

# Genetic improvement technologies to support the sustainable growth of UK aquaculture

Tim Regan<sup>1</sup> , Tim P. Bean<sup>1</sup>, Tim Ellis<sup>2</sup>, Andrew Davie<sup>3</sup>, Stefano Carboni<sup>3</sup>, Herve Migaud<sup>3</sup> and Ross D. Houston<sup>1</sup> 

<sup>1</sup> The Roslin Institute, University of Edinburgh, Roslin, EH25 9RG, UK

<sup>2</sup> Cefas Weymouth Laboratory, Barrack Road, The Nothe, Weymouth, Dorset, DT4 8UB, UK

<sup>3</sup> Institute of Aquaculture, University of Stirling, Stirling, FK9 4LA, UK

## Correspondence

Tim Regan, The Roslin Institute, University of Edinburgh, Roslin EH25 9RG, UK.

Email: tim.regan@roslin.ed.ac.uk

Received 25 July 2020; In Revised form 18 January 2021; accepted 21 February 2021.

## Abstract

While the UK is the fourth largest aquaculture producer in Europe by volume, it is the second largest by value with an annual first sale value of around £1 billion. Over 90% of this value is from Atlantic salmon farmed in Scotland, but other fin-fish and shellfish aquaculture species are important to several UK regions. In this review, we describe the state of the art in UK aquaculture breeding and stock supply, and how innovation in genetics technologies can help achieve the Scottish Government's ambitious target of doubling its aquaculture industry by 2030. Particular attention is given to the four most important UK aquaculture species: Atlantic salmon, rainbow trout, blue mussel and Pacific oyster, and we contrast the highly variable level of selective breeding and genomics technologies used in these sectors. A major factor in the success of Atlantic salmon farming has been large-scale investment in modern breeding programmes, including family selection programmes and genomic selection. This has proven cost-effective at scale, leading to improved production efficiency and reduction of some infectious diseases. We discuss the feasibility of applying similar technologies to the UK shellfish sectors, to ensure consistent and robust spat supply and begin trait selection. Furthermore, we discuss species-specific application of modern breeding technologies in a global context, and the future potential of genomics and genome editing technologies to improve commercially desirable traits. Increased adoption of modern breeding technologies will assist UK aquaculture industries to meet the challenges for sustainable expansion, and remain competitive in a global market.

**Key words:** Atlantic salmon, blue mussel, genome editing, genomics, industry benefits, Pacific oyster, rainbow trout, selective breeding.

## Introduction

Aquaculture is the fastest growing farmed food production sector globally (FAO 2020b) and is an important component of the UK economy. The UK aquaculture industry supports employment in remote rural and coastal areas of the Scottish Highlands and Islands, in addition to deprived urban areas where much processing takes place (Alexander *et al.* 2014; Munro 2019; Munro 2020). The UK is the fourth largest aquaculture producer by volume in Europe (5% of total European production) but is the second largest by value with a production value of over £1 billion in 2018 (FAO 2020a). With its fractal coastline measuring over

31 000 km and stretching from warm temperate to cold temperate zones (Marine Management Organisation 2013), the UK provides abundant access to diverse marine environments, and to extensive freshwater resources. This range of conditions provides opportunities to culture a diversity of species, but also the challenge of identifying species most suited to a given region and environments. An example of successful exploitation of the amenable environment is the west coast of Scotland where sea lochs provide sheltered areas of seawater, ideal for salmon farming (Black & Hughes 2017). In fact, farmed Atlantic salmon alone contribute >90% of UK aquaculture production value (FAO 2020a). Since the first UK farm was established in Scotland

in the late 1960s (Munro *et al.* 1979), salmon farming has become a very successful industry, both nationally and globally. The success of UK salmon farming is attributed to many factors, including technical advances in culture systems, for example recirculation aquaculture systems (RAS) for smolt production, husbandry methods, improved control of the lifecycle to ensure year-long supply, advances in feeds and nutrition, better health management, and domestication and breeding of improved strains. These advances have been facilitated by industry consolidation, economies of scale, vertical integration and international cooperation (Ellis *et al.* 2016).

The early uptake and widespread adoption of well-managed selective breeding programmes have been key to this success for Atlantic salmon, with cumulative improvements in growth performance and traits such as disease resistance (Gjedrem & Rye 2018). However, the level of sophistication of genetic technologies varies hugely between species, and these technologies are both advancing rapidly and becoming more affordable and accessible (Houston *et al.* 2020). Therefore, there is likely to be significant untapped potential to improve other sectors of UK aquaculture production and sustainability via innovation and implementation of genetics and breeding technologies. Uptake of these technologies across species sectors is essential for the UK to remain competitive in a global market, and to tackle some pressing challenges currently facing the industry. This review gives an overview of the current status of the major UK aquaculture species, compares selective breeding strategies used for these species in the UK versus the global state of the art in breeding technologies and outlines current and future challenges, together with technical developments and breeding strategies that can help meet these challenges.

## The state of UK aquaculture

Four species dominate UK aquaculture, together accounting for over 98% of production volume and value: *Salmo salar* (Atlantic salmon), *Mytilus* sp. (blue mussel), *Oncorhynchus mykiss* (rainbow trout) and *Crassostrea gigas* (Pacific oyster) (Table 1). The political, regulatory, media and technical interests of the industry sectors for the main farmed species are represented by separate trade bodies: most salmon production is represented by the Scottish Salmon Producers Organisation (SSPO); The British Trout Association represents 80% of UK trout production; The Shellfish Association of Great Britain is composed of shellfish farmers, fishermen, fishermen associations, processors, commercial traders and retail companies (Carvalho *et al.* 2018). The features of the production systems for each of these four main aquaculture species are discussed below.

### Atlantic salmon (*Salmo salar*)

Atlantic salmon, the UK's biggest food export (FDEA 2020), is by far the most valuable aquaculture species in the UK. The UK is the third largest producer of Atlantic salmon in the world (after Norway and Chile) with almost all of its farms based in Scotland (Black & Hughes 2017). Due to the diverse lifecycle requirements, high feed and capital costs, and time to harvest (Fig. 1), salmon are typically farmed by large multinational companies. A benefit of this structure is that industry investment in research and development is significant, which extends to selective breeding technology. Although over 24 companies are involved in hatchery rearing, smolt production and sea farming of salmon in the UK (Munro 2019), five were responsible for 94% of the total harvest in 2018: Mowi (formerly Marine Harvest), Scottish Sea Farms, The Scottish Salmon Company, Cooke Aquaculture and Grieg Seafood (Mowi 2019).

### Rainbow trout (*Oncorhynchus mykiss*)

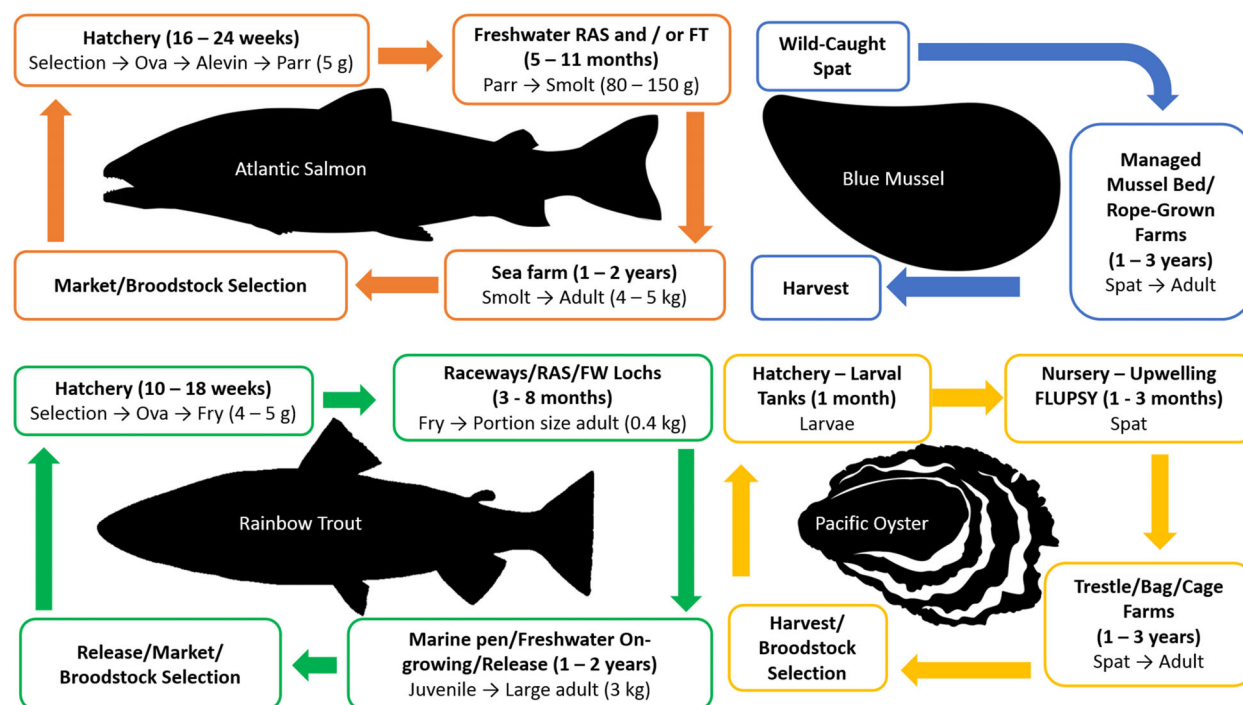
Native to northwest America, rainbow trout were introduced to Britain in the 19<sup>th</sup> century (Nash 2011). Adaptable to many environments, these hardy fish are relatively easy to breed, saltwater tolerant and suitable for cultivation. Although rainbow trout farming expanded rapidly in the UK during the 1980s, it has remained at an almost constant and relatively low level since (Hambrey & Evans 2016). Similar to Atlantic salmon, rainbow trout undergo multiple life stages, each requiring different husbandry and management (Fig. 1). Historically, rainbow trout were harvested at portion size (ca 400 g). However, the price of larger fish is generally higher (Hambrey & Evans 2016), leading to an increase in rainbow trout marine net-pen farms growing fish to a similar harvest size as Atlantic salmon. Over half of the rainbow trout tonnage produced in Scotland is now grown in sea lochs, similar to Atlantic salmon (Munro 2019), making up a quarter of total UK rainbow trout production volume since 2014 (FAO 2020a). In the UK, the majority (90%) of trout farmed for the table and stocking waters for angling are produced by members of the British Trout Association (Robinson 2015), comprising over 50 farming companies mostly in Central and Southern Scotland, Southern England and North Yorkshire. Many of these members are directly affiliated with large multinational breeding companies.

### Blue mussel (*Mytilus* spp.)

Compared with finfish, shellfish aquaculture is relatively small scale across the UK, representing 11% by weight of all marketed species (~22 000 tonnes) and valued at around £36 million (Table 1). However, mussel farming is the

*Reviews in Aquaculture* (2021) **13**, 1958–1985  
© 2021 The Authors. *Reviews in Aquaculture* published by John Wiley & Sons Australia, Ltd.

Species & use of production		Sea/fresh water	Scotland		England		Wales		Northern Ireland		UK total				
			Tonnes	£ value	Tonnes	£ value	Tonnes	£ value	Tonnes	£ value	Tonnes	%	£ value	%	
Finfish – consumption, sport angling & cleaner fish	<i>Salmo salar</i>	Atlantic salmon	170 421	787 837 562											
	<i>Oncorhynchus mykiss</i>	Rainbow trout	7038	18 917 829	5234	16 226 616	216	839 645	639	2 609 358	170 421	82.34%	787 837 562	90.41%	
	<i>Salmonidae</i>	Salmonids – nei	0.8	3236	10	224 957	0.1	1847	449	2 968 590	460	0.22%	3 198 630	0.37%	
	<i>Salmo trutta</i>	Brown trout	42	119 743	229	1 707 512	11	82 181			282	0.14%	1 909 436	0.22%	
	<i>Dicentrarchus labrax</i>	European seabass					84	376 500			84	0.04%	376 500	0.04%	
	<i>Oreochromis niloticus</i>	Nile tilapia			45	158 795					45	0.02%	158 795	0.02%	
	<i>Osteichthyes</i>	Marine fish nei	41	504 900			0				41	0.02%	504 900	0.06%	
	<i>Hippoglossus hippoglossus</i>	Atlantic halibut	30	263 164							30	0.01%	263 164	0.03%	
	<i>Salvelinus alpinus</i>	Arctic char			12	64 803					12	0.01%	64 803	0.01%	
	<i>Cyprinus carpio</i>	Common carp (inc. hybrids)			5	74 298					5	<0.01%	74 298	0.01%	
Finfish – coarse angling	<i>Cyclopterus lumpus</i>	Lumpfish	2	NA							2	<0.01%	NA		
	<i>Labrus bergylla</i>	Balkan wrasse	0.54	NA							1	<0.01%	NA	<0.01%	
	<i>Osteichthyes</i>	Freshwater fish nei			0.2	2438	0.01	22	0.02	283	0.2	<0.01%	2742	<0.01%	
	<i>Cyprinus carpio</i>	Common carp (inc. hybrids)			160	2 325 343			0.1	1148	160	0.08%	2 326 491	0.27%	
	<i>Osteichthyes</i>	Freshwater fish nei			25	529 377	0.04	609			25	0.01%	529 986	0.06%	
	Finfish total	<i>Mytilidae</i>	Blue mussel spp.	177 574	807 646 433	5720	21 314 139	312	1 300 804	1088	5 579 380	184 694	89.24%	835 840 756	95.92%
				7425	9 023 706	1979	3 116 287	5295	8 593 765	3113	3 723 298	17 811	8.61%	24 457 056	2.81%
				274	1 278 792	956	2 305 744	15	34 233	631	1 811 488	1876	0.91%	5 430 257	0.62%
				17	123 750	12	54 008					29	0.01%	177 758	0.02%
				5	66 764							5	<0.01%	66 764	0.01%
Crustaceans- consumption	<i>Aequipecten opercularis</i>	Queen scallop	4	10 750							4	<0.01%	10 750	<0.01%	
			Whiteleg shrimp												
Shellfish total	<i>Litopenaeus vannamei</i>	185 298	5496	10 887 509	5309	8 627 999	3745	5 536 614	22 274	11%	35 555 882	4.1%			
			11 216	32 201 648	5621	9 928 802	4833	11 115 994	206 968	100%	871 396 638	100%			



**Figure 1** Typical rearing life cycle of the top four UK aquaculture species by production volume.

second largest aquaculture sector by production volume in the UK after salmon. UK mussel farming relies entirely on collection of wild spat, either by natural settlement on ropes, or by harvest from natural mussel beds before on-growing in farms (Fig. 1; Adamson *et al.* 2018). The main species cultivated is the native blue mussel, *Mytilus edulis*, although hybridization with Mediterranean (*Mytilus galloprovincialis*) and soft-shelled or foolish (*Mytilus trossulus*) mussels is present in Scottish farms (Dias *et al.* 2009). This latter hybridization has been associated with less desirable commercial traits such as reduced yield and softer shells (Michalek *et al.* 2016). Mussels filter-feed on wild phytoplankton and particulate organic matter without requiring additional feed input. The farming cooperative, the Scottish Shellfish Marketing Group, trades most of Scotland's mussel crop with members throughout Scotland. The Shetland region provides the greatest contribution, accounting for 80% of Scotland's total harvest in 2019 (Munro 2020). All mussel farming in Scotland is on suspended raft and long-line systems, which depend on natural settlement of spat. Elsewhere in the UK, bottom cultivation is also practised. The Menai Strait in Wales was historically the largest mussel producing area in the UK. Following spat collection, mussels are grown on the intertidal bed of the Menai Strait over roughly 10 km<sup>2</sup>. In recent years, production has fallen below that of Scotland, due to a low availability of mussel seed (Addison 2018). Offshore Shellfish Ltd., situated in

Brixham, Devon recently developed the first fully offshore, large-scale, suspended rope grown farm in the UK (Antrobus 2017). At full production capacity, the 15.4 km<sup>2</sup> farm aims to harvest around 10 000 tonnes of mussels each year from its three offshore sites in Lyme Bay. This production is predicted to offset the recent decline in UK mussel production (STECF 2018).

#### Pacific oyster (*Crassostrea gigas*)

Unlike mussel farming, Pacific oyster (also known as the Japanese oyster) farming in the UK is dependent on hatchery sourced oyster spat. A non-native species from the North West Pacific, *C. gigas* constitutes the bulk of hatchery-produced bivalves in the UK at present. Most oyster farmers in the UK are supplied by one of two oyster hatcheries – Guernsey Sea Farms in the Channel Islands and Morecambe Bay Oysters, Lancashire (Adamson *et al.* 2018). Hatcheries in the UK do not currently run selective breeding programmes. The developing larvae are provided with warm-temperate water and algal feeding systems for the first few months of the life cycle. The feed is produced using a combination of indoor high-density microalgal systems and inoculation and blooming of outdoor ponds. The production of large volumes of several microalgae species to fulfil larval and spat nutritional requirements represents the bulk of production costs for UK oyster hatcheries. This

results in a higher seed cost than mussel farming, although oysters reach a higher market value per weight (Table 1). UK growers begin their phase of oyster culture with spat, several months old, which are commonly maintained in bags or in cages elevated from the seabed on trestle structures (Adamson *et al.* 2018). The growing oysters are regularly inspected for damage, graded for size and turned to ensure even access to food and the development of a uniform, deep cupped shell. They are typically on-grown for one to three years before harvest (Fig. 1).

### Atlantic salmon

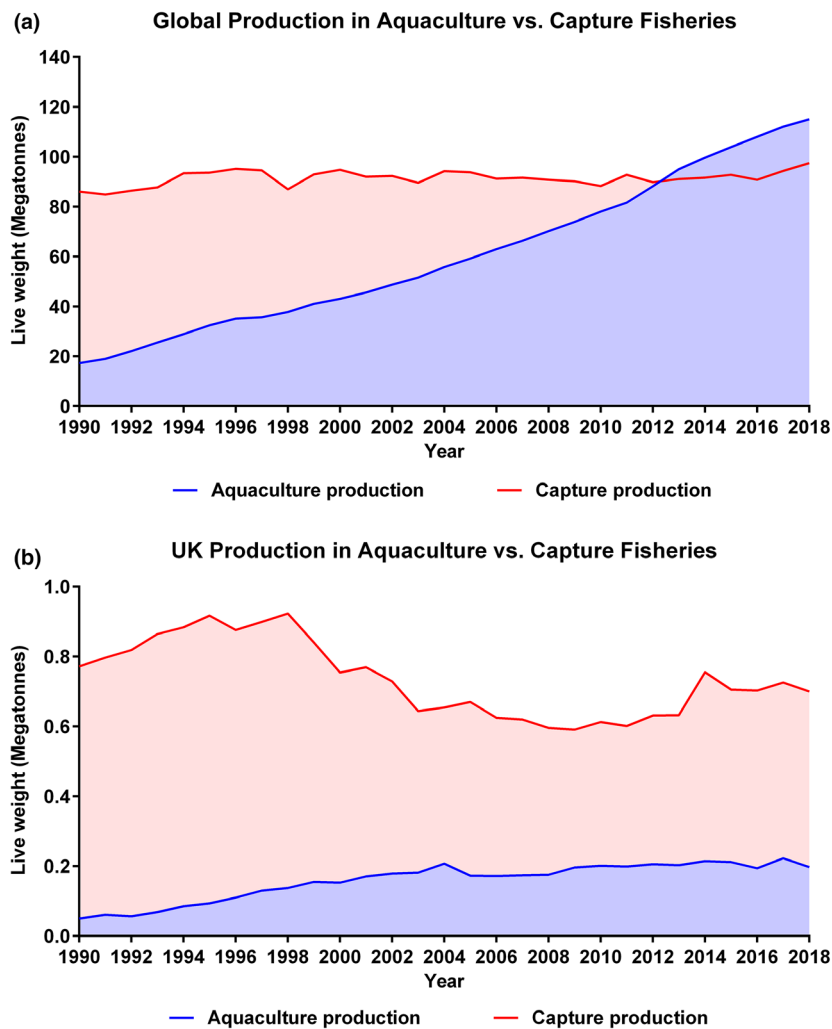
Fertilized ova are typically incubated to eyed stage (from 250 °days) by the breeding company and then transferred to RAS or flow through (FT) salmon hatcheries (usually at 400 °days) where they hatch (500 °days), first feed (from 850 °days) and become parr (from 1500 °days to 5 g). This takes 16–24 weeks. Fish are then on-grown in either RAS or freshwater (inc. loch net-pens) and undergo the parr–smolt transformation also known as smoltification. This process occurs naturally (from August of year 1 to April/May of year 2), or may be controlled for out of season transfer to seawater. Smoltification manipulation is done using standardized photoperiodic regimes (400 °days of simulated short days followed by 400 °days of long days). It takes 5–11 months from parr (5 g) to seawater transfer (80–150 g) depending on smolt cohort produced (usually known as quarter of the year) and systems used (RAS or ambient/FT). Fish are then on-grown in seawater pens, traditionally in sea lochs but also more exposed locations in the Scottish western isles and harvested 1–2 years after marine transfer at a harvest weight of 4–5 kg (Mowi 2019). Rainbow trout: Fertilized ova from selected broodstock are incubated up to eyed stage (from 160 °days) by the breeding company and then transferred to FT hatcheries where they hatch (300 °days), first feed (500 °days) and become fry/fingerlings (1000 °days to 4–5 g). This takes from 10 to 18 weeks. Fry are then on-grown until harvest in either freshwater raceways, tanks, earth ponds or pens in FW lochs. Fish are harvested at 0.4 kg (portion size and restocking) or 3 kg (large) taking between 8 and 24 months, respectively, from fry stage (5 g) (British Trout Association 2019; Munro 2019). Alternatively, fry may be on-grown in marine pens and harvested at 3 kg (Taylor *et al.* 2007). Mussels: Wild spat settle naturally on specialized ropes and are on-grown at sea, commonly on long-line floating systems. Spat can be collected at productive sites and then transferred to other sites to compensate for local shortages. Alternatively, spat are harvested from natural mussel beds for relaying on intertidal beds and moved out to subtidal beds as they grow. Mussels are typically harvested after 1–3 years of

growth (Antrobus 2017; Munro 2020). Pacific oyster: Oyster larvae are reared in tanks at a hatchery where they are kept in warm temperate water and fed with microalgae. Following settlement, 1-month-old oysters are transferred to a nursery, typically in indoor high-density upwelling systems or outdoor using a floating upwelling system (FLUPSY) and upwelled raceways. After 1–3 months of growth in the nursery, oyster spat have developed enough resilience for growing in the sea.

### Current challenges to UK aquaculture

In the past decade, worldwide production from aquaculture has grown rapidly and overtook capture fisheries in 2018 (FAO 2020b). In the UK, however, aquaculture production growth is substantially lower than the global rate (Fig. 2), despite governmental and industry aspirations for expansion and abundant evidence of the contribution to the UK economy and food security (Alexander *et al.* 2014). Development of aquaculture in England, Wales and Northern Ireland has been stagnant or declining for many years (Hambrey & Evans 2016). Plans for the sustainable development of aquaculture in the UK have been published (DEFRA 2015), and aquaculture development within England is currently being addressed within The Seafood 2040 Strategic Framework (Seafish 2015). The Scottish government stated their support to double aquaculture production and economic contribution from £1.8 billion in 2016, to £3.6 billion, and double the number of jobs to 18 000 by 2030 (The Scottish Government 2017). To achieve these ambitious goals, there are a number of challenges that must be addressed. Current obstacles to expansion include concerns about environmental impact, animal welfare, disease outbreaks, social licensing, limitations in site availability and size, oyster and mussel seed supply, public perception and competition with other sectors such as tourism and agriculture. On top of this, climate change is likely to bring stormier coastal environments, less predictable plankton blooms including harmful jellyfish and algae (Moore *et al.* 2008; Carvalho *et al.* 2018), changes in seawater temperature, freshwater availability (rainfall), salinity and acidity. Furthermore, each of these factors is likely to add to the burden of emerging or novel pathogenic diseases and influx of non-native invasive species. These challenges are all interlinked and will require significant innovation and investment to overcome them.

Two factors limiting expansion are site availability with adequate water quality and carrying capacity, and in the case of finfish, environmental impact. However, increased development of offshore or more exposed net-pen facilities, and recirculating aquaculture systems (RAS) on land and semi-contained at sea (Black & Hughes 2017) could overcome many of the issues associated with space



**Figure 2** Production volume of aquaculture versus capture fisheries (a) worldwide and (b) in the UK (FAO 2020a).

requirements, and reduce environmental impact (James & Slaski 2006). Additionally, growing larger size smolt and post-smolt on land to reduce time spent in marine net-pens and enabling more frequent harvests has been further enabled via introduction of RAS (Carvalho *et al.* 2018).

Typically, aquaculture feed (aquafeed) comprises 50–60% of the operating costs for a finfish production business (Black & Hughes 2017). During the last two decades, a trend towards changing the formulation and sourcing of aquafeeds with more sustainable products, using less fish meal (FM) and fish oil (FO) has been a priority (Napier *et al.* 2020). This trend is likely to continue (Kok *et al.* 2020), posing the challenges of maintaining good health and performance of the fish as they adapt to these new diets including antinutritional factors (Glencross *et al.* 2020; Vera *et al.* 2020), and increased competition for land to grow raw ingredients.

Since most farming takes place in open systems and at high stocking densities, pathogens from wild reservoirs of disease are difficult to avoid and can spread rapidly (Yáñez *et al.* 2014a). Infectious disease is estimated to cause a loss of 10% across all cultured aquatic animals, amounting to >10 billion USD annually on a global scale (Evensen 2016). Control of the frequent emergence of previously unknown pathogens is made more difficult by the lack of knowledge surrounding background microbial diversity in farm systems (Stentiford *et al.* 2017). This has led to calls for improved 'pathobiome' definitions, to better understand microbial communities affecting the health of farming environments rather than focusing on single pathogens as disease causing agents (Gilbert *et al.* 2016; Bass *et al.* 2019). In particular, this highlights the need for improving the overall resilience of the farmed animals to better withstand challenges from multiple pathogens.

Selective breeding will have a significant role to play in most of the aforementioned challenges (prevention of disease, adaptation to vegetarian diets, reducing environmental impact and adapting to climate change) (Gjedrem *et al.* 2012). For example, host resistance to many aquaculture pathogens is demonstrably heritable (Ødegård *et al.* 2011; Yáñez *et al.* 2014b; Gjedrem 2015), meaning breeding of stocks with enhanced resistance is feasible. As UK aquaculture expands, selective breeding can also play a key role in the adaptation of a given species or strain to different locations, environments, aquafeeds and rearing techniques, for example RAS, and in improving the overall efficiency of production for a given environmental impact. Selective breeding may also be used synergistically with other approaches to improve aquaculture, such as environmental programming, functional feeds or preventive disease treatments. For example, to reduce cost and increase sustainability, fish can be selectively bred for the ability to thrive on plant-based feeds (Quinton *et al.* 2007; Callet *et al.* 2017).

### Genetic improvement via selective breeding

In order to sustain healthy and productive aquaculture systems, a reliable supply of good quality stocks is required. Compared with terrestrial farm animals and crops, which have typically been domesticated over hundreds or thousands of years, domestication of aquaculture species is in its infancy (Teletchea & Fontaine 2014; Yanez *et al.* 2015). Therefore, there remains a high level of genetic variation in aquaculture species across strains, lines, families and individuals (Abdelrahman *et al.* 2017). Well-managed breeding programmes can maintain and harness this genetic variation to improve production traits in a sustainable manner. For example, finfish breeding programmes have demonstrated that genetic gains in economically important traits of 10–14% per generation can be achieved (Gjedrem *et al.* 2012). These gains are substantially higher than those typically reported in terrestrial livestock (Hickey *et al.* 2017). Traits such as growth and disease resistance have as much as 0.3–0.6 and 0.1–0.5 heritability, respectively (Duncan *et al.* 2013). However, to harness this genetic variation to improve production requires significant investment in selective breeding technology. Approximately 75% of production of the top 10 global finfish, crustacean and mollusc species (Houston *et al.* 2020), and 80% of all European aquaculture production by volume benefit from some form of modern selective breeding programme (Janssen *et al.* 2017). However, a wide range of breeding technologies are used by different sectors, from reliance on wild seed/fish stocks, to family-based selection augmented with use of genomic tools. This variation can clearly be observed in the UK; the mussel industry relies entirely on wild spat for

production, while Atlantic salmon aquaculture employs the highest level of technology, including advanced trait recording and routine use of genomic selection for multiple traits in selection indices. A parallel may be drawn here with Chile, which has similar divergence in the level of breeding technologies used across its salmonid and mussel aquaculture sectors (Lhorente *et al.* 2019; FAO 2020b).

The terminology involved with several aspects of genetic technologies and breeding strategies can appear quite complex. Box 1 provides definitions for the breeding tools and technologies, which we refer to throughout this review. Selective breeding programmes are based on selecting the best individuals to breed from, according to records of traits of interest measured in the broodstock and/or relatives, together with tracking of genetic relationships via pedigree recording or use of genetic markers (typically 100–450) for post-hoc reconstruction of pedigrees (Vandeputte & Haffray 2014). Family-based selection requires the traceability of family origin, and is used to maximize genetic gain without the risk of inbreeding depression, that is avoiding expression of recessive deleterious mutations (Charlesworth & Willis 2009). This method of selection has long been used in salmon breeding (Gjedrem 2010). Individual tagging and tracking is performed using Passive Integrated Transponder (PIT) tags, physical marks, or post hoc parentage assignment with genetic markers. In addition to minimizing inbreeding, tracking of pedigree allows recording and improvement of traits which cannot be measured easily in the selection candidates themselves, such as disease resistance, feed conversion efficiency, environmental tolerance and product quality (Yanez *et al.* 2015). For these traits, the EBVs of their siblings are used in a process known as sib-testing or sib selection (Box 1). As such, for these traits, breeding values can only be estimated at the family level without genomic data and therefore do not capitalize on the within-family, or Mendelian sampling component of genetic variation (Hill 2013).

In the sib-testing schemes described above, improvements in selection accuracy can be achieved via the use of genetic markers associated with variation in the phenotype of interest. There are two main routes by which this can be achieved: marker-assisted selection (MAS) and genomic selection. In both cases, it is important to first determine the genetic architecture of the trait in question; specifically whether it is controlled by single or few quantitative trait loci (QTL) of large effect, or many QTL of small effect.

Marker-assisted selection involves the detection and use of genetic markers linked to specific QTL affecting the trait of interest, and has been applied to several aquaculture species worldwide including Atlantic salmon and rainbow trout grown in the UK (Yue 2014; Liu *et al.* 2018; Shen & Yue 2019; Houston *et al.* 2020; Fraslin *et al.* 2020). By identifying genetic markers, usually SNPs, which segregate non-

**Box 1. Breeding tools and technologies**

Phenotype	An observable trait or characteristic of an organism.
Genotype	The genetic characteristics that contribute to a phenotype.
Mass selection	Selection of individuals for breeding based on ranking according to a desirable phenotype
Heritability	The amount of phenotypic variation attributable to genetics.
EBV (Estimated Breeding Value)	The estimated additive genetic merit of an individual for a given trait.
QTL (Quantitative Trait Locus)	A region of the genome which is associated with variation in a quantitative trait in a population.
Single-Nucleotide Polymorphism (SNP)	The substitution of an individual nucleotide (A/G/C/T) in a specific position of the genome.
SNP chip/SNP array	A small piece of silicon glass (chip) to which a large number of synthetic single-stranded DNA sequences have been chemically bonded. Used to determine genotypes at many SNPs simultaneously for a given DNA sample.
Marker-assisted selection (MAS)	Selection of individuals for breeding partly based on their genotype at genetic markers linked to a trait of interest.
Family selection	Selection of whole families for breeding based on recording of traits of interest and tracking of pedigree in a broodstock population.
Sib testing/selection	Family selection based on trait recording on siblings of selection candidates. Particularly useful for traits difficult or impossible to measure on breeding candidates themselves.
Genomic Selection (GS)	The selection of individuals for improvement of traits of interest based on the use of genome-wide genetic markers to estimate genomic breeding values.
Genome-Wide Association Study (GWAS)	Testing the statistical association between SNPs across the genome and target traits in a large population of animals.
Genomic Breeding Values (GEBV)	Breeding values for a given trait obtained by summing the additive effects of all genetic markers across the genome.
Genotyping-in-Thousands by sequencing (GT-seq)	A method of comparing specific DNA sequences (genotyping) between up to thousands of individuals simultaneously using a relatively small (~500) panel of SNPs.
Genetic Modification (GM) and Genetically Modified Organism (GMO)	Changing the genome of an organism by inserting genomic material from another organism or a synthetic source. Allows production of a GMO with traits which may never have been achieved using conventional selective breeding.
Genome editing (GE) and Gene-edited Organism (GEO)	Using precise genomic engineering tools (e.g. CRISPR/Cas9) to make targeted changes at a defined location in the genome of interest. The change may correspond to naturally occurring variation in a population of interest.
Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/Cas	CRISPR/Cas is part of prokaryotic (bacteria and archaea) immunity. In these organisms, a short RNA 'guide' sequence directs the Cas protein to a specific sequence of viral DNA/RNA to be cut by Cas. This mechanism has been adapted by molecular biologists, in particular as a precise molecular scissors used in genome editing.

randomly with QTL, one may employ marker-assisted selection to enhance family-based selective breeding at relatively low additional cost. However, for this to be effective, it is important that the specific QTL targeted have a large effect, and are consistent in their effect across families and populations. Encouragingly, there are notable examples of where this is the case. In the case of delaying sexual maturity, two independent studies identified the gene *vgll3* being responsible for 33–39% of the phenotypic variation (Ayllon *et al.* 2015; Barson *et al.* 2015). Another desirable trait is disease resistance, (Moen *et al.* 2007; Yáñez *et al.* 2014a; Gonen *et al.* 2015) and one of the most successful cases of breeding for disease resistance using MAS is that of

infectious pancreatic necrosis virus (IPNV). Here, one major QTL was identified as being responsible for 29% of the observed phenotypic variance in disease resistance (Houston *et al.* 2010). Using this information, MAS was effective in reducing disease incidence in freshwater salmon fry from 47% to 9% in one year alone (Norris 2017). This discovery and subsequent implementation is estimated to have saved £26.4 million gross value added (GVA) per year and 750 jobs in the Scottish salmon industry (Houston *et al.* 2010). Similar techniques are being tested to tackle other major diseases affecting the UK aquaculture industry at present such as Oyster Herpes virus (OsHV-1) resistance in Pacific oysters (Gutierrez *et al.* 2018a) and resistance to



the *Bonamia* parasite which is the biggest challenge to *Ostrea edulis* (flat oyster) cultivation at present (Vera *et al.* 2019).

Genomic selection (GS) expands on MAS by utilizing genome-wide markers (usually SNPs) to predict genomic breeding values (GEBVs) for selection candidates (Box 1). It is based on the theory that with sufficient numbers of loci across the genome, most QTLs will be in strong linkage disequilibrium with at least one marker (Meuwissen *et al.* 2001). The estimated breeding value for a given trait is calculated by taking into account the combined effects of all markers, and these are estimated in a training population where all animals are genotyped and measured for traits of interest. The data from the training population are used to train the genomic prediction statistical model which is then applied to calculate breeding values for selection candidates. As such, while MAS is more affordable, GS is particularly useful for breeding oligo- or polygenic traits, that is traits influenced by many loci of relatively minor effect such as growth and resistance to most diseases, overcoming many of the limitations associated with MAS (Zenger *et al.* 2018). The efficacy of genomic selection can be assessed by using the genomic prediction model to predict traits in a test population in which trait values are known but masked, often using a process known as cross-validation (Zenger *et al.* 2018). To date, the use of genomic selection has resulted in higher prediction accuracy of breeding value than pedigree information alone for every aquaculture species it has been applied to including Atlantic salmon (Yanez *et al.* 2015) and rainbow trout (Vallejo *et al.* 2017). One of the reasons for the improvement accuracy is that genomic relationships estimated by genetic markers can capture realized relationships between individuals rather than the approximations used in a pedigree-based relationship matrix. For example, while traditional additive genetic matrices assume a relationship between full siblings of 0.5, the realized relationship between pairs of full siblings varies substantially around this mean, in theory from 0 to 1 (Ødegård & Meuwissen 2012).

Transformative rearing technologies and husbandry regimes are integral to realizing the benefits of breeding programmes by ensuring optimal performances of the stocks. For example, cryopreservation of finfish milt (sperm) (Cabrita *et al.* 2001; Yang *et al.* 2018) and bivalve larvae (Suquet *et al.* 2014; Rodriguez-Riveiro *et al.* 2019) enables long-term storage of genetic material from optimal selection candidates. The high fecundity of aquatic species means that genetically improved stock can be disseminated from a single nucleus to a broad geographical and environmental range. Other innovations include the photoperiod manipulation of parr–smolt transformation (smoltification) and early maturation during the first year

at sea, and land based RAS. There is a global trend for adopting RAS more universally for aquaculture (Espinal & Matulić 2019), and they are likely to become more important in the UK. For example, most rainbow trout farming in Denmark is now performed in RAS, largely driven by strict environmental legislation (Jokumsen & Svendsen 2010). While minimizing water use and reducing effluent discharge, adoption RAS in farming practice also enables a full control of the environment, minimizing exposure to pathogens. Additionally, this environmental control could improve production traits and mitigate potential health and welfare issues through early life programming. Early-life experiences associated with, for example feed, temperature and microbiome can have long-term impacts on performance, robustness and welfare of farmed stocks (Clarkson *et al.* 2017; Vera *et al.* 2017; Martos-Sitcha *et al.* 2020). These effects are largely attributed to epigenetic modifications, that is changes that do not alter DNA but can regulate gene expression, which can in some cases be retained not only later in life but also by subsequent generations (Jonsson & Jonsson 2014; Gavery & Roberts 2017). Our current understanding of these closed rearing systems is still developing (Good & Davidson 2016; Hines *et al.* 2019). Investigations are underway to apply this concept towards overcoming problems encountered later in the production cycle such as disease, poor acceptance of alternative aquafeed or malformations in Atlantic salmon and rainbow trout (Geurden *et al.* 2013; Clarkson *et al.* 2017; Uren Webster *et al.* 2018).

However, despite these potential advantages, there are complexities associated with rearing healthy fish in these land-based systems. Crucially, when dealing with adaptations to different environments such as these, there may be a strong genotype by environment interaction ( $G \times E$ ) effect (Sae-Lim *et al.* 2016).  $G \times E$  occurs where the performance of the selected animals varies markedly across diverse production environments, which results in re-ranking of genotypes and effectively reduces the overall response to selection within a breeding programme (Sae-Lim *et al.* 2016). This presents a major issue for aquaculture species' breeding programmes, which often operate on a global scale. The on-growing of many species occurs under 'natural' conditions in ponds or seawater pens, which can be strikingly different from the controlled conditions of breeding nuclei and experimental challenge facilities. Furthermore, technological advances in production settings mean that breeding goals need to be adapted to new production environments, for example RAS, or environments which are likely to be affected by climate change. This may require separate breeding programmes, or targeted breeding for robustness to reduce the  $G \times E$  effect in these new rearing systems.

## History and current status of selective breeding in the UK

The aquaculture industry in the UK is heavily dominated by salmon production, followed by rainbow trout, mussels and oysters. The domestication of these species occurred over very different timescales – the earliest records for blue mussel and Pacific oyster cultivation date from the 13<sup>th</sup> and 17<sup>th</sup> centuries respectively (Fujiya 1970; Prou & Goulletquer 2002) whereas rainbow trout and Atlantic salmon cultivation only began in the 19<sup>th</sup> century (Nash 2011). However, the first scientific reports of breeding each of these species for a specific trait were all published in the 20<sup>th</sup> century (Lewis 1944; Strömngren & Nielsen 1989; Gjedrem *et al.* 1991; Kong *et al.* 2015). Of these, the most advanced selective breeding programmes, and the most advanced genetic tools, are available for the two largest industries—Atlantic salmon and rainbow trout.

### Atlantic salmon

The first efforts to collect, incubate and hatch salmon eggs in the UK date from 1838 and were aimed at restocking rivers with wild stocks (Shaw 1840). However, the first salmon farm on-growing fish to harvest did not open until 1969 at Loch Ailort, Inverness-shire. Currently, the vast majority of salmon stock originates from established, large-scale and well-managed breeding programmes with routine trait and pedigree recording. This level of industrial investment in selective breeding research for Atlantic salmon is much greater than any other sector of aquaculture globally and has led to rapid advances in the use of genomic tools such as SNP-chips to improve farmed stocks (Houston & Macqueen 2019). Currently in the UK, key priority traits include resistance to parasitic infection (Amoebic Gill Disease AGD and sea lice), feed efficiency, early maturation and overall stock robustness (Migaud & Houston 2017). Improvements in these traits translate to a rapid gain in commercial production (Gjedrem & Rye 2018). Importantly, disease resistance can also reduce the environmental impacts of chemotherapeutant discharge in the water and pathogen transmission to wild populations (Wargelius 2019).

In 2018, 87% of salmon ova laid down to hatch in Scotland were imported from outside the UK (Munro 2019). UK producers largely source genetically improved eggs from large consolidated pedigree-based selective breeding programmes. Such consolidation of industry research and development activities is necessary due to the high costs. Ova are imported from: AquaGen, based in Norway but with new broodstock facilities opened in Scotland in 2018; Benchmark, based in Norway (Salmobreed) and Iceland (StofnFiskur); and one producer (Mowi) runs its own integrated breeding programme in Norway (Mowi 2019).

However, relying on imported stock also has disadvantages. For example, G × E could play a major role in the performance of similar genetic material disseminated to diverse environments. It is well-established in aquaculture species that G × E can be significant for growth and disease resistance traits, and this can cause family re-ranking which reduces the realized impact of genetic gain on commercial production (Sae-Lim *et al.* 2016). Another disadvantage is the potential risk of importing infectious pathogens, and/or the potential bans on egg imports due to changes in governmental regulations, for example following detection of notifiable pathogens. This has been the case recently for ISAV, which has prevented import of eggs from Norway to the UK since 2019 (Marine Scotland Directorate 2020). This clearly highlights the need to establish UK-based breeding programmes to reduce reliance on Norwegian or Icelandic imports, and to select stocks for improved performance under UK environmental conditions and farming practices. Within the UK, Hendrix Genetics runs breeding programmes (Yáñez *et al.* 2015) and specialized companies, for example Xelect, provide genetic management services for in-house breeding programmes of some small- to medium-sized UK producers, for example Loch Duart and Wester Ross Salmon (Munro 2019; SAIC 2019b).

UK research and development programmes related to selective breeding and genomics have been underway for several decades, focussed on several economically important traits, including growth, survival, fillet colour and late sexual maturation (reduced grilising rate) and in particular, disease resistance. Since the 1990s, Norwegian-owned Mowi Scotland (formerly Marine Harvest Scotland) has been involved in genetic improvement programmes aiming at targeting disease resistance traits in farmed stocks in the UK and globally, including sea lice (Jones *et al.* 2002), AGD (Aslam *et al.* 2020), cardiomyopathy (Boison *et al.* 2019) and Pancreas Disease (PD) (Gonen *et al.* 2015). The first successful documented example of MAS being used for any aquaculture species was the IPN resistance project discussed earlier. This was developed in parallel by UK and Norwegian research groups working with Hendrix Genetics and AquaGen, respectively (Houston *et al.* 2008; Moen *et al.* 2009) and was followed by several other collaborative projects between UK and Norwegian academic researchers (Robledo *et al.* 2016; Ulrich *et al.* 2018; Rodríguez *et al.* 2019). It is often the case that breeding research begins via such academic and industry collaborations, before being translated to widespread industry application when it becomes cost-effective. Research projects targeting resistance to the two biggest pathogenic threats to the UK salmon industry at present, sea lice (Tsai *et al.* 2016; Robledo *et al.* 2019) and AGD (Robledo *et al.* 2020) have also successfully produced genome-wide SNP chips suitable for

research (Houston *et al.* 2014; Lien *et al.* 2016). Subsequently, several SNP chips have also been developed and widely applied for industry implementation.

### Rainbow trout

Since the first 'table trout' farm established in Lincolnshire in 1950, almost 300 rainbow trout farms now exist across the UK, with the majority based in southern England, North Yorkshire and Southern to central Scotland (British Trout Association 2019). Similar to the salmon industry, most of the eggs are sourced from outside the UK, the majority coming from Denmark and Norway, with Northern Ireland contributing 20% of the total UK supply, helping mitigate potential G x E effects (Murphy 2015; Munro 2019). Formerly, stock tended to be all-female, which eliminated male maturation in portion size fish. However, reflecting the trend in the industry for larger marine on-grown fish, most eggs are now triploid which prevents maturation in larger fish. Gender manipulation and induced sterility are important stock management tools in aquaculture which will be discussed later.

Several trout producing companies have invested heavily in UK selective breeding projects. The Seven Springs Trout Hatchery Ltd. in Northern Ireland selectively bred broodstock via a partnership between Dawnfresh Ltd. (a major UK trout farming company) and Hendrix Genetics. This attracted Troutex, a large Danish trout breeding company and ova supplier to purchase a 66% share in the hatchery in 2011 (Troutex ApS 2019). UK producers often source genetically improved eggs through four main external specialized breeding companies, Troutex (based in Denmark), AquaGen (based in Norway), Troutlodge (based in Isle of Man) and AquaSearch (based in Jelling, Denmark). Earlier academic efforts to optimize rainbow trout husbandry in the UK focussed on heritability of stress responses and osmoregulation in the context of stocking density and salt-water tolerance respectively (Pottinger & Carrick 1999; Pottinger & Pickering 2011; Le Bras *et al.* 2011). In addition to improving growth and feed conversion ratios, breeding programmes have also selected for disease resistance. Successes include increased resistance to *Flavobacterium psychrophilum*, the causative agent of rainbow trout fry syndrome (RTFS) also known as bacterial coldwater disease (BCWD) (Gulla *et al.* 2016). US-based company Troutlodge was one of the first companies in the world to apply genomic techniques to produce a commercial strain of trout resistant to BCWD (Vallejo *et al.* 2017; Liu *et al.* 2018). In the UK, this company is integrated with Hendrix Genetics and continues to use selective breeding to improve survivability, growth, quality, feed conversion rate, meat characteristics and animal welfare. AquaGen is another company heavily invested in selectively breeding trout. In

collaboration with UK-based aquaculture companies Cooke Aquaculture Scotland and Dawnfresh Seafoods Ltd., AquaGen are involved in researching the heritability of resistance to diseases such as BCWD in trout (SAIC 2017; Hoare 2018).

*Flavobacterium columnare* is a bacterial pathogen which causes Columnaris Disease or Bacterial Warm Water Disease (BWWD) affecting many aquaculture species besides salmonids, although as the name implies, usually in warmer water. As such, it is not yet a major concern in the UK but could emerge as a disease for UK trout. This disease can cause very high mortality rates and antibiotics are currently the only successful treatment (Declercq *et al.* 2013). However, efforts to identify resistance markers are underway including a genome-wide analysis (Silva *et al.* 2018; Silva *et al.* 2019) which should aid UK efforts to breed resistance. Recent (ARRAINA 2013; FISHBOOST 2014) and ongoing (AquaIMPACT 2019; FutureEUAqua 2019) European Commission funded projects have been advancing knowledge and developing tools for selective breeding in rainbow trout as well as salmon and other commercially important species in Europe.

### Mussel

British growers of mussels, the third most commercially important UK aquaculture species, have long relied on natural settlement of wild spat. Therefore, there has been relatively little demand for hatchery produced seed. Wild sourcing is typically cheaper than hatchery production and is likely to result in genetically diverse stocks negating the risks of inbreeding associated with closed breeding populations. However, this process is susceptible to large temporal and geographical variations in availability, deleterious hybridization with the invasive foolish mussel, climate change and disease. The recent development of species diagnostic SNPs panel (Wilson *et al.* 2018), potentially linked to QTL affecting important traits such as meat yield and shell strength, has the potential to significantly inform current wild spat collection strategies for establishing base populations and selective breeding trials. A large bivalve hatchery has also been established in the Shetland Islands to mitigate against current and future challenges to wild spat supply, and will be discussed later (Adamson *et al.* 2018).

### Pacific oyster

Two British bivalve hatcheries produce Pacific oyster seed, and unlike hatcheries elsewhere in Europe, both are confirmed as free from all shellfish diseases listed with notification obligations by the OIE or EU (based on their potential social and economic impact) including OsHV-1 and

protozoan parasites of the *Bonamia* genus (Adamson *et al.* 2018). Combined, these hatcheries are the sole supply for all *C. gigas* seed to UK growers in disease-free areas. However, there would likely be a national seed shortage should conditions change to affect the ability of either hatchery to produce disease-free seed. Substantial research efforts have been made into selective breeding for improved disease resilience and stock husbandry to safeguard against such threats to the UK market (Gutierrez *et al.*, 2018a, 2018b).

### Other species

While the four main UK aquaculture species described above represent 98% of production by value, there are several other minor species (Table 2) with important roles and future potential in diversification of production. The UK has recently started producing cleaner fish for sea lice control in the salmon industry (Table 2), which is predicted to increase significantly in coming years to meet demand (Carvalho *et al.* 2018). Since 2010, several hatcheries have been established throughout the UK by Mowi, Otter Ferry Seafish and Scottish Sea Farms growing both ballan wrasse (*Labrus bergylta*) and lumpfish (*Cyclopterus lumpus*). Ongoing research in the UK is looking at QTL analysis of growth and gender with the view to establish marker-assisted selection in the near future. Additionally, their delousing efficacy is also critical and likely to be heritable and therefore amenable to genetic improvement (Leclercq *et al.* 2014; Imsland *et al.* 2016; Brooker *et al.* 2018).

Atlantic halibut (*Hippoglossus hippoglossus*) farming began in the UK in 1983 (Baynes *et al.* 2006) with harvest tonnage peaking in 2005 at 287 tonnes (FAO 2020a). Currently, the UK industry is centred round a single hatchery and associated land based on-growing site with an annual harvest

volume of circa 60 tonnes in 2019 (Otterferry Seafish Ltd., Tighnabruaich, Scotland, UK). A long generation time of more than 6 years has hindered the establishment of self-sustaining selective breeding programmes, with relatively few specialized hatcheries worldwide (Puvanendran & Mortensen 2009; Reith *et al.* 2011). Progress has been made in gender manipulation technology with the first monosex production started in Scotland in 2013 (Palaikostas *et al.* 2013) and genetic management tools (Reid *et al.* 2007; Reith *et al.* 2011).

Atlantic cod (*Gadus morhua*) farming started in the UK and Norway in the early 21<sup>st</sup> century driven by reduced wild catches, rising market prices and the potential to use existing salmon farming systems. On-growing production in Shetland peaked at 1822 tonnes in 2008 (Walker 2009), however cod farming collapsed in 2007–2008, partly due to the global financial crisis. While UK operations have not yet restarted, Norwegian family-based selective breeding programmes operated by Nofima have continued, targeting growth, maturation (Kolstad *et al.* 2006) and disease resistance (Ødegård *et al.* 2010; Bangera *et al.* 2011).

The native brown trout (*Salmo trutta*) has a relatively small aquaculture industry in the UK, with the majority of farms based in England. Most of these are freshwater sites growing for stocking angling waters (Munro 2019). Several grow-out farms for rearing warm-water fish *Oreochromis niloticus* (Nile tilapia) were established throughout the UK in the past two decades, although none have remained operational. In 2017, however, the first commercial tilapia hatchery in the UK and the second in Europe was established (Fletcher 2017) which attract new UK-based grow-out farming.

The European flat oyster (*Ostrea edulis*) is the UK's native edible oyster. As yet, no selective breeding programmes exist, although two hatcheries now commercially

**Table 2** Annual UK aquaculture output from hatcheries/nurseries of juveniles reported by number for on-growing, averaged over the period 2013–2018. Excludes juveniles on-grown within the same farm, released for angling/restocking and sold to ornamental fish trade. 'nei' (not elsewhere included) used to combine production of minor species and confidential figures, and groupings differ to Table 1 to preserve anonymity; due to limited number of UK producers, Bivalvia species grouped for confidentiality. Source: Cefas compilation of UK statistics for Eurostat and FAO

Species & destination for on-grown production			Produced from Sea/ Fresh water	UK total (millions per annum)
Finfish – on-grown for consumption, as cleaner fish and for sport angling	<i>Salmo salar</i>	Atlantic salmon	FW	49.006
	<i>Oncorhynchus mykiss</i>	Rainbow trout	FW	18.050
	<i>Cyclopterus lumpus</i>	Lumpfish	SW	1.720
	<i>Salmo trutta</i>	Brown trout	FW	0.687
	<i>Labridae</i>	Wrasses, hogfish, etc. nei	SW	0.178
	<i>Osteichthyes</i>	Marine fish nei	SW	0.050
	<i>Osteichthyes</i>	Freshwater fish nei	FW	0.002
	<i>Salmonidae</i>	Salmonids – nei	FW	0.001
	<i>Cyprinus carpio</i>	Common carp (inc. hybrids)	FW	0.125
Finfish – on-grown for coarse angling	<i>Osteichthyes</i>	Freshwater fish nei	FW	0.049
Shellfish – on-grown for consumption	<i>Bivalvia</i>	Oysters, clams, etc. nei	SW	53.606

produce them, including a single species hatchery recently established in Orkney (Orkney Shellfish Hatchery 2020). While great Atlantic scallop cultivation is practised in the UK, this is entirely reliant on wild spat collection and due to the limited production outputs, there is currently no demand for a domestic hatchery. Although scallops earn a high price on the market, they are slow to grow in British waters and wild stocks are still available, which limits commercial prospects to intensify farming activities. Until recently, all seed production was managed by the Scalpro hatchery in Norway using UK broodstock (Adamson *et al.* 2018). Scope to increase spat availability and quality and improve growth rate to reduce time to market remain valuable goals in the progression of UK scallop aquaculture.

A small number of warm-water shrimp farms have been established in the UK over many years, for example Pacific whiteleg shrimp (*Litopenaeus vannamei*) are being grown by Great British Prawns Ltd. in Stirlingshire, Scotland in 2019 using Clearwater RAS technology. This company has established its own hatchery and at full capacity, aims to produce 50 tonnes of *L. vannamei* per year which should replace some of the UK's reliance on imported shrimp, mostly from SE Asia (Fletcher 2019). Hatchery techniques for the production of juvenile European lobster (*Homarus gammarus*) from wild-caught egg-bearing females were pioneered in the UK (Beard *et al.* 1985). Efforts to improve hatchery conditions for lobster larval rearing have been underway for some time (Hughes *et al.* 1972; Middlemiss *et al.* 2015; Small *et al.* 2015), but several husbandry issues remain. Recent advancements have been made to close the breeding cycle and improve genomic tools available for UK lobster (Jenkins *et al.* 2019). This should synergize well with efforts to domesticate this species, such as AquaLeap, a major UK academic-industry research project aiming to improve the genetics and breeding for salmon, lobster, flat oyster and lumpfish (SAIC 2019a).

Reports suggest that the UK offers suitable environments for seaweed aquaculture (Capuzzo & McKie 2016), which can provide a source of biofuel production, carbon sequestration and food (Hughes *et al.* 2012). Although in early stages relative to finfish aquaculture, the potential for genetic improvement of commercially important traits is well recognized (Robinson *et al.* 2013). While seaweed cultivation and macroalgae processing industries are not yet established at scale in the UK, this is predicted to change in coming years as technology develops and demand increases, in particular for biofuels (Capuzzo & McKie 2016; Wood *et al.* 2017).

### Sterility and gender manipulation

In aquaculture, it is often desirable to produce monosex or sterile stock. Hatchery-reared aquaculture stock are

selectively bred for phenotypes suited to farming, which are often not reflective of genotypes found in the wild. Many view this as a significant concern for the open-culture systems used in all major sectors of UK aquaculture due to the potential for escapees to negatively impact on wild populations (Glover *et al.* 2017). In particular for wild freshwater and anadromous fish such as salmon with relatively small effective population sizes, gene pools found in nature can be significantly affected by inflow of genes from farmed animals (Hindar *et al.* 2006; Glover *et al.* 2017). Conversely, it has been suggested that interbreeding with captive native oyster stock may benefit sparse wild populations by contributing to genetic variation (Varney *et al.* 2018; Hornick & Plough 2019). Besides preventing introgression effects of escapees from farms, sterility can also avoid early maturation during on-growing, which may negatively affect growth, welfare and product quality leading to harvest downgrades. Importantly, sterility can also be used to protect intellectual property (IP) generated from long-term improvement programmes run by breeding companies.

The triploid methodology was first implemented in the rainbow trout industry in the 1980's and has since been adopted by farmers all over Europe, including the UK (Munro 2019), in conjunction with monosex female (discussed below). Triploidy is induced by exposing the fertilized eggs to hydrostatic pressure or temperature shock. All female offspring are produced by fertilizing normal female eggs with milt from masculinized genetic females (Dunham 2004; Shen & Wang 2018). Following a UK Environment Agency policy in 2015, rivers and lakes containing native brown trout populations can no longer be stocked with fertile (diploid) farmed strains as for stocking of rainbow trout. This effort to safeguard wild populations from the introgression of farmed fish genetics has led increased production of triploid brown trout, similar to rainbow trout (Preston *et al.* 2013; Orrego 2015).

Despite the widespread use of induced sterility in UK trout, it has yet to be similarly adopted for UK salmon farming (Leclercq *et al.* 2010; Gabian *et al.* 2019). Although the UK has been at the forefront of salmonid sterility research from the 1970s (Johnstone *et al.* 1979; Lincoln & Scott 1983; Bye & Lincoln 1986) and more recently over the last twelve years with Stirling led Salmotrip projects funded by EU, BBSRC and industry (Taylor *et al.* 2007; Taylor *et al.* 2013; Taylor *et al.* 2015), sterile triploid Atlantic salmon are mainly supplied to Norwegian salmon producers by most breeders (Aquagen, Salmobreed, StofnFiskur). This follows the launch of green licences in 2013 (Hersoug 2015) to tackle demonstrated impacts of farmed salmon escapees in Norwegian rivers (Glover *et al.* 2017). Over recent years, knowledge of triploid salmon physiology has progressed vastly, leading to recommendations and protocols to address challenges faced by the

industry, for example suboptimal growth and welfare, reduced robustness, environmental sensitivity and nutritional requirements (Taylor *et al.* 2013; Taylor *et al.* 2015). However, a basic understanding of triploid salmon genetics is still lacking, and the genetic correlation between target traits for breeding observed in conventional diploids and in triploids is not well known. As such, tailored breeding programmes may be required to support routine triploid production.

Besides induced sterility or triploidy, it may also be desirable to control the age of sexual maturation. The gene *vgl3* has been discovered to explain 30–40% of phenotypic variation in maturation age (Verta *et al.* 2020). A technology which could radically progress these efforts in fish is the direct disruption of genes involved in germ cell development through gene editing (Güralp *et al.* 2020), which will be discussed later.

Alongside induced sterility, gender manipulation is routinely performed in several commercially important finfish species, including rainbow trout (monosex female), tilapia (monosex male) and more recently monosex female in halibut (Palaikostas *et al.* 2013). Many aquaculture fish species exhibit strong sexual dimorphism for a number of commercially relevant traits such as growth and age of maturity (Leclercq *et al.* 2010). This has led to interest in understanding sex determination and methods to control it. For instance, male tilapia display 40% faster growth rates and higher FCR than females (Mair & Abella 1997; Beardmore *et al.* 2001). Following an eight year breeding study within the UK Department for International Development (formerly ODA) Fish Genetics Research Programme at Swansea University, Wales (Scott *et al.* 1989), a genetically unique form of Supermale tilapia was developed with a YY genotype rather than the usual XY. The result is all-male offspring without the use of chemical or hormonal treatment. This strain is known as Genetically Male Tilapia (GMT), which are produced by the Three-Sixty Aquaculture hatchery in Swansea (Fletcher 2017). This avoids direct hormonal sex reversal using 17 $\alpha$ -Methyldihydrotestosterone (MDHT), widely practised globally but banned in the European Union (Directive 1996).

Concern surrounds the effects of non-native Pacific oyster settlement on UK ecosystems (Herbert *et al.* 2016). This is a significant reason to farm sterile stock, and the only commercially available method is to generate triploid animals. Although heat and chemical shocks can be used to induce triploidy, a common method involves crossing a diploid animal with a fully fertile tetraploid parent, resulting in a triploid individual. As such, any selective breeding programme harnessing triploids would have to consider the performance as triploids and maintain both tetraploid and diploid breeding animals. Triploid oysters are also considered desirable for aquaculture, because more of their

energy is directed towards growth instead of reproduction. This avoids the unfavourable ‘miliness’ which otherwise occurs during the summer spawning period, allowing triploids to be sold year-round. Additionally, use of sterile stock allows farms to establish more easily in new areas (Adamson *et al.* 2018). Triploid Pacific oysters are available to UK farmers but are not always used due to the higher cost of seed.





Triploid induction in blue mussels seeds has been investigated (Kamermans *et al.* 2013). However, because mussels are usually consumed cooked, poorer meat quality during the spawning season is less of an issue than for oysters. Indeed, mussels are harvested year round, and the gonad development preceding spawning contributes to the meat yield and product quality. It will be important to evaluate whether triploidy could produce adequate and more stable meat yields by potentially reducing post-spawning weight loss. Sterility induced by triploidization is to be expected in mussels but has not yet been demonstrated. As discussed earlier, mussel aquaculture in the UK has been negatively affected by the introgression of *M. trossellus* with the native *M. edulis* resulting in softer shells and lower meat yields (Michalek *et al.* 2016). While hatchery-produced spat could ensure native *M. edulis* are cultivated, introgression of hatchery-produced spat genetics may have a negative effect on the wild populations of blue mussel, as suggested for in Atlantic salmon (Glover *et al.* 2017). While selective breeding from local stocks reduces this concern, directional selection in a closed breeding programme will result in cumulative divergence between the improved and wild strains, and the issue will therefore remain.

### Current breeding technology innovations and future applications

With the advancement of aquaculture industries, the tools and resources routinely used in Atlantic salmon breeding and cultivation are becoming adopted by other finfish sectors and increasingly by shellfish farmers. The current status, and likely next steps for breeding technologies applied domestically and globally to each of the four main UK aquaculture sectors is summarized in Table 3. Some of the innovations and developments which are likely to be adopted in coming years are discussed below.

Genomic selection requires a platform to generate high-density SNP marker genotypes across populations of animals. For example, previous studies of genomic selection in Atlantic salmon have typically used sample sizes of 500–3000 individuals (Ødegård & Meuwissen 2014; Tsai *et al.* 2015; Yanez *et al.* 2015; Tsai *et al.* 2016; Robledo *et al.* 2019; Rodríguez *et al.* 2019) which can be prohibitively expensive. Fortunately, the cost of genotyping an animal reduces markedly with scale, and recent studies have

**Table 3** Current level of breeding technologies applied to each of the four main aquaculture species in the UK and globally. In addition to *Mytilus* spp., 'Mussel' includes all *Mytilid* mussel species grown globally, for example *Perna canaliculus* (New Zealand green-lipped mussel)

Breeding technology	Application			
	Atlantic Salmon	Rainbow Trout	Mussel	Pacific Oyster
				
	UK	UK	UK	UK
	Global	Global	Global	Global
Closed breeding cycle	Commercial	Commercial	Commercial	Commercial
Mass selection	–	–	Academic	Commercial
Family selection	Commercial (Domestic and imported stock)	Commercial	–	Commercial
Sib testing/selection	Commercial (Domestic and imported stock)	–	–	–
Gender manipulation/triploidy	Academic	Commercial	–	Commercial
Marker-assisted selection (MAS)	Commercial (Domestic and imported stock)	Commercial	Commercial	Academic
Genomic selection (GS)	Commercial (Imported stock)	Commercial	Commercial (GBS)	Commercial
Genome editing (GE)/	Academic	Academic	–	Academic
Gene-edited organism (GEO)	–	–	–	Academic

suggested that low-density SNP panels are sufficient to achieve accurate genomic predictions (Kriaridou *et al.* 2020), with genotype imputation offering further avenues to improve cost-efficiency. (Tsai *et al.* 2017; Tsairidou *et al.* 2020). One constraint is that low-density SNP panels are effective when the training and test populations are closely related (e.g. within a year group of a breeding programme), but predicting breeding value of more distantly related animals is often inadequate (Meuwissen *et al.* 2014; Tsai *et al.* 2016). This may be resolved by the detection and use of functional variants impacting the trait directly, rather than linked markers, and is becoming more achievable via the routine use of modern genomics, sequencing and genome editing technologies (Houston *et al.* 2020). High-quality reference genome assemblies are important in genomic assisted breeding and use of genomic tools. The available genome assemblies of current and potential future UK aquaculture species are presented in Table 4. While no reference genome assembly has been published yet for blue mussels, there is a mitochondrial genome and a microsatellite linkage map of 791 markers (Boore *et al.* 2004; Lallias *et al.* 2007). Reference genomes for the closely related Mediterranean (*M. galloprovincialis*) and Korean (*M. coruscus*) mussel has been published (Table 4) and will help in assembling the blue mussel genome. Assemblies are also lacking for the native oyster (*Ostrea edulis*), queen scallop (*Aequipecten opercularis*) and European abalone (*Haliotis tuberculata*); although many of these are currently in progress. Assembling a genome is not a trivial task, and many are complicated by the high levels of genomic sequence variation, heterozygosity (sequence variation between chromosome pairs), repetitive sequences of DNA and whole genome duplication events which are common in several aquaculture species (Berthelot *et al.* 2014; Lien *et al.* 2016; Hollenbeck & Johnston 2018).

### State of the art in breeding and genomics of finfish

The adoption and pace of technical innovations in genomics and selective breeding is realized quicker in salmonid species farmed in the UK by large multinational industries who are able to allocate the required budgets. At the moment, genomic selection is the state of the art for salmon breeding (Table 3). Marker-assisted selection and genome-wide marker SNP array platforms have been used to improve salmon stock across several phenotypes (Zenger *et al.* 2018) including disease resistance (Gonen *et al.* 2015; Robledo *et al.* 2016; Robledo *et al.* 2019; Silva *et al.* 2019; Rodríguez *et al.* 2019; Robledo *et al.* 2020), body size and weight (Reid *et al.* 2005; Baranski *et al.* 2010; Gutierrez *et al.* 2012; Tsai *et al.* 2015), but also delaying sexual maturation which can improve growth and meat quality (Pedersen *et al.* 2013; Gutierrez *et al.* 2014; Ayllon

*et al.* 2015; Barson *et al.* 2015). As domestication of farmed Atlantic salmon progresses, genomic tools may also be used to assess impacts of the domestication process, examining the genetic basis for changes in growth, morphology, behaviour and physiology (Glover *et al.* 2017; López *et al.* 2019).

Understanding how a genotype gives rise to an observable phenotype is a major challenge. Closing the genotype to phenotype gap relies initially upon a broad understanding of the variants across a genome which affect a given trait. This depends heavily on accurately measuring and recording detailed trait information for large numbers of individual animals. Due to the nature of their husbandry and number of animals kept, such large-scale trait recording for aquaculture species presents unique challenges. A clear goal for future development should be to improve the range, accuracy and automation of collecting trait measurements on the animals (phenotyping). Major initiatives for functional annotation, that is assigning biological information to regions of a genome sequence, are underway in livestock (Functional Annotation of Animal Genomes (FAANG)) (Andersson *et al.* 2015; Giuffra *et al.* 2019), and more recently for salmonid species including Atlantic salmon and rainbow trout (Macqueen *et al.* 2017). The ambitious efforts of these large projects should prove very useful in improving the application of genomics to UK salmon and trout breeding and production. Outputs from these programmes will also synergize with advances in genome editing tools. Genome editing (discussed below) can be used in laboratory experiments to increase our understanding of salmonid biology, or potentially directly to improve salmonid broodstock in the future.

Assays and computing for such functional annotation is expensive and requires strategic and often international investment. For emerging or new aquaculture species in an earlier state of domestication, sequencing, assembly and more basic sequence annotation should be an initial priority. A good example of these technologies being successfully used to rapidly fast-track domestication of new aquaculture species is that of ballan wrasse and lumpfish for deployment as cleaner fish, the production of which is becoming a major sector in UK aquaculture (Carvalho *et al.* 2018; Brooker *et al.* 2018). The commercial cultivation of ballan wrasse began in the UK in 2010 with the joint venture between Mowi (former Marine Harvest) and Scottish Sea Farms in Machrihanish (Scotland) followed by lumpsucker in 2013 by Ocean Matters in Anglesey, Wales, now also owned by Mowi (Treasurer 2018). Advanced breeding technologies (e.g. gamete assessment, fecundity estimates) led to closing the life cycles of both species (Treasurer 2018; Pountney *et al.* 2020), and reference genomes released to the public domain by 2018 (Treasurer 2018; Lie *et al.* 2018; Knutsen *et al.* 2019). Using these resources, the



**Table 4** Genome assemblies for UK aquaculture industry relevant species

Species	Total size (Mb)	Contig† N50‡ (Kb)	Scaffold§ N50 (Mb)	Sequencing platform	Reference
Atlantic salmon ( <i>Salmo salar</i> )	2967	57.6	1.366	Illumina HiSeq; PacBio; Sanger; Illumina GAllx	GenBank: GCA_000233375.4 (Lien <i>et al.</i> 2016)
Rainbow trout ( <i>Oncorhynchus mykiss</i> )	2333	16 039	85.33	PacBio Sequel	GenBank: GCA_013265735.1
Pacific oyster ( <i>Crassostrea gigas</i> )	648	1564	58.46	PacBio	GenBank: GCA_902806645.1
Mediterranean mussel ( <i>Mytilus galloprovincialis</i> )	1500	2.63	0.29	Illumina HiSeq	GenBank: GCA_001676915.1
Korean mussel ( <i>Mytilus coruscus</i> )	1904	817	898	Illumina HiSeq; PromethION	GenBank: GCA_011752425.1 (Li <i>et al.</i> 2020b)
Ballan wrasse ( <i>Labrus bergylta</i> )	805	703.9	0.80	Illumina HiSeq; PacBio	GenBank: GCA_900080235.1
Lumpfish ( <i>Cyclopterus lumpus</i> )	573	4950.1	23.90	Illumina HiSeq; PacBio	GenBank: GCA_009769545.1
Sea/brown trout ( <i>Salmo trutta</i> )	2372	1703	52.21	PacBio; Hi-C; 10X Genomics Chromium; BioNano	GenBank: GCA_901001165.1 (Pasquier <i>et al.</i> 2016)
Great Atlantic scallop ( <i>Pecten maximus</i> )	918	1258.8	44.82	PacBio; Hi-C; 10X Genomics Chromium	GenBank: GCA_902652985.1
Nile tilapia ( <i>Oreochromis niloticus</i> )	1006	2923.6	38.84	PacBio	GenBank: GCA_001858045.3
Common carp ( <i>Cyprinus carpio</i> )	1714	75.1	7.83	Roche 454, SOLiD, Sanger BAC-end	GenBank: GCA_000951615.2 (Xu <i>et al.</i> 2014)
Turbot ( <i>Scophthalmus maximus</i> )	557	20 466	25.95	PromethION	GenBank: GCA_013347765.1
Atlantic cod ( <i>Gadus morhua</i> )	670	1015.7	28.73	PacBio	GenBank: GCA_902167405.1
Pacific white shrimp ( <i>Litopenaeus vannamei</i> )	1663	86.86	0.61	PacBio, Illumina HiSeq	GenBank: GCA_003789085.1
Atlantic halibut ( <i>Hippoglossus hippoglossus</i> )	597	7020.3	26.31	PacBio; Illumina NovaSeq; Hi-C; DLS	GenBank: GCA_009819705.1
European sea bass ( <i>Dicentrarchus labrax</i> )	676	54.13	26.44	ABI 3730xl; ROCHE 454 FLX Titanium; Illumina GAllx	GenBank: GCA_000689215.1 (Tine <i>et al.</i> 2014)
Arctic charr ( <i>Salvelinus alpinus</i> )	2170	55.6	1.02	Illumina Paired-End; Illumina Mate-Pair; PacBio	GenBank: GCA_002910315.2 (Christensen <i>et al.</i> 2018)

†Contigs are contiguous stretches of sequenced bases (A, C, G or T) without any gaps.

‡The N50 is measure of the quality of genome assembly contiguity. It is a weighted median statistic where 50% of the entire assembly is covered by contigs/scaffolds equal to or longer than this value.

§Scaffolds are made by joining contigs together based on information about the orientation and position of a contig in a genome.

development of SNP-based toolkits for commercial breeding programmes is currently underway. This is an excellent demonstration of what can be achieved using these multifaceted modern technologies.

### State of the art in breeding and genomics of shellfish

Bivalve genetics differ from those of finfish in several ways due to biological phenomena which are well explained in a recent review (Hollenbeck & Johnston 2018). Very high levels of heterozygosity with marked segregation distortion (e.g. higher genotypic frequency than expected) and high levels of polymorphism, even with close/consanguineous breeding, contribute to computational difficulties in assembling a reference genome (Houston *et al.* 2020). However,

these exact phenomena, and very high fecundity, allow bivalves to maintain a high genetic diversity despite intense selection in the wild. For example, studies have shown that bivalves carry high genetic loads (i.e. high levels of genetic mutations, often deleterious), which are expressed differently against various selection backgrounds (Plough 2016; Plough *et al.* 2016). For these reasons, the ratio of within-family to between-family variation is likely to be considerably higher in bivalves than finfish, suggesting that capturing this variation via genomic selection would provide relatively larger gains than in most species. In family-based and mass selection studies across several mollusc species, the average response to selection per generation across all taxa for growth was 10.6%, while selection for disease resistance traits was 15.7% (Hollenbeck & Johnston 2018). Levels and types of segregation in a hatchery extended from

non-existent (Gutierrez *et al.* 2017) through to homozygous or more typically heterozygous deficiencies (Beaumont 2008; Hedgecock *et al.* 2015). However, higher selection intensity could potentially be performed without risking deleterious consequences of inbreeding (Hornick & Plough 2019; Houston *et al.* 2020). To achieve this, understanding the impact of targeted crossing and hatchery culture on long-term population genetic characteristics will be important for well-managed breeding programmes using genomic selection.

For selective breeding in Mytilid mussels, New Zealand aquaculture is arguably leading the way; a government funded Primary Growth Partnership programme has enabled commercial production of Greenshell™ Mussel spat (*Perna canaliculus*). Unlike an industry with wild spat dependence, this move has allowed for generational genetic improvement, and maintenance of pedigree lines (Paredes *et al.* 2012; Adams *et al.* 2015; Rusk *et al.* 2020). Using family selection, the programme aims to supply 30% of New Zealand's production (Symonds *et al.* 2019). In this way, their industry can be safeguarded and future-proofed from perturbations affecting wild spat supply, such as emerging diseases and climate change.

To mitigate against increasing variations in wild spat supply (Avdelas *et al.* 2020), a pilot scale commercial mussel hatchery was established in the Shetland Islands with the ambition to buffer the industry's reliance on wild resources (Hambrey & Evans 2016; Adamson *et al.* 2018). An aim of the Shetland hatchery project is to develop SNP-based stock management tools for *M. edulis* and the establishment of a family selection programme. This move could prove to be greatly beneficial in securing the future of the UK's largest shellfish aquaculture sector. Simple traits to target in early domestication include increased quality of gametes, survival and resilience of the progeny (Brooker *et al.* 2018). Closing the breeding cycle in a robust and reproducible way is the first step to using mass selection with management of genetic diversity, or ultimately family selection for commercially relevant traits such as disease resistance, growth, meat yield and shell strength (Table 3).

The past attempts and successes of industrial and experimental selective breeding programmes for oysters worldwide are well covered in other reviews (Hollenbeck & Johnston 2018; Tan *et al.* 2020). Many of these programmes relied on mass (individual) selection, with some relying on family selection, and some combining the two. Although mass selection has less control for inbreeding, results from these programmes are encouraging, particularly for resistance to diseases threatening UK oyster cultivation – OsHV-1 (*C. gigas*) and bonamiosis (*Ostrea edulis*) (Lallias *et al.* 2008; Dégremont 2011; Camara & Symonds 2014; Symonds *et al.* 2019; Vera *et al.* 2019). As better reference assemblies become available (Table 4), it will be possible to

produce more improved high-density SNP arrays (Qi *et al.* 2017; Gutierrez *et al.* 2018a), or more affordable tools such as Genotyping-in-Thousands by sequencing (GT-seq) (Campbell *et al.* 2015). This enables high-throughput genotyping, making genomic tools more affordable and accessible to future UK oyster hatchery management, ideally incorporating family selection and maintaining pedigree lines (Table 3).

## Genetic engineering

In 1989, AquaAdvantage salmon was created by Aqua-Bounty. It is a genetically modified (GM) transgenic Atlantic salmon with a growth hormone regulator from Chinook salmon inserted under a promoter sequence from ocean pout. This enabled year-round growth free from seasonal restriction, and the insert was found to be stable across generations (Yaskowiak *et al.* 2006; Ignatz *et al.* 2020). It was the first GM animal approved for human consumption in the USA and Canada (Waltz 2017). However, GM animals are not currently approved for human consumption in the UK, or favourable to the UK consumer market (Mehmet 2020). For now, selective breeding remains the preferred and accepted method of genetic improvement of stocks for aquaculture production. However, the increasing availability and accessibility of genome editing tools, with demonstrated success in whole animals for producing disease resistance (Proudfoot *et al.* 2019), may lead to genetic engineering tools becoming more commonplace in providing solutions to problems in food security in general (Godfray *et al.* 2010). Provided appropriate management of GM animals, such as sterility and the use of land-based facilities to avoid escape and introgression, these technologies could greatly benefit aquaculture.

Advancement of genome editing tools, such as CRISPR/Cas9, has arguably the greatest potential to revolutionize livestock and aquaculture breeding at present. This disruptive technology allows researchers to perform functional studies on genomes of a very diverse range of organisms by knocking out (deleting), or upregulating (increasing activity of) genes, in addition to inserting, deleting or even epigenetically manipulating regions of DNA (Knott & Doudna 2018). It has already been used experimentally to induce sterility in several aquaculture species. This can involve disrupting genes involved in sexual maturity, as seen in the Peruvian scallop, *Argopecten purpuratus* (Thresher *et al.* 2014), or ablation of germ cells by knocking out the *dnd* gene in Atlantic salmon (Wargelius *et al.* 2016; Güralp *et al.* 2020) or *piwil2* gene in Nile tilapia (Jin *et al.* 2020). These demonstrations of gene editing technology to control sterility open the door to targeting many other desirable traits. It facilitates testing and identification of variants in aquaculture genomes which directly affect economically

important traits, such as precise identification of the causative SNPs in a QTL region (Gratacap *et al.* 2019; Gratacap *et al.* 2020a). The use of whole organism (*in vivo*) editing to generate genetically modified organisms can rapidly accelerate domestication programmes, or eliminate disease susceptibility in a precise and targeted fashion (Proudfoot *et al.* 2019). An exciting prospect is that genome editing in aquaculture species offers several advantages over other livestock groups. Due to the typically high fecundity and external fertilization, access to thousands of embryos at relatively low cost is achievable. This, coupled with the fact that aquaculture species are in a very early stage of domestication, could lead to incredibly rapid progress in coming decades. However, further studies should focus on reducing negative effects such as incomplete editing across every cell in the organism (mosaicism) when using CRISPR/Cas9 to facilitate direct functional analysis (Jin *et al.* 2020). This can occur when editing takes place at any stage of development beyond embryo and can lead to failure of the desired phenotype being exhibited, or passed on to the next generation.

Beyond creating GMOs, the ability to edit the genome of any study organism allows us to study the effects of individual genetic markers, genes and even SNPs on phenotypic traits (Wargelius *et al.* 2016; Wargelius 2019). The identification of causative SNPs can increase the accuracy of marker-assisted breeding and retain broodstock genetic diversity when selecting for specific traits such as disease resistance. Using reverse genetic screening (studying the effect of gene deletion), we can gain an increased understanding of gene function for a desired phenotype in a rapid and high-throughput manner (Doench 2018; Gratacap *et al.* 2020b). Every step required for these CRISPR screens has now been achieved in salmon cells *in vitro*, including efficient lentiviral vector delivery and antibiotic selection of transduced cells (Gratacap *et al.* 2020b). This important result demonstrates the ability to perform genome-scale CRISPR screens (Hanna & Doench 2020; Li *et al.* 2020a) in salmon.

However, this technology is in a relatively formative stage. Genome editing methods must first be refined to ensure robust and repeatable results. Appropriate agreement with industry stakeholders and the general public on what risks and benefits genome editing entails is essential when considering public and regulatory acceptance of the technology for a production setting. Currently, genome editing in the UK is regulated through a combination of EU and domestic legislation, while regulatory provisions across the world remain varied. Authorization is required by European Regulation (EC) No 1829/2003 to use food or feed containing or consisting of GMOs, and food or feed produced from or containing ingredients produced from GMOs, as required. Once the European Food Safety

Authority (EFSA) panel has finished its assessment, the European Commission and Member States decide whether to grant authorization of the GMO for use in Europe (Brader 2020). The outcome of a case ruling in 2018 (ECJ 2018) meant that the European Court of Justice (ECJ) does not differentiate between gene-edited organisms (GEOs) and transgenic organisms in all respects, including GEOs which are otherwise indistinguishable from organisms bred by conventional means (Wasmer 2019). However, following requests from Members of European Parliament (MEPs) to revise regulation on GEOs, the EU Council requested the Commission (Council Decision (EU) 2019/1904) to submit 'a study in light of the Court of Justice's judgement in Case C-528/16 (ECJ 2018) regarding the status of novel genomic techniques under Union law' (i.e. Directive 2001/18/EC, Regulation (EC) 1829/2003, Regulation (EC) 1830/2003 and Directive 2009/41/EC) in November 2019. This study will take into account an analysis of the ethical and societal implications of gene editing that is being developed by the European Group on Ethics in Science and New Technologies. The outcome of this report is expected to be published by April 2021 and could have enormous impact on future legislation surrounding GEO and GMOs used in European agriculture. The final regulatory position for genome editing in the UK post-Brexit remains to be seen (Brader 2020).

## Conclusion

For the foreseeable future, Atlantic salmon will continue to be the main UK aquaculture species and largest farmed food export. Continued research and development investment by large companies should allow UK salmon farming to keep pace with the integration of latest breeding technologies as production increases. This will include advances in genomic selection to expedite the development of stocks to address key challenges facing the industry; that is, increased robustness and resilience in changing environments (RAS, climate), disease resistance and adaptation of fish to increasingly vegetarian diets. Genome editing is perhaps the next frontier for salmon breeding, and co-investment in research to develop this technology between industry and public funding will facilitate its development. Innovations to tackle key sustainability and environmental concerns (e.g. biological (cleaner fish) control of parasites, reproductive containment (sterility), nutritional imprinting) will drive the salmon farming expansion, whereas trout production is predicted to remain steady in the near future, with reductions in freshwater farming being offset by increased seawater farming (Carvalho *et al.* 2018). While selective breeding in salmonids has received heavy investment globally, domestic selection programmes for both salmon and trout in the UK will reduce reliance on imported stocks and tackle potential G x E effects.

For the shellfish sector, reduction in wild-spawn availability may lead to a further decline in UK mussel production unless offset by offshore mussel farming, and investment in hatchery and breeding technology is critical. Pacific oyster production will likely continue its strong upward trajectory, while native European flat oyster production has been declining since 2008 (Carvalho *et al.* 2018; FAO 2020a). However, increased interest in hatchery production of European flat oyster seed to support restoration efforts may reverse this decline (Pogoda *et al.* 2019). Further government investment into innovation in tailored stock management and breeding technologies is required to ensure the sustainability of these industries. Consolidation of smaller businesses to develop larger shellfish industries through farmer associations and cooperatives would potentially allow adoption of commercial selective breeding practices for hatchery-produced seed, currently restricted by the scale of investment required. The implementation of well-managed breeding programmes can avoid some of the issues with fragmented broodstock populations susceptible to inbreeding depression and problems with disease and competition. For these reasons, the development of disciplined breeding programmes for major aquaculture species should be a research and development priority in shellfish (You & Hedgecock 2019).

The UK is very well placed in terms of its academic, technological and marine resources, in addition to strong local and export markets, to expand established and develop new aquaculture species sectors. As yet, it is unclear how potential changes in post-Brexit trade agreements will affect domestic and export markets for UK aquaculture products. Improved hatchery and culture capabilities, together with investment in routine trait measurement, genetic resource management and genomic tools can all contribute to the sustainability and expansion of the UK Aquaculture sector. This can be helped by consolidation and/or integration of smaller sectors, which could then afford investment in development and application of genetic technology and innovations. Local breeding, and/or phenotyping, programmes based in the UK should also be developed alongside multinational breeding programmes. These efforts will help certification as UK origin and branding, avoid supply risks associated with disease status of imported stocks from foreign hatcheries and potentially help tackle G x E interactions. The prominence of UK aquaculture within Europe is due to the high quality product delivered from well-managed integrated salmon breeding programmes using advanced breeding technologies. In a global market, it is crucial that these modern tools and technologies are embraced and developed to maintain this status for salmon farming, and to realize the potential for other aquaculture species into the future.

## Acknowledgements

The authors acknowledge funding from the Biotechnology and Biological Sciences Research Council (BBSRC; BB/S004343/1 and BB/R008612/1) and Institute Strategic Programme grants (BBS/E/D/20002172, BBS/E/D/30002275 and BBS/E/D/10002070). The authors also acknowledge funding from Scottish Aquaculture Innovation Centre (Ref SL\_2017\_09) and the European Union's Framework programme H2020 under grant agreement 818367 (AquaIMPACT). The authors declare no conflict of interest. Finally, the authors would like to acknowledge the Aquaculture Research Collaborative Hub UK (ARCH-UK) for facilitating the platform used to initiate this review.

## Data availability statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

## References

- Abdelrahman H, ElHady M, Alcivar-Warren A, Allen S, Al-Tobasei R, Bao L *et al.* (2017) Aquaculture genomics, genetics and breeding in the United States: current status, challenges, and priorities for future research. *BMC Genomics* **18**: 191.
- Adams SL, Smith JF, Taylor J, McGowan LT, Tervit HR (2015) Cryopreservation of Greenshell™ mussel (*Perna canaliculus*) sperm. *Cryopreservation and Freeze-Drying Protocols*, pp. 329–336. Springer, New York. [https://link.springer.com/protocol/10.1007/978-1-4939-2193-5\\_14#citeas](https://link.springer.com/protocol/10.1007/978-1-4939-2193-5_14#citeas)
- Adamson E, Syvret M, Woolmer A (2018) *Shellfish Seed Supply for Aquaculture in the UK*. Report on Views Collected from the Industry in 2017, The Fishmongers' Company, London, 20 p.
- Addison J (2018) *Marine Stewardship Council (MSC) Year 2 Annual Surveillance Report*. Control Union Pesca Ltd, Lymington.
- Alexander KA, Gatward I, Parker A, Black K, Boardman A, Potts T *et al.* (2014) *An Assessment of the Benefits to Scotland of Aquaculture*. Scottish Government, Marine Scotland.
- Andersson L, Archibald AL, Bottema CD, Brauning R, Burgess SC, Burt DW *et al.* (2015) Coordinated international action to accelerate genome-to-phenome with FAANG, the Functional Annotation of Animal Genomes project. *Genome Biology* **16**: 57.
- Antrobus L (2017) *Torbay Council Harbour Committee Report*. Torbay Council, Torquay.
- AquaIMPACT (2019) AquaIMPACT. [Cited 25 Jan 2019.] Homepage, Available from URL: <https://www.luke.fi/AquaIMPACT>
- ARRAINA (2013) ARRAINA. [Cited 12 Dec 2016.] Homepage, Available from URL: <https://www.ARRAINA.eu/>

- Aslam ML, Boison SA, Lillehammer M, Norris A, Gjerde B (2020) Genome-wide association mapping and accuracy of predictions for amoebic gill disease in Atlantic salmon (*Salmo salar*). *Scientific Reports* **10**: 6435.
- Avdelas L, Avdic-Mravljic E, Borges Marques AC, Cano S, Capelle JJ, Carvalho N *et al.* (2020) The decline of mussel aquaculture in the European Union: causes, economic impacts and opportunities. *Reviews in Aquaculture* **13** (1): 91–118.
- Ayllon F, Kjaerner-Semb E, Furmanek T, Wennevik V, Solberg MF, Dahle G *et al.* (2015) The vgl3 locus controls age at maturity in wild and domesticated Atlantic Salmon (*Salmo salar* L.) males. *PLoS Genetics* **11**: e1005628.
- Bangera R, Ødegård J, Præbel AK, Mortensen A, Nielsen HM (2011) Genetic correlations between growth rate and resistance to vibriosis and viral nervous necrosis in Atlantic cod (*Gadus morhua* L.). *Aquaculture* **317**: 67–73.
- Baranski M, Moen T, Vage DI (2010) Mapping of quantitative trait loci for flesh colour and growth traits in Atlantic salmon (*Salmo salar*). *Genetics Selection Evolution* **42**: 17.
- Barson NJ, Aykanat T, Hindar K, Baranski M, Bolstad GH, Fiske P *et al.* (2015) Sex-dependent dominance at a single locus maintains variation in age at maturity in salmon. *Nature* **528**: 405–408.
- Bass D, Stentiford GD, Wang HC, Koskella B, Tyler CR (2019) The pathobiome in animal and plant diseases. *Trends in Ecology & Evolution* **34**: 996–1008.
- Baynes S, Verner-Jeffreys D, Howell B (2006) Research on finfish cultivation. *Science Series Technical Report (CEFAS, Lowestoft, UK)* **32**: 1–64.
- Beard TW, Richards PR, Wickins JF (1985) The techniques and practicability of year-round production of lobsters, *Homarus gammarus* (L.), in laboratory recirculation systems. Fisheries research technical report no. 79. Ministry of Agriculture, Fisheries and Food, Directorate of Fisheries Research. ISSN 0308-5589.
- Beardmore JA, Mair GC, Lewis RI (2001) Monosex male production in finfish as exemplified by tilapia: applications, problems, and prospects. *Aquaculture* **197**: 283–301.
- Beaumont AR (2008) Genetic studies of laboratory reared mussels, *Mytilus edulis*: heterozygote deficiencies, heterozygosity and growth. *Biological Journal of the Linnean Society* **44**: 273–285.
- Berthelot C, Brunet F, Chalopin D, Juanchich A, Bernard M, Noel B *et al.* (2014) The rainbow trout genome provides novel insights into evolution after whole-genome duplication in vertebrates. *Nature Communications* **5**: 3657.
- Black K, Hughes A (2017) *Future of the Sea: Trends in Aquaculture*. UK Government, Government Office for Science, London.
- Boison S, Ding J, Leder E, Gjerde B, Bergtun PH, Norris A *et al.* (2019) QTLs associated with resistance to cardiomyopathy syndrome in Atlantic Salmon. *Journal of Heredity* **110**: 727–737.
- Boore JL, Medina M, Rosenberg LA (2004) Complete sequences of the highly rearranged molluscan mitochondrial genomes of the Scaphopod Graptacme eborea and the bivalve *Mytilus edulis*. *Molecular Biology and Evolution* **21**: 1492–1503.
- Brader C (2020) *Gene Editing: Recent Developments and Scientific Status. Debate on 30 January 2020*. House of Lords, Library Briefing, Head of Research Services, House of Lords Library, London.
- British Trout Association (2019) Trout Farming in the UK and its history. [Cited 14 Nov 2019.] Available from URL: <https://britishtrout.co.uk/about-trout/trout-farming/>
- Brooker AJ, Papadopoulou A, Gutierrez C, Rey S, Davie A, Migaud H (2018) Sustainable production and use of cleaner fish for the biological control of sea lice: recent advances and current challenges. *The Veterinary Record* **183**: 383.
- Bye VJ, Lincoln RF (1986) Commercial methods for the control of sexual maturation in rainbow trout (*Salmo gairdneri* R.). *Aquaculture* **57**: 299–309.
- Cabrita E, Robles V, Alvarez R, Herráez M (2001) Cryopreservation of rainbow trout sperm in large volume straws: application to large scale fertilization. *Aquaculture* **201**: 301–314.
- Callet T, Médale F, Larroquet L, Surget A, Aguirre P, Kerneis T *et al.* (2017) Successful selection of rainbow trout (*Oncorhynchus mykiss*) on their ability to grow with a diet completely devoid of fishmeal and fish oil, and correlated changes in nutritional traits. *PLoS One* **12**: e0186705.
- Camara MD, Symonds JE (2014) Genetic improvement of New Zealand aquaculture species: programmes, progress and prospects. *New Zealand Journal of Marine and Freshwater Research* **48**: 466–491.
- Campbell NR, Harmon SA, Narum SR (2015) Genotyping-in-Thousands by sequencing (GT-seq): a cost effective SNP genotyping method based on custom amplicon sequencing. *Molecular Ecology Resources* **15**: 855–867.
- Capuzzo E, McKie T (2016) Seaweed in the UK and abroad—status, products, limitations, gaps and Cefas role, Defra. [Cited 18 Aug 2016.] Available from URL: <https://www.gov.uk/government/publications/the-seaweed-industry-in-the-uk-and-abroad>
- Carvalho N, Nielsen R, Guillen J (2018) *Scientific, Technical and Economic Committee for Fisheries (STECF) – Economic Report of the EU Aquaculture sector (STECF-18-19)*. European Union, Luxembourg.
- Charlesworth D, Willis JH (2009) The genetics of inbreeding depression. *Nature Reviews Genetics* **10**: 783–796.
- Christensen KA, Rondeau EB, Minkley DR, Leong JS, Nugent CM, Danzmann RG *et al.* (2018) The Arctic charr (*Salvelinus alpinus*) genome and transcriptome assembly. *PLoS One* **13**: e0204076.
- Clarkson M, Migaud H, Metochis C, Vera LM, Leeming D, Tocher DR *et al.* (2017) Early nutritional intervention can improve utilisation of vegetable-based diets in diploid and triploid Atlantic salmon (*Salmo salar* L.). *British Journal of Nutrition* **118**: 17–29.
- Declercq AM, Haesebrouck F, Van den Broeck W, Bossier P, Decostere A (2013) Columnaris disease in fish: a review with emphasis on bacterium-host interactions. *Veterinary Research* **44**: 27.

- DEFRA U (2015) *United Kingdom Multiannual National Plan for the Development of Sustainable Aquaculture*. Department for Environment Food & Rural Affairs, UK Government.
- Dégremont L (2011) Evidence of herpesvirus (OsHV-1) resistance in juvenile *Crassostrea gigas* selected for high resistance to the summer mortality phenomenon. *Aquaculture* **317**: 94–98.
- Dias PJ, Dordor A, Tulett D, Piernney S, Davies IM, Snow M (2009) Survey of mussel (*Mytilus*) species at Scottish shellfish farms. *Aquaculture Research* **40**: 1715–1722.
- Directive E (1996) Council Directive 96/22EC of 29 April 1996 concerning the prohibition on the use in stockfarming of certain substances having a hormonal other thyrostatic action and of beta-agonist, and repealing Directives 81/602, pp. 3–9.
- Doench JG (2018) Am I ready for CRISPR? A user's guide to genetic screens. *Nature Reviews Genetics* **19**: 67–80.
- Duncan NJ, Sonesson AK, Chavanne H (2013) 2 - Principles of finfish broodstock management in aquaculture: control of reproduction and genetic improvement. In: Allan G, Burnell G (eds) *Advances in Aquaculture Hatchery Technology*. pp. 23–75. Woodhead Publishing, Sawston, Cambridge.
- Dunham RA (2004) *Aquaculture and Fisheries Biotechnology: Genetic Approaches*. CABI Pub, Wallingford, Oxon, New York.
- ECJ (2018) Judgment of 25 July 2018, Confédération Paysanne a.o. ECLI:EU:C:2018:583.
- Ellis T, Turnbull JF, Knowles TG, Lines JA, Auchterlonie NA (2016) Trends during development of Scottish salmon farming: an example of sustainable intensification? *Aquaculture* **458**: 82–99.
- Espinal CA, Matulić D (2019) Recirculating aquaculture technologies. In: *Aquaponics Food Production Systems*, pp. 35–76. Springer, New York.
- Evensen Ø (2016) Development of fish vaccines: focusing on methods. In: Adams A (ed.) *Fish Vaccines*, pp. 53–74. Springer, Basel.
- FAO (2020a) *Fisheries and Aquaculture Software*. FishStatJ - Software for Fishery and Aquaculture Statistical Time Series. FAO Fisheries and Aquaculture Department, Rome.
- FAO (2020b) *The State of World Fisheries and Aquaculture 2020. Sustainability in Action*, p. 244. FAO, Rome, Italy.
- FDEA (2020) *Food and Drink Federation Exports Snapshot - Full Year 2019*. Food and Drink Federation, Holborn, London.
- FISHBOOST (2014) FISHBOOST homepage. [Cited 01 Feb 2014.] Available from URL: <http://www.fishboost.eu/>
- Fletcher R (2017) Welsh firm sets sights on global tilapia market. The Fish Site.
- Fletcher R (2019) Britain's prawn farming pioneers. The Fish Site.
- Fraslin C, Quillet E, Rochat T, Dechamp N, Bernardet J-F, Collet B *et al.* (2020) Combining multiple approaches and models to dissect the genetic architecture of resistance to infections in fish. *Front Genet* **11**: 677.
- Fujiya M (1970) Oyster farming in Japan. *Helgoländer wissenschaftliche Meeresuntersuchungen* **20**: 464–479.
- FutureEUAqua (2019) FutureEUAqua homepage. [Cited 1 Mar 2019.] Available from URL: <https://futureeuaqua.eu/>
- Gabian M, Moran P, Fernandez AI, Villanueva B, Chtioui A, Kent MP *et al.* (2019) Identification of genomic regions regulating sex determination in Atlantic salmon using high density SNP data. *BMC Genomics* **20**: 764.
- Gavery MR, Roberts SB (2017) Epigenetic considerations in aquaculture. *PeerJ* **5**: e4147.
- Geurden I, Borchert P, Balasubramanian MN, Schrama JW, Dupont-Nivet M, Quillet E *et al.* (2013) The positive impact of the early-feeding of a plant-based diet on its future acceptance and utilisation in rainbow trout. *PLoS One* **8**: e83162.
- Gilbert JA, Quinn RA, Debelius J, Xu ZZ, Morton J, Garg N *et al.* (2016) Microbiome-wide association studies link dynamic microbial consortia to disease. *Nature* **535**: 94–103.
- Giuffra E, Tuggle CK, Consortium F (2019) Functional Annotation of Animal Genomes (FAANG): current achievements and roadmap. *Annual Review of Animal Biosciences* **7**: 65–88.
- Gjedrem T (2010) The first family-based breeding program in aquaculture. *Reviews in Aquaculture* **2**: 2–15.
- Gjedrem T (2015) Disease resistant fish and shellfish are within reach: a review. *Journal of Marine Science and Engineering*. **3**: 146–153.
- Gjedrem T, Gjøen HM, Gjerde B (1991) Genetic origin of Norwegian farmed Atlantic salmon. *Aquaculture* **98**: 41–50.
- Gjedrem T, Robinson N, Rye M (2012) The importance of selective breeding in aquaculture to meet future demands for animal protein: a review. *Aquaculture* **350**: 117–129.
- Gjedrem T, Rye M (2018) Selection response in fish and shellfish: a review. *Reviews in Aquaculture* **10**: 168–179.
- Glencross BD, Baily J, Berntssen MHG, Hardy R, MacKenzie S, Tocher DR (2020) Risk assessment of the use of alternative animal and plant raw material resources in aquaculture feeds. *Reviews in Aquaculture* **12**: 703–758.
- Glover KA, Solberg MF, McGinnity P, Hindar K, Verspoor E, Coulson MW *et al.* (2017) Half a century of genetic interaction between farmed and wild Atlantic salmon: status of knowledge and unanswered questions. *Fish and Fisheries* **18**: 890–927.
- Godfray HCJ, Beddington JR, Crute IR, Haddad L, Lawrence D, Muir JF *et al.* (2010) Food security: the challenge of feeding 9 billion people. *Science* **327**: 812.
- Gonen S, Baranski M, Thorland I, Norris A, Grove H, Arnesen P *et al.* (2015) Mapping and validation of a major QTL affecting resistance to pancreas disease (salmonid alphavirus) in Atlantic salmon (*Salmo salar*). *Heredity (Edinb)* **115**: 405–414.
- Good C, Davidson J (2016) A review of factors influencing maturation of Atlantic Salmon, *Salmo salar*, with focus on water recirculation aquaculture system environments. *J World Aquacult Soc* **47**: 605–632.
- Gratacap RL, Jin YH, Mantsopoulou M, Houston RD (2020a) Efficient genome editing in multiple salmonid cell lines using ribonucleoprotein complexes. *Marine Biotechnology* **22**: 717–724.

- Gratacap RL, Regan T, Dehler CE, Martin SA, Boudinot P, Collet B *et al.* (2020b) Efficient CRISPR/Cas9 genome editing in a salmonid fish cell line using a lentivirus delivery system. *BMC Biotechnology* **20**: 1–9.
- Gratacap RL, Wargelius A, Edvardsen RB, Houston RD (2019) Potential of genome editing to improve aquaculture breeding and production. *Trends in Genetics* **35**: 672–684.
- Gulla S, Lund V, Kristoffersen AB, Sørum H, Colquhoun DJ (2016) vapA (A-layer) typing differentiates *Aeromonas salmonicida* subspecies and identifies a number of previously undescribed subtypes. *Journal of Fish Diseases* **39**: 329–342.
- Güralp H, Skaftnesmo KO, Kjærner-Semb E, Straume AH, Kleppe L, Schulz RW *et al.* (2020) Rescue of germ cells in dnd crispant embryos opens the possibility to produce inherited sterility in Atlantic salmon. *Scientific Reports* **10**: 18042.
- Gutierrez AP, Bean TP, Hooper C, Stenton CA, Sanders MB, Paley RK *et al.* (2018a) A genome-wide association study for host resistance to ostreid herpesvirus in Pacific Oysters (*Crassostrea gigas*). *G3 (Bethesda)* **8**: 1273–1280.
- Gutierrez AP, Lubieniecki KP, Davidson EA, Lien S, Kent MP, Fukui S *et al.* (2012) Genetic mapping of quantitative trait loci (QTL) for body-weight in Atlantic salmon (*Salmo salar*) using a 6.5 K SNP array. *Aquaculture* **358**: 61–70.
- Gutierrez AP, Lubieniecki KP, Fukui S, Withler RE, Swift B, Davidson WS (2014) Detection of Quantitative Trait Loci (QTL) related to grilising and late sexual maturation in Atlantic Salmon (*Salmo salar*). *Marine Biotechnology* **16**: 103–110.
- Gutierrez AP, Matika O, Bean TP, Houston RD (2018b) Genomic selection for growth traits in Pacific Oyster (*Crassostrea gigas*): potential of low-density marker panels for breeding value prediction. *Frontiers in Genetics* **9**: 391.
- Gutierrez AP, Turner F, Gharbi K, Talbot R, Lowe NR, Peñaloza C *et al.* (2017) Development of a medium density combined-species SNP array for Pacific and European Oysters. *G3 (Bethesda)* **7**: 2209–2218.
- Hambrey J, Evans S (2016) *Aquaculture in England, Wales and Northern Ireland: An Analysis of the Economic Contribution and Value of the Major Sub-Sectors and the Most Important Farmed Species*. The Seafish Domestic Aquaculture Strategy Programme, John Hambrey and, Sue Evans, Hambrey Consulting, Strathpeffer, UK.
- Hanna RE, Doench JG (2020) Design and analysis of CRISPR–Cas experiments. *Nature Biotechnology* **38**: 813–823.
- Hedgecock D, Shin G, Gracey AY, Den Berg DV, Samanta MP (2015) Second-generation linkage maps for the Pacific Oyster *Crassostrea gigas* reveal errors in assembly of genome scaffolds. *G3 (Bethesda)* **5**: 2007–2019.
- Herbert RJH, Humphreys J, Davies CJ, Roberts C, Fletcher S, Crowe TP (2016) Ecological impacts of non-native Pacific oysters (*Crassostrea gigas*) and management measures for protected areas in Europe. *Biodiversity and Conservation* **25**: 2835–2865.
- Hersoug B (2015) The greening of Norwegian salmon production. *Maritime Studies* **14**: 16.
- Hickey JM, Chiurugwi T, Mackay I, Powell W, Eggen A, Kilian A *et al.* (2017) Genomic prediction unifies animal and plant breeding programs to form platforms for biological discovery. *Nature Genetics* **49**: 1297–1303.
- Hill WG (2013) On estimation of genetic variance within families using genome-wide identity-by-descent sharing. *Genetics Selection Evolution* **45**: 32.
- Hindar K, Fleming IA, McGinnity P, Diserud O (2006) Genetic and ecological effects of salmon farming on wild salmon: modelling from experimental results. *ICES Journal of Marine Science* **63**: 1234–1247.
- Hines CW, Fang YC, Chan VKS, Stiller KT, Brauner CJ, Richards JG (2019) The effect of salinity and photoperiod on thermal tolerance of Atlantic and coho salmon reared from smolt to adult in recirculating aquaculture systems. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology* **230**: 1–6.
- Hoare R (2018) Improving disease resistance in Atlantic salmon and Rainbow trout to *Flavobacterium psychrophilum*, the causative agent of Rainbow Trout Fry Syndrome (RTFS). [Cited 1 Jan 2018.] Available from URL: <https://www.stir.ac.uk/research/hub/contract/349159>
- Hollenbeck CM, Johnston IA (2018) Genomic tools and selective breeding in molluscs. *Frontiers in Genetics* **9**: 253.
- Hornick KM, Plough LV (2019) Tracking genetic diversity in a large-scale oyster restoration program: effects of hatchery propagation and initial characterization of diversity on restored vs. wild reefs. *Heredity* **123**: 92–105.
- Houston RD, Bean TP, Macqueen DJ, Gundappa MK, Jin YH, Jenkins TL *et al.* (2020) Harnessing genomics to fast-track genetic improvement in aquaculture. *Nature Reviews Genetics* **21**: 389–409.
- Houston RD, Haley CS, Hamilton A, Guy DR, Tinch AE, Taggart JB *et al.* (2008) Major quantitative trait loci affect resistance to infectious pancreatic necrosis in Atlantic salmon (*Salmo salar*). *Genetics* **178**: 1109–1115.
- Houston RD, Haley CS, Hamilton A, Guy DR, Mota-Velasco JC, Gheyas AA *et al.* (2010) The susceptibility of Atlantic salmon fry to freshwater infectious pancreatic necrosis is largely explained by a major QTL. *Heredity* **105**: 318–327.
- Houston RD, Macqueen DJ (2019) Atlantic salmon (*Salmo salar* L.) genetics in the 21st century: taking leaps forward in aquaculture and biological understanding. *Animal Genetics* **50**: 3–14.
- Houston RD, Taggart JB, Cézard T, Bekaert M, Lowe NR, Downing A *et al.* (2014) Development and validation of a high density SNP genotyping array for Atlantic salmon (*Salmo salar*). *BMC Genomics* **15**: 90.
- Hughes AD, Black KD, Campbell I, Davidson K, Kelly MS, Stanley MS (2012) Does seaweed offer a solution for bioenergy with biological carbon capture and storage? *Greenhouse Gases: Science and Technology* **2**: 402–407.
- Hughes JT, Sullivan JJ, Shleser R (1972) Enhancement of lobster growth. *Science* **177**: 1110–1111.

- Ignatz EH, Braden LM, Benfey TJ, Caballero-Solares A, Hori TS, Runighan CD *et al.* (2020) Impact of rearing temperature on the innate antiviral immune response of growth hormone transgenic female triploid Atlantic salmon (*Salmo salar*). *Fish & Shellfish Immunology* **97**: 656–668.
- Imslund AK, Reynolds P, Eliassen G, Mortensen A, Hansen ØJ, Puvanendran V *et al.* (2016) Is cleaning behaviour in lumpfish (*Cyclopterus lumpus*) parentally controlled? *Aquaculture* **459**: 156–165.
- James MA, Slaski R (2006) Appraisal of the opportunity for off-shore aquaculture in UK waters. In: Report of Project FC0934. DEFRA and Seafish from FRM Ltd, p. 119.
- Janssen K, Chavanne H, Berentsen P, Komen H (2017) Impact of selective breeding on European aquaculture. *Aquaculture* **472**: 8–16.
- Jenkins TL, Ellis CD, Triantafyllidis A, Stevens JR (2019) Single nucleotide polymorphisms reveal a genetic cline across the north-east Atlantic and enable powerful population assignment in the European lobster. *Evolutionary Applications* **12**: 1881–1899.
- Jin YH, Liao B, Migaud H, Davie A (2020) Physiological impact and comparison of mutant screening methods in piwi2 KO founder Nile tilapia produced by CRISPR/Cas9 system. *Scientific Reports*, **10** (1), <http://dx.doi.org/10.1038/s41598-020-69421-0>.
- Johnstone R, Simpson TH, Youngson AF, Whitehead C (1979) Sex reversal in salmonid culture: Part II. The progeny of sex-reversed rainbow trout. *Aquaculture* **18**: 13–19.
- Jokumsen A, Svendsen LM (2010) *Farming of Freshwater Rainbow Trout in Denmark*. Aqua-rapport, DTU Aqua, Lyngby.
- Jones CS, Lockyer AE, Verspoor E, Secombes CJ, Noble LR (2002) Towards selective breeding of Atlantic salmon for sea louse resistance: approaches to identify trait markers. *Pest Management Science* **58**: 559–568.
- Jonsson B, Jonsson N (2014) Early environment influences later performance in fishes. *Journal of Fish Biology* **85**: 151–188.
- Kamermans P, Galley T, Boudry P, Fuentes J, McCombie H, Batista FM *et al.* (2013) Blue mussel hatchery technology in Europe. In: Allan G, Burnell G (eds) *Advances in Aquaculture Hatchery Technology*, pp. 339–373. Sawston, Cambridge: Elsevier.
- Knott GJ, Doudna JA (2018) CRISPR-Cas guides the future of genetic engineering. *Science* **361**: 866–869.
- Knutsen TM, Kirubakaran GT, Mommens M, Moen T (2019) *Lumpfish (Cyclopterus lumpus) Draft Genome Assembly*. Aqua-gen AS, Trondheim.
- Kok B, Malcorps W, Tlustý MF, Eltholth MM, Auchterlonie NA, Little DC *et al.* (2020) Fish as feed: using economic allocation to quantify the Fish In:Fish Out ratio of major fed aquaculture species. *Aquaculture* **528**, 735474.
- Kolstad K, Thorland I, Refstie T, Gjerde B (2006) Genetic variation and genotype by location interaction in body weight, spinal deformity and sexual maturity in Atlantic cod (*Gadus morhua*) reared at different locations off Norway. *Aquaculture* **259**: 66–73.
- Kriaridou C, Tsairidou S, Houston RD, Robledo D (2020) Genomic prediction using low density marker panels in aquaculture: performance across species, traits, and genotyping platforms. *Frontiers in Genetics* **11**.
- Lallias D, Arzul I, Heurtebise S, Ferrand S, Chollet B, Robert M *et al.* (2008) Bonamia ostreae-induced mortalities in one-year old European flat oysters *Ostrea edulis*: experimental infection by cohabitation challenge. *Aquatic Living Resources* **21**: 423–439.
- Lallias D, Lapègue S, Hecquet C, Boudry P, Beaumont AR (2007) AFLP-based genetic linkage maps of the blue mussel (*Mytilus edulis*). *Animal Genetics* **38**: 340–349.
- Le Bras Y, Dechamp N, Krieg F, Filangi O, Guyomard R, Bous-saha M *et al.* (2011) Detection of QTL with effects on osmoregulation capacities in the rainbow trout (*Oncorhynchus mykiss*). *BMC Genetics* **12**: 46.
- Leclercq E, Davie A, Migaud H (2014) Delousing efficiency of farmed ballan wrasse (*Labrus bergylta*) against *Lepeophtheirus salmonis* infecting Atlantic salmon (*Salmo salar*) post-smolts. *Pest Management Science* **70**: 1274–1282.
- Leclercq E, Taylor JF, Hunter D, Migaud H (2010) Body size dimorphism of sea-reared Atlantic salmon (*Salmo salar* L.): Implications for the management of sexual maturation and harvest quality. *Aquaculture* **301**: 47–56.
- Lewis RC (1944) Selective breeding of rainbow trout at Hot Creek Hatchery. *California Fish and Game* **30**, 95–97.
- Lhorente JP, Araneda M, Neira R, Yáñez JM (2019) Advances in genetic improvement for salmon and trout aquaculture: the Chilean situation and prospects. *Reviews in Aquaculture* **11**: 340–353.
- Li B, Clohisey SM, Chia BS, Wang B, Cui A, Eisenhaure T *et al.* (2020a) Genome-wide CRISPR screen identifies host dependency factors for influenza A virus infection. *Nature Communications* **11**: 164.
- Li R, Zhang W, Lu J, Zhang Z, Mu C, Song W *et al.* (2020b) The whole-genome sequencing and hybrid assembly of *Mytilus coruscus*. *Frontiers in Genetics* **11**.
- Lie KK, Tørresen OK, Solbakken MH, Rønnestad I, Tooming-Klunderud A, Nederbragt AJ *et al.* (2018) Loss of stomach, loss of appetite? Sequencing of the ballan wrasse (*Labrus bergylta*) genome and intestinal transcriptomic profiling illuminate the evolution of loss of stomach function in fish. *BMC Genomics* **19**: 186.
- Lien S, Koop BF, Sandve SR, Miller JR, Kent MP, Nome T *et al.* (2016) The Atlantic salmon genome provides insights into rediploidization. *Nature* **533**: 200–205.
- Kong N, Li Q, Yu H, Kong LF (2015) Heritability estimates for growth-related traits in the Pacific oyster (*Crassostrea gigas*) using a molecular pedigree. *Aquaculture Research*, **46** (2), 499–508. <http://dx.doi.org/10.1111/are.12205>.
- Lincoln R, Scott A (1983) Production of all-female triploid rainbow trout. *Aquaculture* **30**: 375–380.
- Liu S, Vallejo RL, Evenhuis JP, Martin KE, Hamilton A, Gao G *et al.* (2018) Retrospective evaluation of marker-assisted selection for resistance to bacterial cold water disease in three



- generations of a commercial rainbow trout breeding population. *Frontiers in Genetics* **9**: 286.
- López ME, Linderroth T, Norris A, Lhorente JP, Neira R, Yáñez JM (2019) Multiple selection signatures in farmed Atlantic salmon adapted to different environments across hemispheres. *Frontiers in Genetics* **10**: 901.
- Macqueen DJ, Primmer CR, Houston RD, Nowak BF, Bernatchez L, Bergseth S *et al.* (2017) Functional Annotation of All Salmonid Genomes (FAASG): an international initiative supporting future salmonid research, conservation and aquaculture. *BMC Genomics* **18**.
- Martos-Sitcha JA, Mancera JM, Prunet P, Magnoni LJ (2020) Editorial: Welfare and stressors in fish: Challenges facing aquaculture. *Frontiers in Physiology*, **11**. <http://dx.doi.org/10.3389/fphys.2020.00162>
- Mair G, Abella T (1997) *Technoguide on the Production of Genetically Male Tilapia (GMT)*. PHIL-FISHGEN, Freshwater Aquaculture Center, Central Luzon State University, Philippines.
- Marine Management Organisation (2013) *Strategic Scoping Report August 2013*. UK Government, London.
- Marine Scotland Directorate (2020) Salmon Ova imports data: EIR release. In: *Information Request and Response Under the Environmental Information (Scotland) Regulations 2004*. Scottish Government, Edinburgh.
- Mehmet S (2020) Survey suggests public concerns remain over safety of GM foods. [Cited 7 Jan 2020.] Available from URL: <https://www.newfoodmagazine.com/news/101598/survey-suggests-public-concerns-remain-over-safety-of-gm-foods/>
- Meuwissen TH, Hayes BJ, Goddard ME (2001) Prediction of total genetic value using genome-wide dense marker maps. *Genetics* **157**: 1819–1829.
- Meuwissen THE, Odegard J, Andersen-Ranberg I, Grindflek E (2014) On the distance of genetic relationships and the accuracy of genomic prediction in pig breeding. *Genetics Selection Evolution* **46**: 49.
- Michalek K, Ventura A, Sanders T (2016) *Mytilus* hybridisation and impact on aquaculture: a minireview. *Marine Genomics* **27**: 3–7.
- Middlemiss KL, Daniels CL, Urbina MA, Wilson RW (2015) Combined effects of UV irradiation, ozonation, and the probiotic *Bacillus* spp. on growth, survival, and general fitness in European lobster (*Homarus gammarus*). *Aquaculture* **444**: 99–107.
- Migaud H, Houston R (2017) ARCH-UK Working Group Report. In: *Report from Working Group 5: Stock Improvement*. Aquaculture Research Collaborative Hub Aquaculture Research Collaborative Hub.
- Moen T, Baranski M, Sonesson AK, Kjøglum S (2009) Confirmation and fine-mapping of a major QTL for resistance to infectious pancreatic necrosis in Atlantic salmon (*Salmo salar*): population-level associations between markers and trait. *BMC Genomics* **10**: 368.
- Moen T, Sonesson AK, Hayes B, Lien S, Munck H, Meuwissen TH (2007) Mapping of a quantitative trait locus for resistance against infectious salmon anaemia in Atlantic salmon (*Salmo salar*): comparing survival analysis with analysis on affected/resistant data. *BMC Genetics* **8**: 53.
- Moore SK, Trainer VL, Mantua NJ, Parker MS, Laws EA, Backer LC *et al.* (2008) Impacts of climate variability and future climate change on harmful algal blooms and human health. *Environmental Health* **7**: S4.
- Mowi (2019) *Salmon Farming Industry Handbook 2019*. Mowi, Bergen.
- Munro A, Waddell I, Elson K (1979) *Report of the Growth of Scottish Salmonid Fish Farms and their Production and Manpower in 1979*. Department of Agriculture and Fisheries for Scotland, London.
- Munro LA (2019) *Scottish Fish Farm Production Survey 2018*. Scottish Government, Marine Scotland Science, Aberdeen.
- Munro LA (2020) *Scottish Shellfish Farm Production Survey 2019*. Scottish Government, Marine Scotland Science, Aberdeen.
- Murphy D (2015) Import data: live fish from EU to England and Wales 2013 and 2014 CEFAS. Cefas, Weymouth. [Cited 6 Nov 2015.] Available from URL: <https://marinescience.blog.gov.uk/2015/11/06/import-data-fish-fish-eu-england-wales/>
- Napier JA, Haslam RP, Olsen R-E, Tocher DR, Betancor MB (2020) Agriculture can help aquaculture become greener. *Nature Food* **1**: 680–683.
- Nash CE (2011) *The History of Aquaculture*. Blackwell Publishing Ltd., John Wiley & Sons, Hoboken, NJ.
- Norris A (2017) Application of genomics in salmon aquaculture breeding programs by Ashie Norris: who knows where the genomic revolution will lead us? *Marine Genomics* **36**: 13–15.
- Ødegård J, Baranski M, Gjerde B, Gjerdem T (2011) Methodology for genetic evaluation of disease resistance in aquaculture species: challenges and future prospects. *Aquaculture Research* **42**: 103–114.
- Ødegård J, Meuwissen THE (2012) Estimation of heritability from limited family data using genome-wide identity-by-descent sharing. *Genetics Selection Evolution* **44**: 16.
- Ødegård J, Meuwissen TH (2014) Identity-by-descent genomic selection using selective and sparse genotyping. *Genetics Selection Evolution* **46**: 1–8.
- Ødegård J, Sommer A-I, Præbel AK (2010) Heritability of resistance to viral nervous necrosis in Atlantic cod (*Gadus morhua* L.). *Aquaculture* **300**: 59–64.
- Orkney Shellfish Hatchery (2020) Orkney shellfish hatchery. [Cited 1 Oct 2020.] Available from URL: <https://www.orkneyshellfishhatchery.co.uk/>
- Orrego R (2015) Repositioning British trout in the market place FishFarmingExpert. [Cited 19 Jun 2015.] <https://www.fishfarmingexpert.com/article/repositioning-british-trout-in-the-market-place/>
- Palaiokostas C, Bekaert M, Davie A, Cowan ME, Oral M, Taggart JB *et al.* (2013) Mapping the sex determination locus in the Atlantic halibut (*Hippoglossus hippoglossus*) using RAD sequencing. *BMC Genomics* **14**.
- Paredes E, Adams S, Tervit H, Smith J, McGowan L, Gale S *et al.* (2012) Cryopreservation of Greenshell™ mussel (*Perna canaliculus*) trochophore larvae. *Cryobiology* **65**: 256–262.

- Pasquier J, Cabau C, Nguyen T, Jouanno E, Severac D, Braasch I *et al.* (2016) Gene evolution and gene expression after whole genome duplication in fish: the PhyloFish database. *BMC Genomics* **17**: 368.
- Pedersen S, Berg PR, Culling M, Danzmann RG, Glebe B, Leadbeater S *et al.* (2013) Quantitative trait loci for precocious parr maturation, early smoltification, and adult maturation in double-backcrossed trans-Atlantic salmon (*Salmo salar*). *Aquaculture* **410**: 164–171.
- Plough LV (2016) Genetic load in marine animals: a review. *Current Zoology* **62**: 567–579.
- Plough LV, Shin G, Hedgecock D (2016) Genetic inviability is a major driver of type III survivorship in experimental families of a highly fecund marine bivalve. *Molecular Ecology* **25**: 895–910.
- Pogoda B, Brown J, Hancock B, Preston J, Pouvreau S, Kammernans P *et al.* (2019) The Native Oyster Restoration Alliance (NORA) and the Berlin Oyster Recommendation: bringing back a key ecosystem engineer by developing and supporting best practice in Europe. *Aquatic Living Resources* **32**: 13.
- Pottinger TG, Carrick TR (1999) Modification of the plasma cortisol response to stress in rainbow trout by selective breeding. *General and Comparative Endocrinology* **116**: 122–132.
- Pottinger T, Pickering A (2011) Genetic basis to the stress response: selective breeding for stress-tolerant fish. In: Iwama GK, Pickering AD, Sumpter JP, Schreck CB (eds) *Fish Stress and Health in Aquaculture*, pp. 171–195. Cambridge University Press, Cambridge, UK.
- Pountney SM, Lein I, Migaud H, Davie A (2020) High temperature is detrimental to captive lumpfish (*Cyclopterus lumpus*, L.) reproductive performance. *Aquaculture* **522**: 735121.
- Preston AC, Taylor JF, Craig B, Bozzolla P, Penman DJ, Migaud H (2013) Optimisation of triploidy induction in brown trout (*Salmo trutta* L.). *Aquaculture* **414–415**: 160–166.
- Prou J, Gouilletquer P (2002) The French mussel industry: present status and perspectives. *Bulletin-Aquaculture Association of Canada* **102**, 17–23.
- Proudfoot C, Lillico S, Tait-Burkard C (2019) Genome editing for disease resistance in pigs and chickens. *Animal Frontiers* **9**: 6–12.
- Puvanendran V, Mortensen A (2009) 24 - Farming cod and halibut: biological and technological advances in two emerging cold-water marine finfish aquaculture species. In: Burnell G, Allan G (eds) *New Technologies in Aquaculture*, pp. 771–803. Woodhead Publishing, Sawston, Cambridge.
- Qi H, Song K, Li C, Wang W, Li B, Li L *et al.* (2017) Construction and evaluation of a high-density SNP array for the Pacific oyster (*Crassostrea gigas*). *PLoS One* **12**: e0174007.
- Quinton CD, Kause A, Koskela J, Ritola O (2007) Breeding salmonids for feed efficiency in current fishmeal and future plant-based diet environments. *Genetics Selection Evolution* **39**: 431.
- Reid DP, Smith C-A, Rommens M, Blanchard B, Martin-Robichaud D, Reith M (2007) A genetic linkage map of Atlantic halibut (*Hippoglossus hippoglossus* L.). *Genetics* **177**: 1193.
- Reid DP, Szanto A, Glebe B, Danzmann RG, Ferguson MM (2005) QTL for body weight and condition factor in Atlantic salmon (*Salmo salar*): comparative analysis with rainbow trout (*Oncorhynchus mykiss*) and Arctic charr (*Salvelinus alpinus*). *Heredity* **94**: 166–172.
- Reith M, Reid D, Martin-Robichaud D, Benfey T (2011) Genetic and genomic approaches to Atlantic halibut broodstock management. *Aquaculture Biotechnology*.
- Robinson N, Winberg P, Kirkendale L (2013) Genetic improvement of macroalgae: status to date and needs for the future. *Journal of Applied Phycology* **25**: 703–716.
- Robinson O (2015) *British Trout Farming - Overview for English Aquaculture Consultation Group*. Seafish, Edinburgh/Grimsby.
- Robledo D, Gutiérrez AP, Barriá A, Lhorente JP, Houston RD, Yáñez JM (2019) Discovery and functional annotation of quantitative trait loci affecting resistance to sea lice in Atlantic Salmon. *Frontiers in Genetics* **10**: 56.
- Robledo D, Hamilton A, Gutiérrez AP, Bron JE, Houston RD (2020) Characterising the mechanisms underlying genetic resistance to amoebic gill disease in Atlantic salmon using RNA sequencing. *BMC Genomics* **21**: 271.
- Robledo D, Taggart JB, Ireland JH, McAndrew BJ, Starkey WG, Haley CS *et al.* (2016) Gene expression comparison of resistant and susceptible Atlantic salmon fry challenged with Infectious Pancreatic Necrosis virus reveals a marked contrast in immune response. *BMC Genomics* **17**: 279.
- Rodríguez FH, Flores-Mara R, Yoshida GM, Barriá A, Jedlicki AM, Lhorente JP *et al.* (2019) Genome-wide association analysis for resistance to infectious pancreatic necrosis virus identifies candidate genes involved in viral replication and immune response in rainbow trout (*Oncorhynchus mykiss*). *G3 (Bethesda)* **9**: 2897–2904.
- Rodríguez-Riveiro R, Heres P, Troncoso J, Paredes E (2019) Long term survival of cryopreserved mussel larvae (*Mytilus galloprovincialis*). *Aquaculture* **512**: 734326.
- Rusk AB, Alfaro AC, Young T, Watts E, Adams SL (2020) Development stage of cryopreserved mussel (*Perna canaliculus*) larvae influences post-thaw impact on shell formation, organogenesis, neurogenesis, feeding ability and survival. *Cryobiology* **93**: 121–132.
- Sae-Lim P, Gjerde B, Nielsen HM, Mulder H, Kause A (2016) A review of genotype-by-environment interaction and micro-environmental sensitivity in aquaculture species. *Reviews in Aquaculture* **8**: 369–393.
- SAIC (2017) *Improving Disease Resistance in Atlantic Salmon and Rainbow Trout to Flavobacterium psychrophilum*. Scottish Aquaculture Innovation Centre, Stirling.
- SAIC (2019a) *AQUALEAP: Innovation in Genetics & Breeding to Advance UK Aquaculture Production*. Scottish Aquaculture Innovation Centre, Stirling.
- SAIC (2019b) *Scottish Consortium Takes Giant Leap Forward for Salmon Gill Health*. Scottish Aquaculture Innovation Centre, Scottish Aquaculture Innovation Centre, Stirling, UK.
- Scott AG, Penman DJ, Beardmore JA, Skibinski DOF (1989) The 'YY' supermale in *Oreochromis niloticus* (L.) and its potential in aquaculture. *Aquaculture* **78**: 237–251.

- Huntington T, Cappell R (2015) English Aquaculture Strategy. Final Report. Produced by Poseidon Aquatic Resources Management Ltd for the Seafish Industry Authority. 80 pp + appendices. Seafish, Edinburgh.
- Shaw J (1840) XXVII.—Account of experimental observations on the development and growth of salmon-fry, from the exclusion of the Ova to the age of two years. *Earth and Environmental Science Transactions of The Royal Society of Edinburgh* **14**: 547–566.
- Shen Y, Yue G (2019) Current status of research on aquaculture genetics and genomics-information from ISGA 2018. *Aquaculture and Fisheries* **4**: 43–47.
- Shen ZG, Wang HP (2018) Environmental sex determination and sex differentiation in teleost—how sex is established. In: Wang HP, Piferrer F, Chen SL (eds) *Sex Control in Aquaculture: Theory and Practice (Chapter 4)*. Wiley-Blackwell, Hoboken, NJ. Available from URL: <https://doi.org/10.1002/9781119127291.ch4>
- Silva RMO, Evenhuis JP, Vallejo RL, Tsuruta S, Wiens GD, Martin KE *et al.* (2018) Variance and covariance estimates for resistance to bacterial cold water disease and columnaris disease in two rainbow trout breeding populations1. *Journal of Animal Science* **97**: 1124–1132.
- Silva RMO, Evenhuis JP, Vallejo RL, Gao G, Martin KE, Leeds TD *et al.* (2019) Whole-genome mapping of quantitative trait loci and accuracy of genomic predictions for resistance to columnaris disease in two rainbow trout breeding populations. *Genetics Selection Evolution* **51**: 42.
- Small DP, Calosi P, Boothroyd D, Widdicombe S, Spicer JI (2015) Stage-specific changes in physiological and life-history responses to elevated temperature and Pco2 during the larval development of the European Lobster *Homarus gammarus* (L.). *Physiological and Biochemical Zoology* **88**: 494–507.
- STECF STaECff (2018) *Economic Report of the EU Aquaculture Sector*. Publications Office of the European Union, Luxembourg.
- Stentiford GD, Sritunyalucksana K, Flegel TW, Williams BAP, Withyachumnarnkul B, Itsathitphaisarn O *et al.* (2017) New paradigms to help solve the global aquaculture disease crisis. *PLoS Path* **13**: e1006160.
- Strömberg T, Nielsen MV (1989) Heritability of growth in larvae and juveniles of *Mytilus edulis*. *Aquaculture* **80**: 1–6.
- Suquet M, Labbé C, Puyo S, Mingant C, Quittet B, Boulais M *et al.* (2014) Survival, growth and reproduction of cryopreserved larvae from a marine invertebrate, the Pacific oyster (*Crassostrea gigas*). *PLoS One* **9**: e93486.
- Symonds JE, Clarke SM, King N, Walker SP, Blanchard B, Sutherland D *et al.* (2019) Developing successful breeding programs for New Zealand aquaculture: a perspective on progress and future genomic opportunities. *Frontiers in Genetics* **10**.
- Tan K, Zhang H, Zheng H (2020) Selective breeding of edible bivalves and its implication of global climate change. *Reviews in Aquaculture* **12**: 2559–2572.
- Taylor JF, Needham MP, North BP, Morgan A, Thompson K, Migaud H (2007) The influence of ploidy on saltwater adaptation, acute stress response and immune function following seawater transfer in non-smolting rainbow trout. *General and Comparative Endocrinology* **152**: 314–325.
- Taylor JF, Sambras F, Mota-Velasco J, Guy DR, Hamilton A, Hunter D *et al.* (2013) Ploidy and family effects on Atlantic salmon (*Salmo salar*) growth, deformity and harvest quality during a full commercial production cycle. *Aquaculture* **410**: 41–50.
- Taylor JF, Waagbo R, Diez-Padrisa M, Campbell P, Walton J, Hunter D *et al.* (2015) Adult triploid Atlantic salmon (*Salmo salar*) have higher dietary histidine requirements to prevent cataract development in seawater. *Aquaculture Nutrition* **21**: 18–32.
- Teletchea F, Fontaine P (2014) Levels of domestication in fish: implications for the sustainable future of aquaculture. *Fish and Fisheries* **15**: 181–195.
- The Scottish Government (2017) *A Nation with Ambition: The Government's Programme for Scotland 2017–2018*. APS Group Scotland, Edinburgh.
- Thresher RE, Hayes K, Bax NJ, Teem J, Benfey TJ, Gould F (2014) Genetic control of invasive fish: technological options and its role in integrated pest management. *Biological Invasions* **16**: 1201–1216.
- Tine M, Kuhl H, Gagnaire P-A, Louro B, Desmarais E, Martins RST *et al.* (2014) European sea bass genome and its variation provide insights into adaptation to euryhalinity and speciation. *Nature Communications* **5**: 5770.
- Treasurer J (2018) *Cleaner fish Biology and Aquaculture Applications*, 5th edn. Publishing Ltd.
- Troutex ApS (2019) Troutex. [Cited 26 Oct 2020.] Available from URL: <https://troutex.dk/en/about.html>
- Tsai HY, Hamilton A, Tinch AE, Guy DR, Gharbi K, Stear MJ *et al.* (2015) Genome wide association and genomic prediction for growth traits in juvenile farmed Atlantic salmon using a high density SNP array. *BMC Genomics* **16**.
- Tsai HY, Hamilton A, Tinch AE, Guy DR, Bron JE, Taggart JB *et al.* (2016) Genomic prediction of host resistance to sea lice in farmed Atlantic salmon populations. *Genetics Selection Evolution* **48**.
- Tsai H-Y, Matika O, Edwards SM, Antolín-Sánchez R, Hamilton A, Guy DR *et al.* (2017) Genotype imputation to improve the cost-efficiency of genomic selection in farmed Atlantic salmon. *G3: Genes|Genomes|Genetics* **7**: 1377.
- Tsairidou S, Hamilton A, Robledo D, Bron JE, Houston RD (2020) Optimizing low-cost genotyping and imputation strategies for genomic selection in Atlantic salmon. *G3: Genes|Genomes|Genetics* **10**: 581.
- Ulrich K, Wehner S, Bekaert M, Di Paola N, Dilcher M, Muir KF *et al.* (2018) Molecular epidemiological study on Infectious Pancreatic Necrosis Virus isolates from aquafarms in Scotland over three decades. *Journal of General Virology* **99**: 1567–1581.

- Uren Webster TM, Consuegra S, Hitchings M, Garcia de Leaniz C (2018) Interpopulation variation in the Atlantic salmon microbiome reflects environmental and genetic diversity. *Applied and Environmental Microbiology* **84**.
- Vallejo RL, Leeds TD, Gao G, Parsons JE, Martin KE, Evenhuis JP *et al.* (2017) Genomic selection models double the accuracy of predicted breeding values for bacterial cold water disease resistance compared to a traditional pedigree-based model in rainbow trout aquaculture. *Genetics Selection Evolution* **49**: 17.
- Vandeputte M, Haffray P (2014) Parentage assignment with genomic markers: a major advance for understanding and exploiting genetic variation of quantitative traits in farmed aquatic animals. *Frontiers in Genetics* **5**.
- Varney RL, Watts JC, Wilbur AE (2018) Genetic impacts of a commercial aquaculture lease on adjacent oyster populations. *Aquaculture* **491**: 310–320.
- Vera LM, Hamre K, Espe M, Hemre G-I, Skjærven K, Lock E-J *et al.* (2020) Higher dietary micronutrients are required to maintain optimal performance of Atlantic salmon (*Salmo salar*) fed a high plant material diet during the full production cycle. *Aquaculture* **528**, 735551.
- Vera LM, Metochis C, Taylor JF, Clarkson M, Skjærven KH, Migaud H *et al.* (2017) Early nutritional programming affects liver transcriptome in diploid and triploid Atlantic salmon, *Salmo salar*. *BMC Genomics* **18**: 886.
- Vera M, Pardo BG, Cao A, Vilas R, Fernandez C, Blanco A *et al.* (2019) Signatures of selection for bonamiosis resistance in European flat oyster (*Ostrea edulis*): new genomic tools for breeding programs and management of natural resources. *Evolutionary Applications* **12**: 1781–1796.
- Verta J-P, Debes PV, Piavchenko N, Ruokolainen A, Ovaskainen O, Moustakas-Verho JE *et al.* (2020) *Cis*-regulatory differences in isoform expression associate with life history strategy variation in Atlantic salmon. *bioRxiv* 777300.
- Walker AJ (2009) *Scottish Fish Farm Production Survey 2009*. Marine Scotland, Aberdeen.
- Waltz E (2017) First genetically engineered salmon sold in Canada. *Nature* **548**: 148.
- Wargelius A (2019) Application of genome editing in aquatic farm animals: Atlantic salmon. *Transgenic Research* **28**: 101–105.
- Wargelius A, Leininger S, Skaftnesmo KO, Kleppe L, Andersson E, Taranger GL *et al.* (2016) Dnd knockout ablates germ cells and demonstrates germ cell independent sex differentiation in Atlantic salmon. *Scientific Reports* **6**.
- Wasmer M (2019) Roads forward for European GMO Policy—uncertainties in wake of ECJ judgment have to be mitigated by regulatory reform. *Frontiers in Bioengineering and Biotechnology* **7**.
- Wilson J, Matejusova I, McIntosh RE, Carboni S, Bekaert M (2018) New diagnostic SNP molecular markers for the *Mytilus* species complex. *PLoS One* **13**: e0200654.
- Wood D, Capuzzo E, Kirby D, Mooney-McAuley K, Kerrison P (2017) UK macroalgae aquaculture: what are the key environmental and licensing considerations? *Marine Policy* **83**: 29–39.
- Xu P, Zhang X, Wang X, Li J, Liu G, Kuang Y *et al.* (2014) Genome sequence and genetic diversity of the common carp, *Cyprinus carpio*. *Nature Genetics* **46**: 1212–1219.
- Yáñez JM, Houston RD, Newman S (2014a) Genetics and genomics of disease resistance in salmonid species. *Frontiers in Genetics* **5**: 415.
- Yáñez JM, Lhorente JP, Bassini LN, Oyarzún M, Neira R, Newman S (2014b) Genetic co-variation between resistance against both *Caligus rogercresceyi* and *Piscirickettsia salmonis*, and body weight in Atlantic salmon (*Salmo salar*). *Aquaculture* **433**: 295–298.
- Yáñez JM, Newman S, Houston RD (2015) Genomics in aquaculture to better understand species biology and accelerate genetic progress. *Frontiers in Genetics* **6**: 128. <https://doi.org/10.3389/fgene.2015.00128>
- Yang H, Hu E, Buchanan JT, Tiersch TR (2018) A Strategy for sperm cryopreservation of Atlantic salmon, *Salmo salar*, for remote commercial-scale high-throughput processing. *Journal of the World Aquaculture Society* **49**: 96–112.
- Yaskowiak ES, Shears MA, Agarwal-Mawal A, Fletcher GL (2006) Characterization and multi-generational stability of the growth hormone transgene (EO-1 $\alpha$ ) responsible for enhanced growth rates in Atlantic Salmon. *Transgenic Research* **15**: 465–480.
- You W, Hedgecock D (2019) Boom-and-bust production cycles in animal seafood aquaculture. *Reviews in Aquaculture* **11**: 1045–1060.
- Yue GH (2014) Recent advances of genome mapping and marker-assisted selection in aquaculture. *Fish and Fisheries* **15**: 376–396.
- Zenger KR, Khatkar MS, Jones DB, Khalilisamani N, Jerry DR, Raadsma HW (2018) Genomic selection in aquaculture: application, limitations and opportunities with special reference to marine shrimp and pearl oysters. *Frontiers in Genetics* **9**: 693.