental & physiological processes	Change in μ (signature of selective sweeps) between declining and non-declining population status of Atlantic salmon; Redundancy analysis (RDA) for detection of outliers, polygenic risk scores	Lehnert et al. (2019)
Soft selective sweeps	Identification of new alleles to intermediate frequency against a background of unusually long haplotypes of low nucleotide diversity	Integrated haplotype scores (iHS)	Voight et al. (2006)
Soft selective sweeps	Identification of selected alleles nearing or having achieved fixation in one population but that remains polymorphic in the wider group of populations.	Extended cross population haplotype homozygosity (XP-EHH)	Sabeti et al. (2007)
Soft selective sweeps	Detection of positive selection acting to increase haplotype homozygosity; combines distribution of fragment lengths between mutations and number of segregating sites between all pairs of chromosomes; ratio of haplotype homozygosity for derived & ancestral alleles.	Number of segregating sites by length (nSL); similar to iHS but (1) a genetic map is not required and (2) more robust to recombination and/or mutation rate variation	Ferrer-Admetlla et al. (2014)

Table continued on next page

Table 2 (continued)

Method	Comparison	Statistics/Tests	Reference
Machine learning	Correlates of habitat/environmental variables with observed genetic structure	Random Forest; PCA loadings; outlier detection	Sylvester et al. (2018a)
Machine learning	Detection of loci of small phenotypic effect on a key life-history variable (e.g. run timing) across multiple populations	Random forest; outlier detection; PCA	Brieuc et al. (2015)
(B) Changes in neutral diversity or effective population size			
Effective population size	Single-sample method based on linkage disequilibrium to estimate effective populations size	Contemporary N_e	Waples & Do (2010), Waples et al. (2016)
Effective population size	Single-sample method to estimate changes in contemporary N_e by comparing linkage disequilibrium estimates with recombination rates estimated from physical linkage or genomic position	Contemporary N_e estimates at various times in the past	Hollenbeck et al. (2016)
Effective population size	Application of Hollenbeck et al. (2016) for range-wide populations of Atlantic salmon and associations of genomic regions to decline status	Contemporary N_e estimates over time	Lehnert et al. (2019)

the presence of selection is either the comparison of representative pre- and post-impact genetic samples in the absence of hybridization or the examination of situations with the capacity to quantify and correct for signatures of recent or current hybridization (Leitwein et al. 2019). For time series analysis of changes in allele frequency associated with selection, differentiation measures such as the fixation index (F_{ST}) are commonly used, and several tests have been recently proposed using bi-allelic loci, including the empirical likelihood ratio test (ELRT) and the frequency increment test (FIT) (Feder et al. 2014). Recent temporal comparisons of natural selection in ecological, climate adaptation, and fishery-impact studies have revealed detectable increases in genomic differentiation over even short timeframes (e.g. 1 to 4 generations; Bitter et al. 2019, Leitwein et al. 2019, Therkildsen et al. 2019), indicating genomic tools show high power to detect changes in natural selection when recent pre-impact baselines are available. Where replicate temporal comparisons across sites can be made, this may allow uncovering parallel patterns and non-parallel signatures of adaptation. Knowledge of pre-impact genomic variation across replicates could quantify both the source and magnitude of non-reproductive genetic impacts; sites with similar starting genomic variation are more likely to show parallel responses, unless source or strength of selection differs.

In the absence of pre-impact samples, traditional tests for the presence of outliers (e.g. Foll & Gaggiotti 2008, Luu et al. 2017), trait associations, or selective sweeps (e.g. Nielsen 2005) may be applied using genome-wide polymorphism data, though the ability to attribute a given impact to these loci may be problematic. Similar to pre- and post-impact temporal comparisons, tests for genomic differentiation using metrics such as F_{ST} between sites with differing levels of exposure to stressors can be used to detect the magnitude and location of genomic change between these impacted and pristine sites (e.g. Dayan et al. 2019, Oziolor et al. 2019). Genome-wide association and genome-environment association methods also show promise in measuring aquaculture impacts, but have traditionally been used to estimate correlations between genomic variants and trait or environmental variation (Rellstab et al. 2015, Santure & Garant 2018). A recent genomic study by Lehnert et al. (2019) instead used

decline status as the trait in genome-wide association and uncovered polygenic associations with population decline and variation in immune and developmental genes. This approach could be further refined in future studies by incorporating continuous measures of aquaculture exposure such as magnitude of escape, site proximity, or pathogen load.

Rapid evolutionary change is often associated with selection on standing genetic variation ('soft sweeps') rather than new mutations (Messer et al. 2016, Hermisson & Pennings 2017). Methods that utilize differences in frequency and diversity of haplotypes such as integrated haplotype score (iHS; Voight et al. 2006), extended cross population haplotype homozygosity (XP-EHH; Sabeti et al. 2007), and number of segregating sites by length (nSL; Ferrer-Admetlla et al. 2014) can identify signatures of soft selective sweeps. Identification of sweep signatures that are exclusive to aquaculture-impacted populations may provide an additional way of both validating genomic changes induced by non-reproductive genetic impacts and uncovering implicated target genes. Machine learning approaches have also shown promise in identifying subtle signatures of environment (Sylvester et al. 2018a), trait associations (Brieuc et al. 2015), and selective sweep signatures (Kern & Schrider 2018). These provide additional research areas for future studies into the genetic impacts of aquaculture exposure that may not be detected by traditional statistical approaches. Lastly, gene ontology (Rivals et al. 2007) and gene set (Daub et al. 2017) enrichment methods can be used to characterize functional impacts and parallel responses at biological levels above changes at individual genes (Jacobs et al. 2020) and can help clarify potential targets of selection from aquaculture interactions.

3.2. Detecting changes in neutral diversity or effective population size

Genomic approaches can also be applied in the context of resolving a loss of diversity due to demographic declines associated with non-reproductive genetic impacts and applied to quantify genome-wide trends in diversity over time or estimate trends in the effective population size (Table 2B; see Waples & Do 2010). Large genomic datasets offer new opportunities for enhanced estimates of effective population size (Waples et al. 2016) as well as retrospective estimates of changes in effective population size over time (e.g. Hollenbeck et al. 2016). For example, B. Watson (pers. comm.) evaluated the performance of

estimates of effective population size (N_e) using large genomic datasets to assess and approximate population declines. This was used to establish a genomic baseline to detect non-reproductive genetic interactions in southern Newfoundland Atlantic salmon populations following the use of largely sterile Atlantic salmon in aquaculture. Their results suggest that large genomic datasets (≥ 1000 SNPs) were able to detect population declines significantly earlier, and with increased accuracy, than small genetic or genomic datasets (25 microsatellites or 100 SNPs). However, monitoring using effective size requires samples from multiple time points, which is not always possible. As an alternative, Hollenbeck et al. (2016) present a method that uses linkage information to bin loci by rates of recombination and reconstruct trends in N_e decades into the past. Lehnert et al. (2019) applied this method to Atlantic salmon across the North Atlantic and estimated that 60% of all populations have declined in recent decades. Finally, molecular approaches to mark-recapture abundance estimation (i.e. CKMR, Bravington et al. 2016) also offer the potential to quantify changes in population size over time and have been used in marine and freshwater fish species (Bravington et al. 2016, Waples et al. 2018, Ruzzante et al. 2019). Such approaches could be used to quantify population trends in effective size in the absence of assessment data and monitor for ecological and non-reproductive genetic interactions in future.

4. CONCLUSIONS

Ultimately, despite an abundance of relevant and informative research, the relative importance of hybridization and non-reproductive genetic interactions between domestic individuals and wild populations remains largely unresolved. Nonetheless, the literature suggests that ecological interactions arising from salmon aquaculture have the realistic potential to result in substantial genetic change in wild salmon populations, as well as other species. It is worth noting that, at present, there is a significant knowledge gap regarding the non-reproductive genetic impacts of increased predation or competition due to salmon aquaculture on wild populations. Fortunately, recent advances in genetic and genomic methods present a new scope for quantifying these impacts. However, careful experimental design and pre-impact comparisons will in most cases be needed to accurately attribute any genetic change to non-reproductive genetic interactions with salmon aquaculture activities.

Future research should explore the sensitivities and power of these approaches to detect changes in genetic diversity and character over time. Given that both reproductive and non-reproductive interactions co-occur within the native range of Atlantic salmon, there may be benefit to focus studies on instances where interbreeding is unlikely or impossible. This could involve the study of ecological and genetic impacts in other species such as Pacific salmon species or in Atlantic salmon in regions where sterility is employed as a containment or mitigation measure. Alternatively, genomic approaches could potentially be used to disentangle reproductive and non-reproductive interactions from indirect interactions based on the identification of hybrids, introgressed ancestry blocks, or signatures of selection.

Our review suggests that non-reproductive genetic interactions represent both a broad reaching and largely unresolved source of genetic impact on wild populations exposed to Atlantic salmon aquaculture activities. Thus, further study is urgently needed to support an integrated understanding of aquaculture–ecosystem interactions, their implications for ecosystem stability, and the identification of potential pathways of effect. This information will be essential to the development of potential mitigation and management strategies.

Acknowledgements. This review was conducted as part of the ICES Working Group on Genetic Applications to Fisheries and Aquaculture between 2018 and 2020. Funding was provided through the Fisheries and Oceans Program for Aquaculture Regulatory Research. This work also benefited greatly from a 3-year Canada-EU Galway Statement for the Transatlantic Ocean Research Alliance Working Group on modelling genetic interactions among wild and farm escaped Atlantic salmon in the North Atlantic. The authors thank Brian Dempson and several anonymous reviewers for comments on this manuscript.

LITERATURE CITED

- Bitter MC, Kapsenberg L, Gattuso JP, Pfister CA (2019) Standing genetic variation fuels rapid adaptation to ocean acidification. *Nat Commun* 10:5821
- Bjørn PA, Finstad B, Kristoffersen R (2001) Salmon lice infection of wild sea trout and Arctic char in marine and freshwaters: the effects of salmon farms. *Aquacult Res* 32: 947–962
- Bøhn T, Gjelland KØ, Serra-Llinares RM, Finstad B and others (2020) Timing is everything: survival of Atlantic salmon *Salmo salar* postsmolts during events of high salmon lice densities. *J Appl Ecol* 57:1149–1160
- Bolstad GH, Hindar K, Robertsen G, Jonsson B and others (2017) Gene flow from domesticated escapes alters the life history of wild Atlantic salmon. *Nat Ecol Evol* 1:0124
- Børretzen Fjørtoft H, Nilsen F, Besnier F, Espedal PG and others (2020) Aquaculture-driven evolution: distribution of pyrethroid resistance in the salmon louse throughout the North Atlantic in the years 2000–2017. *ICES J Mar Sci* 77:1806–1815
- Bourret V, O'Reilly PT, Carr JW, Berg PR, Bernatchez L (2011) Temporal change in genetic integrity suggests loss of local adaptation in a wild Atlantic salmon (*Salmo salar*) population following introgression by farmed escapees. *Heredity* 106:500–510
- Bradbury IR, Duffy S, Lehnert SJ, Jóhannsson R and others (2020) Model-based evaluation of the genetic impacts of farm-escaped Atlantic salmon on wild populations. *Aquacult Environ Interact* 12:45–59
- Bravington MV, Grewe PM, Davies CR (2016) Absolute abundance of southern bluefin tuna estimated by close-kin mark-recapture. *Nat Commun* 7:13162
- Brieuc MSO, Ono K, Drinan DP, Naish KA (2015) Integration of Random Forest with population-based outlier analyses provides insight on the genomic basis and evolution of run timing in Chinook salmon (*Oncorhynchus tshawytscha*). *Mol Ecol* 24:2729–2746
- Bürger R, Lynch M (1995) Evolution and extinction in a changing environment: a quantitative genetic analysis. *Evolution* 49:151–163
- Callier MD, Byron CJ, Bengtson DA, Cranford PJ and others (2018) Attraction and repulsion of mobile wild organisms to finfish and shellfish aquaculture: a review. *Rev Aquacult* 10:924–949
- Connors BM, Krkošek M, Ford J, Dill LM (2010) Coho salmon productivity in relation to salmon lice from infected prey and salmon farms. *J Appl Ecol* 47:1372–1377
- Consuegra S, de Eyto E, McGinnity P, Stet RJM, Jordan WC (2011) Contrasting responses to selection in class I and class II α major histocompatibility-linked markers in salmon. *Heredity* 107:143
- Correa K, Lhorente JP, Bassini L, López ME and others (2017) Genome wide association study for resistance to *Caligus rogercresseyi* in Atlantic salmon (*Salmo salar* L.) using a 50K SNP genotyping array. *Aquaculture* 472:61–65
- Coughlan J, McGinnity P, O'Farrell B, Dillane E and others (2006) Temporal variation in an immune response gene (MHC I) in anadromous *Salmo trutta* in an Irish river before and during aquaculture activities. *ICES J Mar Sci* 63:1248–1255
- Cross TF, King J (1983) Genetic effects of hatchery rearing in Atlantic salmon. *Aquaculture* 33:33–40
- Daub JT, Moretti S, Davydov II, Excoffier L, Robinson-Rechavi M (2017) Detection of pathways affected by positive selection in primate lineages ancestral to humans. *Mol Biol Evol* 34:1391–1402
- Dayan DI, Du X, Baris TZ, Wagner DN, Crawford DL, Oleksiak MF (2019) Population genomics of rapid evolution in natural populations: polygenic selection in response to power station thermal effluents. *BMC Evol Biol* 19:61
- de Eyto E, McGinnity P, Consuegra S, Coughlan J and others (2007) Natural selection acts on Atlantic salmon major histocompatibility (MH) variability in the wild. *Proc R Soc B* 274:861–869
- de Eyto E, McGinnity P, Huisman J, Coughlan J and others (2011) Varying disease-mediated selection at different life-history stages of Atlantic salmon in fresh water. *Evol Appl* 4:749–762
- Denholm SJ, Hoyle AS, Shinn AP, Paladini G, Taylor NGH, Norman RA (2016) Predicting the potential for natural recovery of Atlantic salmon (*Salmo salar* L.) populations

- following the introduction of *Gyrodactylus salaris* Malmberg, 1957 (Monogenea). PLOS ONE 11:e0169168
- DFO (2016) Proposed use of European-strain triploid Atlantic salmon in Marine cage aquaculture in Placentia Bay, NL. DFO Can Sci Advis Sec Sci Resp 2016/034. <https://waves-vagues.dfo-mpo.gc.ca/Library/40621248.pdf>
- DFO (2018) Review of the environmental impact statement for the Placentia Bay Atlantic salmon aquaculture project. DFO Can Sci Advis Sec Sci Resp 2018. <https://waves-vagues.dfo-mpo.gc.ca/Library/40738899.pdf>
- ✦ Dionne M, Miller KM, Dodson JJ, Caron F, Bernatchez L (2007) Clinal variation in MHC diversity with temperature: evidence for the role of host-pathogen interaction on local adaptation in Atlantic salmon. *Evolution* 61: 2154–2164
- ✦ Dionne M, Miller KM, Dodson JJ, Bernatchez L (2009) MHC standing genetic variation and pathogen resistance in wild Atlantic salmon. *Philos Trans R Soc B* 364: 1555–1565
- ✦ Diserud OH, Fiske P, Sægrov H, Urdal K and others (2019) Escaped farmed Atlantic salmon in Norwegian rivers during 1989–2013. *ICES J Mar Sci* 76:1140–1150
- ✦ Feder AF, Kryazhinskiy S, Plotkin JB (2014) Identifying signatures of selection in genetic time series. *Genetics* 196: 509–522
- ✦ Ferrer-Admetlla A, Liang M, Korneliussen T, Nielsen R (2014) On detecting incomplete soft or hard selective sweeps using haplotype structure. *Mol Biol Evol* 31:1275–1291
- ✦ Fjellidal PG, Hansen TJ, Karlsen Ø, Wright DW (2019) Effects of laboratory salmon louse infection on Arctic char osmoregulation, growth and survival. *Conserv Physiol* 7:coz072
- ✦ Fleming IA, Jonsson B, Gross MR (1994) Phenotypic divergence of sea-ranched, farmed, and wild salmon. *Can J Fish Aquat Sci* 51:2808–2824
- ✦ Fleming IA, Jonsson B, Gross MR, Lamberg A (1996) An experimental study of the reproductive behaviour and success of farmed and wild Atlantic salmon (*Salmo salar*). *J Appl Ecol* 33:893–905
- ✦ Fleming IA, Hindar K, Mjølnerød IB, Jonsson B, Balstad T, Lamberg A (2000) Lifetime success and interactions of farm salmon invading a native population. *Proc R Soc B* 267:1517–1524
- ✦ Foll M, Gaggiotti O (2008) A Genome-scan method to identify selected loci appropriate for both dominant and codominant markers: a Bayesian perspective. *Genetics* 180:977–993
- ✦ Ford JS, Myers RA (2008) A global assessment of salmon aquaculture impacts on wild salmonids. *PLOS Biol* 6: e33
- ✦ Forseth T, Barlaup BT, Finstad B, Fiske P and others (2017) The major threats to Atlantic salmon in Norway. *ICES J Mar Sci* 74:1496–1513
- ✦ Garcia de Leaniz C, Fleming IA, Einum S, Verspoor E and others (2007) A critical review of adaptive genetic variation in Atlantic salmon: implications for conservation. *Biol Rev Camb Philos Soc* 82:173–211
- ✦ Garseth ÅH, Ekrem T, Biering E (2013) Phylogenetic evidence of long distance dispersal and transmission of piscine reovirus (PRV) between farmed and wild Atlantic salmon. *PLOS ONE* 8:e82202
- ✦ Gilbey J, Verspoor E, Mo TA, Sterud E and others (2006) Identification of genetic markers associated with *Gyrodactylus salaris* resistance in Atlantic salmon (*Salmo salar*). *Dis Aquat Org* 71:119–129
- ✦ Glover KA, Pertoldi C, Besnier F, Wennevik V, Kent M, Skaala Ø (2013) Atlantic salmon populations invaded by farmed escapees: quantifying genetic introgression with a Bayesian approach and SNPs. *BMC Genet* 14:74
- ✦ Glover KA, Solberg MF, McGinnity P, Hindar K and others (2017) Half a century of genetic interaction between farmed and wild Atlantic salmon: status of knowledge and unanswered questions. *Fish Fish* 18:890–927
- ✦ Gomulkiewicz R, Holt RD (1995) When does evolution by natural selection prevent extinction? *Evolution* 49:201–207
- ✦ Hamoutene D, Cote D, Marshall K, Donnet S and others (2018) Spatial and temporal distribution of farmed Atlantic salmon after experimental release from sea cage sites in Newfoundland (Canada). *Aquaculture* 492:147–156
- ✦ Handeland SO, Björnsson BT, Arnesen AM, Stefansson SO (2003) Seawater adaptation and growth of post-smolt Atlantic salmon (*Salmo salar*) of wild and farmed strains. *Aquaculture* 220:367–384
- ✦ Hermisson J, Pennings PS (2017) Soft sweeps and beyond: understanding the patterns and probabilities of selection footprints under rapid adaptation. *Methods Ecol Evol* 8: 700–716
- ✦ Hollenbeck CM, Portnoy DS, Gold JR (2016) A method for detecting recent changes in contemporary effective population size from linkage disequilibrium at linked and unlinked loci. *Heredity* 117:207
- ✦ Jacobs A, Carruthers M, Yurchenko A, Gordeeva NV and others (2020) Parallelism in eco-morphology and gene expression despite variable evolutionary and genomic backgrounds in a Holarctic fish. *PLOS Genet* 16:e1008658
- ✦ Johnsen BO, Jensen AJ (1991) The *Gyrodactylus* story in Norway. *Aquaculture* 98:289–302
- ✦ Johnsen BO, Jensen AJ (1994) The spread of furunculosis in salmonids in Norwegian rivers. *J Fish Biol* 45:47–55
- ✦ Karbowski CM, Finstad B, Karbowski N, Hedger RD (2019) Sea lice in Iceland: assessing the status and current implications for aquaculture and wild salmonids. *Aquacult Environ Interact* 11:149–160
- ✦ Karlsson S, Moen T, Lien S, Glover KA, Hindar K (2011) Generic genetic differences between farmed and wild Atlantic salmon identified from a 7K SNP-chip. *Mol Ecol Resour* 11(Suppl 1):247–253
- ✦ Karlsson S, Diserud OH, Fiske P, Hindar K (2016) Widespread genetic introgression of escaped farmed Atlantic salmon in wild salmon populations. *ICES J Mar Sci* 73: 2488–2498
- Karlsson S, Bolstad GH, Hansen H, Jansen PA, Moen T, Noble LR (2020) The potential for evolution of resistance to *Gyrodactylus salaris* in Norwegian Atlantic salmon. NINA Report 1812, Norwegian Institute for Nature Research, Trondheim
- ✦ Kennedy GJA, Greer JE (1988) Predation by cormorants *Phalacrocorax carbo* (L.), on an Irish river. *Aquacult Fish Manage* 19:159–170
- ✦ Kern AD, Schrider DR (2018) diploS/HIC: an updated approach to classifying selective sweeps. *G3 (Bethesda)* 8: 1959–1970
- ✦ Keyser F, Wringe BF, Jeffery NW, Dempson JB, Duffy S, Bradbury IR (2018) Predicting the impacts of escaped farmed Atlantic salmon on wild salmon populations. *Can J Fish Aquat Sci* 75:506–512
- ✦ Kirkpatrick M, Barton NH (1997) Evolution of species' range. *Am Nat* 150:1–23
- ✦ Kjærner-Semb E, Ayllon F, Furmanek T, Wennevik V and others (2016) Atlantic salmon populations reveal adap-

- tive divergence of immune related genes — a duplicated genome under selection. *BMC Genomics* 17:610
- ✦ Krkošek M, Lewis MA, Volpe JP (2005) Transmission dynamics of parasitic sea lice from farm to wild salmon. *Proc Biol Sci* 272:689–696
- ✦ Krkošek M, Ford JS, Morton A, Lele S, Myers RA, Lewis MA (2007) Declining wild salmon populations in relation to parasites from farm salmon. *Science* 318:1772–1775
- ✦ Krkošek M, Connors BM, Morton A, Lewis MA, Dill LM, Hilborn R (2011a) Effects of parasites from salmon farms on productivity of wild salmon. *Proc Natl Acad Sci USA* 108:14700–14704
- ✦ Krkošek M, Connors BM, Ford H, Peacock S and others (2011b) Fish farms, parasites, and predators: implications for salmon population dynamics. *Ecol Appl* 21:897–914
- ✦ Lehnert SJ, Kess T, Bentzen P, Kent MP and others (2019) Genomic signatures and correlates of widespread population declines in salmon. *Nat Commun* 10:2996
- ✦ Leitwein M, Cayuela H, Ferchaud AL, Normandeau É, Gagnaire PA, Bernatchez L (2019) The role of recombination on genome-wide patterns of local ancestry exemplified by supplemented brook charr populations. *Mol Ecol* 28:4755–4769
- Luu K, Bazin E, Blum MGB (2017) pcadapt: an R package to perform genome scans for selection based on principal component analysis. *Mol Ecol Resour* 17:67–77
- ✦ Madhun AS, Karlsbakk E, Isachsen CH, Omdal LM and others (2015) Potential disease interaction reinforced: double-virus-infected escaped farmed Atlantic salmon, *Salmo salar* L., recaptured in a nearby river. *J Fish Dis* 38:209–219
- ✦ Madhun AS, Isachsen CH, Omdal LM, Einen ACB and others (2018) Prevalence of piscine orthoreovirus and salmonid alphavirus in sea-caught returning adult Atlantic salmon (*Salmo salar* L.) in northern Norway. *J Fish Dis* 41:797–803
- ✦ McGinnity P, Prodöhl P, Ferguson A, Hynes R and others (2003) Fitness reduction and potential extinction of wild populations of Atlantic salmon, *Salmo salar*, as a result of interactions with escaped farm salmon. *Proc R Soc B* 270:2443–2450
- ✦ Messer PW, Ellner SP, Hairston NG Jr (2016) Can population genetics adapt to rapid evolution? *Trends Genet* 32:408–418
- ✦ Miller KM, Li S, Kaukinen KH, Ginther N and others (2011) Genomic signatures predict migration and spawning failure in wild Canadian salmon. *Science* 331:214–217
- ✦ Morris MRJ, Fraser DJ, Heggelin AJ, Whoriskey FG, Carr JW, O'Neil SF, Hutchings JA (2008) Prevalence and recurrence of escaped farmed Atlantic salmon (*Salmo salar*) in eastern North American rivers. *Can J Fish Aquat Sci* 65:2807–2826
- ✦ Morton A, Routledge R, Hrushowy S, Kibenge M, Kibenge F (2017) The effect of exposure to farmed salmon on piscine orthoreovirus infection and fitness in wild Pacific salmon in British Columbia, Canada. *PLOS ONE* 12:e0188793
- ✦ Nekouei O, Vanderstichel R, Thakur K, Arriagada G and others (2018) Association between sea lice (*Lepeophtheirus salmonis*) infestation on Atlantic salmon farms and wild Pacific salmon in Muchalat Inlet, Canada. *Sci Rep* 8:4023
- ✦ Nielsen R (2005) Molecular signatures of natural selection. *Annu Rev Genet* 39:197–218
- ✦ Nylund A, Brattespe J, Plarre H, Kambestad M, Karlsen M (2019) Wild and farmed salmon (*Salmo salar*) as reservoirs for infectious salmon anaemia virus, and the importance of horizontal- and vertical transmission. *PLOS ONE* 14:e0215478
- ✦ Oziolor EM, Reid NM, Yair S, Lee KM and others (2019) Adaptive introgression enables evolutionary rescue from extreme environmental pollution. *Science* 364:455–457
- ✦ Peacock SJ, Krkošek M, Proboyszcz S, Orr C, Lewis MA (2013) Cessation of a salmon decline with control of parasites. *Ecol Appl* 23:606–620
- ✦ Price MH, Proboyszcz SL, Routledge RD, Gottesfeld AS, Orr C, Reynolds JD (2011) Sea louse infection of juvenile sockeye salmon in relation to marine salmon farms on Canada's west coast. *PLOS ONE* 6:e16851
- ✦ Pritchard VL, Mäkinen H, Vähä JP, Erkinaro J, Orell P, Primmer CR (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
- ✦ Rellstab C, Gugerli F, Eckert AJ, Hancock AM, Holderegger R (2015) A practical guide to environmental association analysis in landscape genomics. *Mol Ecol* 24:4348–4370
- ✦ Rivals I, Personnaz L, Taing L, Potier MC (2007) Enrichment or depletion of a GO category within a class of genes: which test? *Bioinformatics* 23:401–407
- ✦ Robertsen G, Reid D, Einum S, Aronsen T and others (2019) Can variation in standard metabolic rate explain context-dependent performance of farmed Atlantic salmon offspring? *Ecol Evol* 9:212–222
- ✦ Robledo D, Gutiérrez AP, Barría A, Lhorente JP, Houston RD, Yáñez JM (2019) Discovery and functional annotation of quantitative trait loci affecting resistance to sea lice in Atlantic salmon. *Front Genet* 10:56
- ✦ Ruzzante DE, McCracken GR, Førland B, MacMillan J and others (2019) Validation of close-kin mark-recapture (CKMR) methods for estimating population abundance. *Methods Ecol Evol* 10:1445–1453
- ✦ Sabeti PC, Varilly P, Fry B, Lohmueller J and others (2007) Genome-wide detection and characterization of positive selection in human populations. *Nature* 449:913–918
- ✦ Santure AW, Garant D (2018) Wild GWAS — association mapping in natural populations. *Mol Ecol Resour* 18:729–738
- ✦ Serra-Llinares RM, Bøhn T, Karlsen Ø, Nilsen R and others (2020) Impacts of salmon lice on mortality, marine migration distance and premature return in sea trout. *Mar Ecol Prog Ser* 635:151–168
- ✦ Shephard S, Gargan P (2017) Quantifying the contribution of sea lice from aquaculture to declining annual returns in a wild Atlantic salmon population. *Aquacult Environ Interact* 9:181–192
- ✦ Skaala Ø, Glover KA, Barlaup BT, Svåsand T, Besnier F, Hansen MM, Borgstrøm R (2012) Performance of farmed, hybrid, and wild Atlantic salmon (*Salmo salar*) families in a natural river environment. *Can J Fish Aquat Sci* 69:1994–2006
- ✦ Skilbrei OT, Heino M, Svåsand T (2015) Using simulated escape events to assess the annual numbers and destinies of escaped farmed Atlantic salmon of different life stages from farm sites in Norway. *ICES J Mar Sci* 72:670–685
- ✦ Sylvester EVA, Beiko RG, Bentzen P, Paterson I and others (2018a) Environmental extremes drive population structure at the northern range limit of Atlantic salmon in North America. *Mol Ecol* 27:4026–4040
- ✦ Sylvester EVA, Wringe BF, Duffy SJ, Hamilton LC, Fleming IA, Bradbury IR (2018b) Migration effort and wild population size influence the prevalence of hybridization

- between escaped farmed and wild Atlantic salmon. *Aquacult Environ Interact* 10:401–411
- ✦ Therkildsen NO, Wilder AP, Conover DO, Munch SB, Baumann H, Palumbi SR (2019) Contrasting genomic shifts underlie parallel phenotypic evolution in response to fishing. *Science* 365:487–490
- Thorstad EB, Finstad B (2018) Impacts of salmon lice emanating from salmon farms on wild Atlantic salmon and sea trout. NINA Report 1449, Norwegian Institute for Nature Research, Trondheim
- ✦ Tonteri A, Vasemägi A, Lumme J, Primmer CR (2010) Beyond MHC: signals of elevated selection pressure in Atlantic salmon (*Salmo salar*) immune-relevant loci. *Mol Ecol* 19:1273–1282
- ✦ Tsai HY, Hamilton A, Tinch AE, Guy DR and others (2016) Genomic prediction of host resistance to sea lice in farmed Atlantic salmon populations. *Genet Sel Evol* 48:47
- Verspoor E, McGinnity P, Bradbury I, Glebe B (2015) The potential direct and indirect genetic consequences for native Newfoundland Atlantic salmon from interbreeding with European-origin farm escapes. DFO Can Sci Advis Sec Res Document 2015/030:viii + 36. <https://waves-vagues.dfo-mpo.gc.ca/Library/359696.pdf>
- Vitti JJ, Grossman SR, Sabeti PC (2013) Detecting natural selection in genomic data. *Annu Rev Genet* 47:97–120
- ✦ Voight BF, Kudravalli S, Wen X, Pritchard JK (2006) A map of recent positive selection in the human genome. *PLOS Biol* 4:e72
- ✦ Vollset KW, Krontveit RI, Jansen PA, Finstad B and others (2016) Impacts of parasites on marine survival of Atlantic salmon: a meta-analysis. *Fish Fish* 17:714–730
- ✦ Waples RS, Do C (2010) Linkage disequilibrium estimates of contemporary N_e using highly variable genetic markers: a largely untapped resource for applied conservation and evolution. *Evol Appl* 3:244–262
- ✦ Waples RK, Larson WA, Waples RS (2016) Estimating contemporary effective population size in non-model species using linkage disequilibrium across thousands of loci. *Heredity* 117:233–240
- ✦ Waples RS, Grewe PM, Bravington MW, Hillary R, Feutry P (2018) Robust estimates of a high N_e/N ratio in a top marine predator, southern bluefin tuna. *Sci Adv* 4:eaar7759
- ✦ Webb JH, Hay DW, Cunningham PD, Youngson AF (1991) The spawning behaviour of escaped farmed and wild adult Atlantic salmon (*Salmo salar* L.) in a northern Scottish river. *Aquaculture* 98:97–110
- ✦ Webb JH, McLaren IS, Donaghy MJ, Youngson AF (1993a) Spawning of farmed Atlantic salmon in the second year after their escape. *Aquacult Fish Manage* 24:557–561
- ✦ Webb JH, Youngson AF, Thompson CE, Hay DW, Donaghy MJ, McLaren IS (1993b) Spawning of escaped farmed Atlantic salmon, *Salmo salar* L., in western and northern Scottish rivers: egg deposition by females. *Aquacult Fish Manage* 24:663–670
- ✦ Wringe BF, Jeffery NW, Stanley RRE, Hamilton LC and others (2018) Extensive hybridization following a large escape of domesticated Atlantic salmon in the Northwest Atlantic. *Commun Biol* 1:108
- ✦ Wringe BF, Anderson EC, Jeffery NW, Stanley RRE, Bradbury IR (2019) Development and evaluation of SNP panels for the detection of hybridization between wild and escaped Atlantic salmon (*Salmo salar*) in the West Atlantic. *Can J Fish Aquat Sci* 76:695–704
- ✦ Zueva KJ, Lumme J, Veselov AE, Kent MP, Lien S, Primmer CR (2014) Footprints of directional selection in wild Atlantic salmon populations: evidence for parasite-driven evolution? *PLOS ONE* 9:e91672
- ✦ Zueva KJ, Lumme J, Veselov AE, Kent MP, Primmer CR (2018) Genomic signatures of parasite-driven natural selection in north European Atlantic salmon (*Salmo salar*). *Mar Genomics* 39:26–38

Editorial responsibility: Kevin Glover,
Bergen, Norway

Submitted: June 8, 2020; Accepted: August 31, 2020
Proofs received from author(s): October 12, 2020