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Current Advances in Functional Genomics in Aquaculture

Hetron M. Munang'andu and Øystein Evensen

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<http://dx.doi.org/10.5772/intechopen.69883>

Abstract

Gene expression studies in aquaculture have slowly evolved from the traditional reductionist approach of single gene sequencing to high throughput sequencing (HTS) techniques able to sequence entire genomes of living organisms. The upcoming of HTS techniques has led to emergence of metagenomics, nutrigenomics, epigenetics and other omics technologies in aquaculture in the last decade. Metagenomics analyses have accelerated the speed at which emerging pathogens are being discovered, thereby contributing to the design of timely disease control strategies in aquaculture. Using metagenomics, it is easy to identify and monitor microbial communities found in different ecosystems. In vaccine production, genomic studies are being used to identify cross neutralizing antigens against variant strains of the same pathogens. In genetics and epigenetics, genomics traits have been identified that are beginning to gain commercial applications in aquaculture. Nutrigenomics have not only enhanced our understanding of the biological markers for nutrition-related diseases, but they have also enhanced our ability to formulate diets able to maintain a stable immune homeostasis in the gut. Overall, herein, we have shown that functional genomics provide multifaceted applications ranging from monitoring microbial communities in aquatic environments to optimizing production systems in aquaculture.

Keywords: genomics, aquaculture, metagenomics, nutrigenomics, epigenetics

1. Introduction

The ability to decipher the molecular composition of nucleic acids of living organisms is of prime importance in biological sciences. Although the traditional approaches of single gene expression analyses using polymerase chain reaction (PCR) tests [1, 2], quantitative real

time PCRs (qRT-PCRs) [3, 4], competitive PCRs [5] or nested PCRs [6] have been and are still widely used in biological sciences, they inherently lack the ability to provide a global overview of genomic transcripts found in living organisms. However, the recent advent of omics technologies such as metagenomics, nutrigenomics and epigenetics based on high throughput sequencing (HTS) is rapidly enhancing our ability to understand complex systems underlying different biological functions. These omics technologies have not only accelerated whole genome sequencing projects of different aquatic organisms [7, 8], but they also have the capacity to unravel the sequences of entire genomes without prior knowledge of the genes to be sequenced thereby enhancing the discovery and annotation of novel genes in non-model species. And as shown from recent studies, their applications in aquaculture have accelerated our ability to identify emerging pathogens [9], monitor the microbiomes of different aquatic environments [10], develop nutritional diets with less side effects [11, 12] and understand the cellular networks that regulate different biological processes in aquatic organisms [13–15]. It is evident from studies carried out this far that an integrated use of different omics technologies is bound to improve our production systems in aquaculture [10, 12, 16–18]. Hence, this chapter provides an overview of different omics technologies currently used in aquaculture mainly focusing on their overall contribution to transforming genomics studies into functional applications.

2. Application of metagenomics analyses

Studies carried out this far show that metagenomics can be used to identify novel pathogens as well as microbiota found on mucosal surfaces of cultured aquatic organisms.

2.1. Application of metagenomics in diagnostics and discovery of novel pathogens

The rapid expansion of aquaculture to become a leading source of proteins for human consumption in the world has brought with it a rapid increase in the number pathogens infecting farmed aquatic organisms [19]. To expedite the process of identifying emerging pathogens, there has been a shift in recent years from the use of traditional diagnostic tools based on isolation, culture and pathogen characterization to include metagenomics analyses in the identification of novel pathogens in aquaculture [10]. Metagenomics is a culture independent diagnostic tool that does not require prior knowledge of nucleic acids to be sequenced unlike conventional PCR that require prior knowledge of the nucleic acid to be sequenced for the design of primers [20]. Metagenomics analyses have the capacity to sequence all nucleic acids present in a sample at once thereby generating a vast array of data that requires computational analyses for interpretation [20, 21]. As pointed out in our previous studies [9, 10], it has the advantage of identifying co-infections and in the case of viral pathogens, it has the capacity to generate all variable proteins that form complete virions thereby permitting comparative phylogenetic analyses with other viruses present in public databases. Moreover, it is a proactive diagnostic tool able to identify novel pathogens before they cause outbreaks unlike the reactive traditional diagnostic tools in which etiological agents are only identified after

causing disease outbreaks reaching epidemic proportions [21]. Using metagenomics, several novel pathogens have been identified at a much faster rate than traditional approaches in which the duration from first observation of clinical signs to identification of the pathogens is long [10]. For example, infectious pancreatic necrosis (IPN) was first reported as an acute infectious enteritis [22] in salmonids in the 1940s while the etiological was later characterized as IPN virus after 20 years in 1960 [23]. Similarly, viral haemorrhagic septicaemia (VHS) was first reported in the early 1950s in salmonids while the causative agent was characterized later after 10 years in 1962 [24]. This trend was observed for several other diseases such as infectious hematopoietic necrosis virus (IHNV), nervous necrosis virus (NNV), heart and skeletal muscle inflammation (HSMI) and cardiac myopathy syndrome (CMS) in which identification of the etiological agents took long after clinical signs were first reported [25–33]. However, the upcoming of metagenomics has accelerated our discovery of novel pathogens in which the duration from observation of first clinical signs to identification of the etiological agent has been reduced. In fish, viruses discovered using metagenomics include circoviruses from common bream [34] and European eel [35], posavirus [36] and seadornavirus [37] from freshwater carp and totivirus from golden shiner. As shown in our recent study [9], more than 20 novel fish pathogenic viruses have been identified using metagenomics in the last 4 years, which is more than the number identified using traditional diagnostic tools in the last 5 decades, clearly showing the rapid rate at which metagenomics has accelerated our ability to identify novel pathogens compared with traditional diagnostic methods.

In crustaceans, mortalities due to white spot syndrome virus (WSSV) in shrimps were first reported in 1992 while the causative agent was identified in 2001 [38–40]. Mortalities due to taura syndrome virus (TSV) in shrimps were first reported in Ecuador in 1991 [41] and the virus was characterized in 1994 [42]. A similar trend was observed for Yellow head disease virus (YTV) [43, 44], infectious hypodermal and hematopoietic necrosis virus (IHHNV) [45–47], shrimp infectious myonecrosis virus (SIMV) [48] and *Penaeus vannamei* nodavirus (PvNV) [49, 50] in which the duration between the first report of the disease and identification of the etiological agent was long. Shrimps viruses discovered using metagenomics analyses include *Frafantepenaeus duorarum* nodavirus (FdNV) and shrimp hepatopancreas-associated circular nodavirus (ShrimpCDV) [51].

2.2. Monitoring of environmental microbiomes

A good understanding of microbial communities found in freshwater and marine environment used for aquaculture is a prerequisite to designing effective disease control strategies tailored for each ecosystem. Metagenomics analyses provide a unique opportunity to study infectious agents in water samples outside their susceptible hosts [10]. Its ability to sequence all nucleic acids present in a sample at once enables it to profile microbial communities found in different ecosystems. For example, Angly et al. [52] showed that microbial composition varies with latitude gradient with highest diversity being in warm climates around the equator and less diversity in the poles. After analysis of viromes from 32 different marine sites, Dinsdale et al. [53] noted that viral richness decreased from deep sea to surface waters and with distance from shore in surface waters and increased from winter to summer. Given that

over 40% of the global human population live within 100 km of coastlines, anthropogenic activities have been shown to influence the composition of microbial communities in coastal areas where aquaculture activities are mostly carried out [54]. These anthropogenic activities include host species composition changes introduced by aquaculture [55, 56], waste disposal [57], agriculture [58], recreation [59] and industrial activities [59]. As a result, metagenomics is currently being used to monitor the impact of anthropogenic activities on coastal microbial composition. Port et al. [60] found an increase in antibiotic resistance genes caused by coastal effluent discharges, while Morán et al. [61] showed significant changes in bacterial community structures caused by coastal copper disposal in La Lancha and Chañaral bay in the Pacific Ocean. Overall, these studies show that metagenomics is not only used to identify novel pathogens, but it is also used to monitor the impact of human activities on microbial composition in different aquatic environments.

2.3. Application of metagenomics in recirculation systems

In contrast to outdoor aquaculture systems that are dependent on natural water basins such as rivers and oceans, the recirculation aquaculture system (RAS) uses water that is filtered before it is recycled back into culture tanks in closed systems. Water used in RAS is subjected to several treatment processes such as biofiltration to reduce ammonium, removal of solids, oxygenation, pH control and pathogen denaturation using ozone and UV-light. Although a well-designed state-of-the-art RAS has the potential to reduce the presence of waterborne microorganisms, some pathogens are able to resist RAS disinfection. Bacteria phyla detected from RAS biofilters include Actinobacteria [62], Firmicutes, Bacteroides [63–65], Proteobacteria [63, 65], Verrucomicrobia [65] and Sphingobacteria [62, 65]. Hence, some microorganisms are being used as biosafety indicators whose dominance points to increase in the proliferation of pathogenic microorganisms [66]. As a result, metagenomics analyses are being used to monitor the increase in proliferation of pathogens in RAS [67].

2.4. Metagenomics analyses of mucosa microbiota

Given that mucosal surfaces are the major portals of microbial invasion, there has been a growing interest to study mucosal microbiota of cultured aquatic organisms. Metagenomics studies show that different environmental factors influence the composition of mucosal microbiota on different fish species.

2.4.1. Skin mucosa microbiota

Larsen et al. [68] compared the skin microbiota of six different fish species (*Mugil cephalus*, *Lutjanus campechanus*, *Cynoscion nebulosus*, *Cynoscion arenarius*, *Micropogonias undulatus* and *Lagodon rhomboides*) from the Gulf of Mexico and showed that Proteobacteria was the predominant phylum followed by Firmicutes and Actinobacteria across all species. Although *Aeribacillus* was found in 19% of all fish species examined, genera such as *Neorickettsia* and *Microbacterium* were fish species-specific pointing to existence of phyla and genera associated

with particular fish species. Lokesh and Kiron [69] showed that the bacterial operational taxonomy unit (OTU) composition on the skin of Atlantic salmon (*Salmo salar* L.) changed significantly as a result of transfer from fresh to seawater. Proteobacteria was the dominant phylum both in fresh and seawater while Bacteroidetes, Actinobacteria, Firmicutes, Cyanobacteria and Verrucomicrobia were the most abundant in freshwater. The genus *Oleispira* was the most abundant in seawater. Similarly, Wilson et al. [70] showed that bacterial communities from the epidermal mucus of Atlantic cod (*Gadus morhua*) from the Baltic, Iceland and North seas collected over three seasons mainly comprised of *Psychrobacter*, *Bacteroides* and *Photobacterium* OTUs in all seasons although there were significant inter-site and seasonal variations in community composition.

Boutin et al. [71] combined 16S RNA metagenomics and QTL analyses to show that host genotype can regulate the microbiota composition on the skin surface of brook charr (*Salvelinus fontinalis*). They found a strong negative correlation between *Flavobacterium* and *Methylobacterium*, pointing to a mutually competitive relationship between pathogenic and non-pathogenic bacteria on the skin mucosa of brook charr. *Flavobacterium* is known to be pathogenic among different fish species, while *Methylobacteria* provide protection against pathogenic bacterial infections on skin surfaces suggesting that a shift from *Methylobacteria* to *Flavobacterium* dominance on the skin mucosal could point to increase in susceptibility to bacterial infection. Hence, by monitoring changes on mucosal bacteria composition, metagenomics can be used to determine the susceptibility of fish to microbial infections.

2.4.2. Gut mucosal microbiota

As pointed out by Lyons et al. [72] that to better understand the gut microbiome and its impact on the health status of aquatic organisms, it is vital to determine its structure, diversity and potential functional capacity. Gajardo et al. [12] analysed the microbiota profile of the digesta and gut mucosal of Atlantic salmon (*S. salar* L.) fed commercial diets and showed that microbiota richness and diversity differed significantly between the digesta and gut. The digesta had a higher and diverse richness than the gut mucosa. Proteobacteria was the dominant phyla in the mucosa whereas Proteobacteria and Firmicutes were dominant in the digesta. In addition, there were significant differences in microbiota composition in different segments of the gut. Actinobacteria was dominant in the posterior intestinal (PI) than the mid-intestinal (MI) mucosa. Moreover, the PI showed presence of Spirochaetes that were not found in the MI showing that metagenomics can be used to identify microbial communities that inhabit different segments of the gut. In another study, Gajardo et al. [11] identified bacterial groups associated with diet-induced gut dysfunction that could serve as biological markers of the gut health status in Atlantic salmon. Mouchet et al. [73] compared the gut microbiota of 15 fish species from the Atlantic Ocean near Brazil and showed that the microbiota genetic diversity was highly influenced by the fish species, geographical location and diet. Put together, these studies show that metagenomics can be used to profile bacteria species on mucosal surfaces of different fish species and that different factors such as host species, geographical areas and diet influence mucosal microbiota in fish.

2.5. Metagenomics technologies and their limitations

Of the most widely used NGS technologies, both 454 pyrosequencing Roche and Illumina sequencers have been widely used in the metagenomics analyses of different aquatic organisms. For example, 454 pyrosequencing Roche has been used to study microbial communities of different fish species including rainbow trout (*Oncorhynchus mykiss*) [74], Atlantic cod (*G. morhua*) [75], Atlantic salmon [76], brook trout (*S. fontinalis*) [77], brown trout (*Salmo trutta*) [78], zebrafish (*Dario rerio*) [79], Gizzard shad (*Dorosoma cepedianum*) [80], silver carp (*Hypophthalmichthys molitrix*) [81], common carp (*Cyprinus carpio*) [82], grass carp (*Ctenopharyngodon idellus*) [83], orange spotted grouper (*Epinephelus coioides*) [84] and Senegalese sole (*Solea senegalensis*) [85]. On the other hand, Illumina sequencers have been used for the analyses of microbiota found in seabass (*Lates calcarifer*) [86], blunt snout bream (*Megalobrama amblycephala*) [87], grass carp (GC) [87], mandarin fish (*Siniperca chuatsi*) [87], topmouth culter (*Culter alburnus*), common carp [87] and Crucian carp (*Carassius auratus*) [87], silver carp [87] and bighead carp (*Hypophthalmichthys nobilis*) [87]. In terms of assembly, both whole genome shotgun and marker gene guided sequencing have been used on different aquatic organisms. The commonly used marker gene in metagenomics analyses is the 16S ribosomal RNA (16S rRNA), which has been widely used to characterize the microbiota of different aquatic organisms including rainbow trout [88, 89], Atlantic salmon [11, 12], turbot (*Scophthalmus maximus*) [90], lamprey (*Lampetra morii*) [91] and Baleen whale [92]. Whole genome shotgun sequencing has also been widely used in the study of environmental microbial communities and pathogens infecting different aquatic organisms. The major advantage with this approach is that it can be used to sequence whole genomes of known or unknown organisms using *de novo* assemblies unlike guided marker assemblies that are dependent on a reference gene [93–96].

Despite its positive contribution to the discovery of novel pathogens and environmental monitoring of microbial communities, metagenomics has significant limitations that require the support of other tools [95]. The immense metagenome data generated using NGS technologies require the support of other tools for clustering, classification and annotation of individual sequences [95]. For *de novo* assembled sequences, the most reliable annotation approach is by homology search using reference sequences available in public databases. However, the number of existing public databases for aquatic organisms is limited, which makes it difficult to identify novel pathogens [97]. In general, functional annotation lags behind the rate at which metagenome data is generated. Alternative methods used to identify novel pathogens include motif or pattern-based identification [98, 99], phylogenetic profiling [100] and neighbourhood tree alignments [101, 102].

3. Nutrigenomics in aquaculture

Nutrigenomics is the study of the role of nutrition on gene expression. Galduch-Giner et al. [103] showed that there was specialization in the functional properties of different components of the intestinal tract of the European seabass (*Dicentrarchus labrax*). They observed that

molecular markers linked to nutrient digestion and absorption were high in the anterior (AI) and middle intestine (MI) while the posterior intestine (PI) predominantly expressed genes linked to immune defence mechanisms. These observations are in line with other scientists who showed that the AI and MI are mainly responsible for nutrient digestion and absorption [104, 105] while the PI is responsible for induction of innate immune responses linked to activation of adaptive immunity in teleosts fish [106–109].

Different scientists have studied the genomic changes induced by various nutrients in the guts of different fish species. Krol et al. [110] compared the differential response of the Atlantic salmon gut to soybean meal (SBM) and fish meal (FM) as positive and negative controls for enteritis, respectively. They noted that SBM altered the gut histology and induced extensive transcriptomic changes linked to underlying mechanisms of SBM-induced enteropathy. They found 18 enriched pathways linked to inflammation and immune responses induced by SBM enteropathy. Among these were the NF- κ B and IL-8 signalling pathways known to induce the synthesis of various pro-inflammatory cytokines. Phagocytic pathways such as the Fc γ receptor mediated phagocytosis and monocyte pathways were highly enriched. In another study, Torrecillas et al. [111] showed downregulation of TCR β , COX-2, TNF α , IL-8, IL-6, IL-10, TGF β and IgM when MHC-II was upregulated in European seabass fed to Soya-bean oil (SBO). Expression of these genes corresponded with reduced lengths of intestinal folds and mucus density in the gut. Conversely, mannan oligosaccharides (MOS) diets increased the length of intestinal folds and mucus density and upregulated MHC-CD4, COX-2, TNF α and IgM expression. Combined MOS and SBO diets reduced the harmful effects of SBO diets by moderating the downregulation of GALT-related genes. Therefore, these observations show the importance of optimizing feed formulation in order to produce balanced diets able to preserve the GALT-immune homeostasis.

Apart from soyabean, nutrigenomics have also been used to evaluate the impact of other nutrients in fish diets. Azeredo et al. [112] showed that the immune status of the European seabass was impaired by arginine dietary supplements. They observed that different cell-mediated immune markers were downregulated in fish fed 1–2% arginine diets. Leukocytes obtained from fish fed arginine diets showed low respiratory burst compared to control fish. After challenge with *Vibrio aguilorum*, fish fed arginine diet supplements showed higher mortality than control fish. Interestingly, reducing arginine levels to 0.5% in the diet supplements significantly increased respiratory burst to levels comparable with control fish. In another study, Estensoro et al. [113] showed that butyrate (BP-70[®]NOREL) helped to restore the intestinal status of marine gilthead sea bream (*Sparus aurata*) fed extremely low diets of fish meal (FM) and fish oil (FO). They observed that extremely low FO and FM diet levels significantly altered the transcriptomic profiles linked to nutrient absorption in the AI and increased expression of inflammatory, antioxidant, permeability and mucus production genes that coincided with increased granulocyte and lymphocyte presence in the PI submucosa. Interestingly, expression of these genes was restored to control values by adding butyrate (BP-70) to the feed. As pointed out by Krol et al. [110], gut transcriptomic profiling is a useful tool for testing the adverse impacts of different feeds and that understanding gut-diet interactions is a prerequisite to designing diets able to prevent induction of diet-related diseases in the gut.

Omics technologies commonly used for nutrigenomics analyses in aquaculture mainly comprise of microarray and RNA-seq. RNA-seq has been widely used to study the impact of different diets in various fish species including Atlantic salmon [114], rainbow trout [115], channel catfish (*Ictalurus punctatus*) [116], blue catfish (*Ictalurus furcatus*) [117] and zebrafish [118]. On the other hand, microarray has also been widely used to study nutrigenomics in different fish species that include Atlantic salmon, rainbow trout, Atlantic cod (*G. morhua*) and Gilthead sea bream (*S. aurata*). However, the use of RNA-seq and microarray leads to several challenges that include the need for large data processing softwares as well as the need of bioinformatics tools required for differential gene expression, network pathway, alternative splicing and gene duplication analyses. To cope with these challenges, different bioinformatics tools have been developed and new innovations are being invented to cover different aspects of quality assessment of mapped genes, mapping for *de novo* assembled genes, expression quantification, differential expression analyses, alternative splicing and network pathway analyses [119–122]. Different reviews have been published providing in-depth comparative analyses of existing tools highlighting their strengths and weakness that could serve as a guide for end users to select the most appropriate tool suitable for nutrigenomics studies in different aquatic organisms [119, 123, 124].

4. Functional genomics in vaccine development

Given that most pathogens exist as multiple strains having different antigenic proteins, the challenge in vaccine design has been to find cross protective antigens against variant strains of the same pathogen. In the case of viruses, different approaches have been used aiming at finding the most neutralizing epitopes using methods such as epitope mapping, peptide-scan and reverse genetics [125–128]. However, the upcoming of next generation sequencing (NGS) supported with current advances of bioinformatics tools is expected to expedite our ability to identify the most immunogenic proteins for vaccine production against viral diseases. For example, Ou-yang et al. [129] used bioinformatics to identify the antigenic proteins for Singapore grouper iridovirus. They used the 162 open reading frames (ORFs) of SGIV for sequence similarity searches to identify motifs, cellular locations and other prediction domains to identify the most immunogenic epitopes required for vaccine production. They identified 13 genes that were cloned to produce DNA vaccines of which three vaccines produced relative percent survival (RPS) ranging from 58.3 to 66.7% in vaccinated grouper.

In the case of bacterial vaccines, identification of protective antigens can be a challenge given that they contain several antigenic proteins such as capsular antigens, fimbriae, pili and outer membrane proteins [130–132]. Some of these proteins lead to serotype, biovar or strain differences leading to antigenic diversity within bacterial species. Hence, the challenge is to identify broad neutralizing antigens able to confer cross protection against variant bacterial strains can be a difficult task. To overcome this problem, Handfield et al. [133] developed an *in vivo* induced antigen technology (IVIAT) that uses antibodies generated from individuals infected by the bacterial strain homologous to the vaccine strain to probe for immunogenic proteins using an *in vitro* expression system. To do this, a genomic library is generated using DNA fragments from the bacteria strain to be used for vaccine production. The DNA fragments are digested using

restriction enzymes and cloned into plasmid vectors. Induced colonies of the expression library are probed using pooled sera from bacterial infected individuals as shown in **Figure 1**. Reactive clones are purified and used as vaccine candidates [133]. This technology has been widely used to identify antigenic proteins for different bacteria species such as *Streptococcus iniae* [134], *Vibrio anguillarum* [135], *Aeromonas salmonicida* [136, 137], *Edwardsiella tarda* [138] and *Streptococcus parauberis* [139]. Jia et al. [138] used the IVIAT to identify a 510 aa peptidase protein, which they used to produce a subunit vaccine against *E. tarda* in Japanese flounder. Sun et al. [134] used the IVIAT technique to identify a secretory antigen, which they designated as Sia10, and cloned it to produce a DNA vaccine against *S. iniae*. In vaccinated turbot, the Sia10 protein was detected in the muscle, liver, kidney and spleen by 7 days post-vaccination (dpv) lasting until 49 dpv. Post-challenge RPS showed 73.9 and 92.3% in fish challenged with high- and low-challenge dose, respectively. In addition, the Sia10 protein produced protective antibodies in passively vaccinated fish. In another study, Sun et al. [140] used the IVIAT method to identify a surface

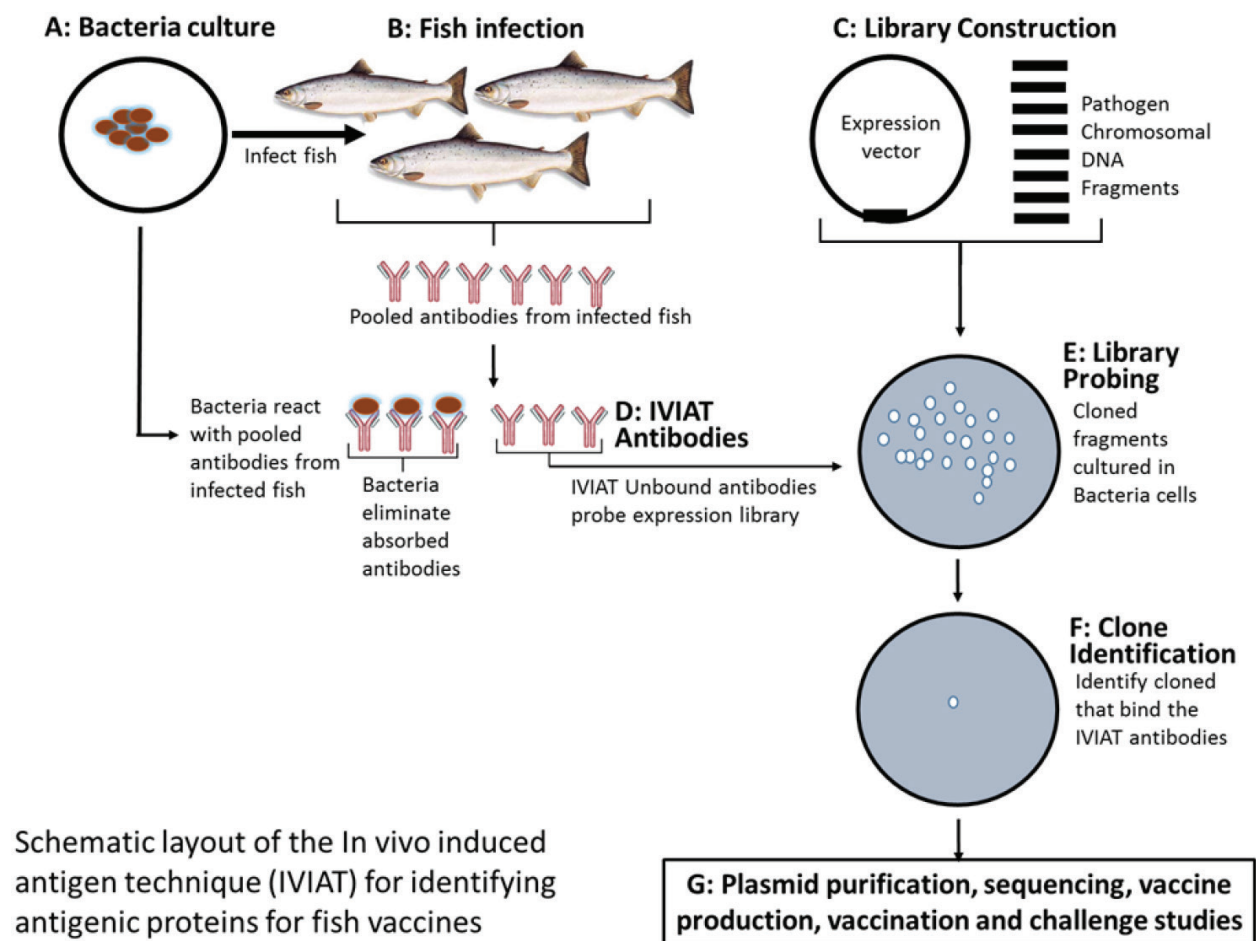


Figure 1. Schematic layout of the IVIAT technique for the identification of bacterial antigenic proteins essential for the production of fish vaccines: A: bacteria culture. B: bacteria infection in fish and the sera from infected fish is pooled. C: library construction using chromosomal DNA fragments of the bacteria cultured in (A). D: bacteria eliminate absorbed antibodies from sera while IVIAT unbound antibodies are used to probe the library constructed in (C). E: clones from fragments of bacterial chromosomal DNA are probed with IVIAT pooled sera. F: after probing with pooled sera from infected fish, clones depicting binding capacity to IVIAT sera are sub-cultured. G: the identified clones are purified, sequenced and used for subunit or DNA vaccine production followed by vaccination and challenge trials.

antigen designated as *Esa1*, which they used to produce a DNA vaccine against *E. tarda* in Japanese flounder. They showed that the p*CEsa1* vaccine enhanced respiratory burst, acid phosphatase activity and bactericidal activity of headkidney macrophages. In addition, it produced RPS = 57% in passively vaccinated fish. Overall, these studies show that genomics approaches can be used to identify the most immunogenic proteins for different bacterial strains in order to produce the most protective vaccines for use in aquaculture.

5. Marker-assisted selection of growth and disease resistance traits

5.1. Growth traits

Genetic selection in which individuals with the best growth traits are selected as parent stock for the next generation is one of the major strategies used for improving production in aquaculture. And as such, several breeding programmes have been going on using natural selection approaches [141–143]. The major drawback with this approach is that it takes several generation cycles to identify individuals having positive growth traits. To expedite the process of identifying genetic traits for optimal growth performance, marker-assisted selection (MAS) processes such as single nucleotides polymorphism (SNP), microsatellite, amplified fragment length polymorphism (AFLP), random amplified polymorphism DNA (RAPD), restriction fragment length polymorphism (RFLP) and quantitative trait loci (QTL) are being used to scan chromosomal DNA of different farmed aquatic organisms. Among these, the most widely used is QTL analysis, which has been applied across most of the commercial fish and crustacean species used in aquaculture [144–147]. As defined by Geldermann [148], QTLs are chromosomal regions made of single genes or gene clusters determining a quantitative character of a given trait. Given their high heritability, mapped QTLs have proved to be a useful tool in selective breeding, which has played an important role in accelerating genetic improvement in aquaculture.

As shown in **Tables 1** and **2**, the most important genetic traits sought for in aquaculture are growth rate, body weight and length. These traits influence the commercial value of farmed aquatic organisms. Traits for body weight and length have been identified in several fish species such as Atlantic salmon [149], rainbow trout [150], Big heard carp (*H. nobilis*) [151], common carp [152, 153] and tilapia (*Oreochromis niloticus*) [154], nine spined stickleback (*Pungitius pungitius*) [155] and Arctic char (*Salvelinus alpinus*) [156]. In shrimps and prawns, body weight and length traits have been identified in kruma shrimp [157, 158], Chinese shrimp [159], Giant fresh water prawn [160], Ridge white prawn [161] and Oriental river prawns [162]. Another important trait, which has contributed to improved production in aquaculture is sexual maturation. It has been shown that in some some species, sex is closely related to growth. For example, Sun and Liang [163] showed that in common carp, females grow bigger than males at the same age, while in tilapia, the males grow faster than females [164]. Hence, the selection of males for aquaculture increases production in tilapia while the females increase production in carp. Important traits related to improving meat quality include muscle quality [154], muscle fibre [165], texture [165], colour [166, 167], fat percentage [166] and dressed weight percentage [166].

Fish species	Trait	Method	References
Blue bream (<i>Ballerus ballerus</i>) (Cyprinidae)	Thyroid hormones	Transcriptome	[241]
Blunt snout bream (<i>Megalobrama amblycephala</i>)	Growth trait	Transcriptome	[242]
Turbot (<i>Scophthalmus maximus</i>)	Growth trait	Transcriptome	[243]
Grouper hybrids (<i>Epinephelus fuscogutatus</i>)	Superiority in growth	Transcriptome	[244]
Mandarin fish (<i>Siniperca chuatsi</i>)	Growth traits	Microsatellite	[245]
Atlantic salmon (<i>Salmo salar</i> L.)	Growth traits	SNP/GWAS	[149]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Robustness	Transcriptome	[173]
Nile tilapia (<i>Oreochromis niloticus</i>)	Growth traits	Transcriptome	[154]
Nile tilapia (<i>Oreochromis niloticus</i>)	Skeletal muscle quality	Transcriptome	[154]
gilthead sea bream (<i>Sparus aurata</i>)	Skeletal muscle quality	Transcriptome	[246]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Growth traits	SNP	[150]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Stress factor traits	Transcriptome	[247]
Atlantic cod (<i>Gadus morhua</i>)	Growth/reproduction	Transcriptome	[248]
Lake whitefish pairs (<i>Coregonus</i> spp. <i>Salmonidae</i>)	Reproduction	Transcriptome	[249]
Lake whitefish pairs (<i>Coregonus</i> spp. <i>Salmonidae</i>)	Adaptation	QTL	[250]
Atlantic salmon (<i>Salmo salar</i> L.)	Smoltification	Transcriptome	[177]
Common carp (<i>Cyprinus carpio</i>)	Cold tolerance	QTL	[163]
Arctic char (<i>Salvelinus alpinus</i>)	Temperature tolerance	QTL	[176]
Arctic char (<i>Salvelinus alpinus</i>)	Growth rate	SNP	[251]
Tilapia (<i>Oreochromis niloticus</i>)	Cold tolerance	QTL	[175]
Tilapia (<i>Oreochromis niloticus</i>)	Fish size	QTL	[175]
Coho salmon (<i>Oncorhynchus kisutch</i>)	Flesh colour	QTL	[167]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Spawning time	QTL	[178]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Albinism	QTL	[170]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	High temperature tolerance	QTL	[252]

Table 1. Growth and performance traits for different fish species.

Crustacean species	Trait	Method	References
Pandad shrimp (<i>Pandalus latirostris</i>)		Microsatellite	[253]
Giant freshwater prawn (<i>Macrobrachium rosenbergii</i>)	Growth traits	SNP	[160]
Ridgetail white prawn (<i>Exopalaemon carinicauda</i>)	Growth traits	Transcriptome	[161]
Kuruma shrimp (<i>Marsupenaeus japonicas</i>)	Growth traits	QTL	[157]
Kuruma shrimp (<i>Marsupenaeus japonicas</i>)	High temperature tolerance	QTL	[157]
Kuruma shrimp (<i>Marsupenaeus japonicas</i>)	Growth traits	AFLP	[158]
Pacific white shrimp (<i>Litopenaeus vannamei</i>)	Growth traits	QTL	[147]
Kuruma shrimp (<i>Marsupenaeus japonicas</i>)	Total and carapace length	ALFP	[254]
Indian black tiger shrimp (<i>Penaeus monodon</i>)	Sex determining loci	QTL	[255]
Pacific white shrimp (<i>Litopenaeus vannamei</i>)	Sex determining loci	Microsatellite	[256]
Chinese shrimp (<i>Fenneropenaeus chinensis</i>)	Body length	QTL	[159]
Pacific white shrimp (<i>Litopenaeus vannamei</i>)	Body weight and length	QTL	[257]
oriental river prawn (<i>Macrobrachium nipponense</i>)	Body length	QTL	[162]
Kuruma shrimp (<i>Marsupenaeus japonicas</i>)	Body length	QTL	[158]

Table 2. Growth and performance traits for different crustacean species.

Body appearance traits identified include the red body colour excluding normal black pigmentation in tilapia [168], silvery skin with few spots in rainbow trout [169], albinism in rainbow trout [170] and melanization in threespine sticklebacks (*Gasterosteus aculeatus*) [171]. Genetic traits essential for improving production in fish farming include traits for feed conversion ratio [172], robustness [173], maturation timing [174], cold tolerance [163, 175], high temperature tolerance [176] and salinity tolerance. In anadromous species such as Atlantic salmon, genetic traits for smoltification [177], migration and spawning timing [178] have been determined.

5.2. Disease resistance and susceptibility traits

The rapid expansion of aquaculture to become one of the leading sources of protein in the world has brought with it an increase in infectious diseases in aquaculture. To reduce the disease

burden and prevent the use of antibiotics, which have been shown to have adverse environmental effects, there has been a tremendous increase in genomics studies aimed at identifying disease resistance traits in different cultured organisms. And as such, different approaches such as SNP, MTLs, AFLP, RAPD, RFLP and QTL analyses have been used for the identification of disease resistance and susceptibility traits in different aquatic organisms. In the case of fish viral diseases, QTL resistance traits have been generated for grass carp reovirus (GCRV) infection in grass carp [179], nervous necrosis virus (NNV) in seabass [180], viral hemorrhagic septicemia (VHS) in turbot [181] and rainbow trout [182], infectious salmon anaemia (ISAV) virus in Atlantic salmon, lymphocytic disease virus in Japanese flounder [183] and infectious pancreatic necrosis virus (IPNV) in Atlantic salmon [184, 185]. Among these, the QTL for resistance against IPNV has contributed to significantly reducing the IPNV incidence by >80% from 2008 when IPNV resistance fish were introduced in the Norwegian Atlantic salmon industry to 2015 [186]. Bacteria disease for which QTL resistance traits have been identified include coldwater disease in rainbow trout [187], *Aeromonas hydrophila* in rohu (*Labeo rohita*) [188], *Vibrio anguillarum* in Japanese flounder [189], *Flavobacterium psychrophilum* in rainbow trout [190] and pastuerellosis in Gilthead seabream [191]. As for parasitic diseases, QTL resistance traits have been identified for *Gyrodactylus salaris* in Atlantic salmon [192] and Monohenean parasite (*Benedenia seriolae*) in Yellow tail (*Seriola quinqueradiata*) [193].

In shrimps, resistance traits have been identified for white spot syndrome virus (WSSV) in Indian black tiger shrimp (*Penaeus monodon*) [194, 195], Fenneropenaeus (*Penaeus chinensis*), infectious hypodermal and hematopoietic necrosis virus (IHHNV) resistance in shrimp (*Litopenaeus stylirostris*) [196] and taura syndrome resistance in Pacific white shrimp (*P. vannamei*) [197]. Among these, the QTL for resistance against TSV has contributed to significant reduction of the disease prevalence in shrimps by generating pathogen-specific free disease shrimps for use in breeding programmes in aquaculture.

6. Application of epigenetics in aquaculture

The term 'epigenetics' was first coined by Waddington in 1942 and was defined as changes in the phenotype without inducing changes in the genotype [198, 199]. Studies on chemical modification of DNA bases date as far back as 1948 [200] and by the 1970s, the role of DNA methylation in gene regulation was identified [201]. In subsequent years, the link between DNA methylation and gene expression was established [202] paving way to the discovery of therapeutic drugs such as 5-azacytidine used to block DNA methylation [203]. In principle, epigenetic changes are regulated by (i) chemical modifications on DNA cytosine residues resulting in DNA methylation and, (ii) histone protein modifications on DNA [204, 205]. Current advances in HTS have refined genomic analyses to base-pair resolution making it easier to map entire epigenomes of living organisms enabling us to identify biological markers predictive of the outcome of disease infections, reproduction, growth and adaptation to new environments [206]. As a result of these advances, epigenetics studies in aquaculture have tremendously increased in the last decades with the view to identifying biological markers relevant for improving the production of farmed aquatic organisms. Technologies used for epigenetics analyses in aquaculture include (i) RNA-seq in

Medaka [207] and Nile tilapia [208]; (ii) genome-wide methylated DNA immunoprecipitation sequencing (MeDIP-seq) in Nile tilapia [209] and Medaka [207]; (iii) bisulfite sequencing (BS-seq) in smooth tongue sole (*Cynoglossus semilaevis*) [210, 211], rainbow trout [212] and Nile tilapia [208]; (iv) genetic linkage map analysis using simple sequence length polymorphisms (SSLPs) in medaka [213, 214]; (v) methylation sensitivity amplified polymorphism (MSAP) in Atlantic salmon [18], grass carp [215], brown trout [17], sea urchin (*Glyptocidaris crenularis*) [216] and sea cucumber (*Apostichopus japonicas*) [217]; (vi) 5-methylcytosine immunolocalization in sea lamprey (*Petromyzon marinus*) [218]; (vii) restriction endonuclease hydrolysis of DNA using methylation enzymes in Zebrafish [219] and (viii) bisulfite sequencing PCR in Pacific Oyster (*Crassostrea gigas*) [220] and grass carp [221]. As shown in **Table 3**, epigenetics studies carried out this far include studies on reproduction, growth and adaptation traits. In the case of Atlantic salmon, which is one of the most widely studied species, epigenetic studies have been carried out at different stages of the production cycle as shown in **Figure 2**.

6.1. Embryogenesis and reproduction traits

Embryogenesis and reproduction traits determined by epigenetic analyses in aquatic organisms include sexual dimorphism, embryo development, control of gonadal aromatase and male meiosis [208, 222, 223]. Mhanni and McGowan [219] examined the methylation patterns of the zebrafish genome during early embryogenesis and showed that parental genetic contributions to the zygote were differently methylated with the sperm being more hypermethylated than the oocyte genome. However, immediately after fertilization there was a significant decrease in the embryonic genome methylation, but increased rapidly as the embryo developed to normal levels by the gastrulation stage. These observations are consistent with those seen in mouse [224] suggesting that embryo demethylation/re-methylation is conserved across the vertebrate taxa as of part embryogenesis. As for reproduction traits, Wan et al. [208] found several differentially methylated regions (DMRs) on tilapia chromosomal DNA linked to sexual dimorphism in which the males had high methylation levels after prolonged exposure to high temperature conditions. Similarly, Navarro-Martín et al. [222, 223] showed that European seabass juvenile males had double DNA methylation levels than females in the promoter region of gonadal aromatase, the enzyme that converts androgens to estrogens suggesting that methylation levels on gonadal aromatase were predictive of sex determination. Other fish species for which DNA methylation of aromatase has been linked to sex determination include medaka [225] and Japanese flounder (*Paralichthys olivaceus*) [226]. In crustacean, Gómez et al. [227] analysed the post-translational histone modifications in the testis of *Daphnia magna* and identified cytological markers linked to meiosis progression and the silencing of unsynapsed chromatin. Put together, these studies show that DNA methylation and histone modification can induce reproduction and embryogenesis changes in different aquatic organisms.

6.2. Growth and productivity traits

Epigenetic factors associated with growth and productivity identified in aquatic organisms include early maturation, regulation of muscle growth and disease resistance. Early maturation in Atlantic salmon has emerged to be an interesting topic because prior to migration,

Aquatic organism	Epigenetic trait	References
Zebrafish (<i>Danio rerio</i>)	Carcinogenesis	[258]
Zebrafish (<i>Danio rerio</i>)	Embryo development	[219]
Zebrafish (<i>Danio rerio</i>)	Embryonic cardiogenesis	[259]
Medaka (<i>Oryzias latipes</i>)	Excision of ToL2 transposal	[260]
Medaka (<i>Oryzias latipes</i>)	Control of cardiomyocyte production in response to stress	[214]
Medaka (<i>Oryzias latipes</i>)	Hypoxia and transgenerational reproduction impairment	[207]
Nile tilapia (<i>Oreochromis niloticus</i>)	High temperature induced masculinization of skeletal muscles	[209]
Nile tilapia (<i>Oreochromis niloticus</i>)	Sexual dimorphism	[208]
Atlantic salmon (<i>Salmo salar</i> L.)	Early maturation	[18]
European seabass (<i>Dicentrarchus labrax</i>)	Temperature dependent sex ratio shift	[222, 223]
Tongue sole (Cynoglossidae)	Sex reversal	[210, 211]
Senegalese sole (<i>Solea senegalensis</i>)	Thermal epigenetic regulation of muscle growth	[261]
European eel (<i>Anguillarum anguillarum</i>)	Low cadmium exposure	[232]
European eel (<i>Anguillarum anguillarum</i>)	Abnormal ovarian DNA methylation-gonadal	[262]
Red eared slider turtle (<i>Trachemys scripta elegans</i>)	Control of gonadal aromatase	[263]
<i>Daphnia magna</i>	Male meiosis	[227]
Pacific oyster (<i>Crassostrea gigas</i>)	Growth	[220]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Glucose intolerance	[230]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Migration-related phenotypic divergence	[212]
Atlantic Cod (<i>Gadus morhua</i> L.)	Photoperiod influence	[228, 229]
Grass carp (<i>Ctenopharyngodon idella</i>)	Individual variations	[215]
Grass carp (<i>Ctenopharyngodon idella</i>)	Resistance against grass reovirus	[221]

Table 3. Epigenetics application in aquatic organisms.

parr can reach sexual maturity and successfully fertilize adult females. Up to 60% of total paternity in wild populations has been attributed to these precocious male parr or ‘sneakers’. To determine the underlying causes of early sexual maturation in parr, Morán and Pérez-Figueroa [18] compared genetic and epigenetic differences of two populations of parr and mature fish originating from two different rivers and found no genetic difference between

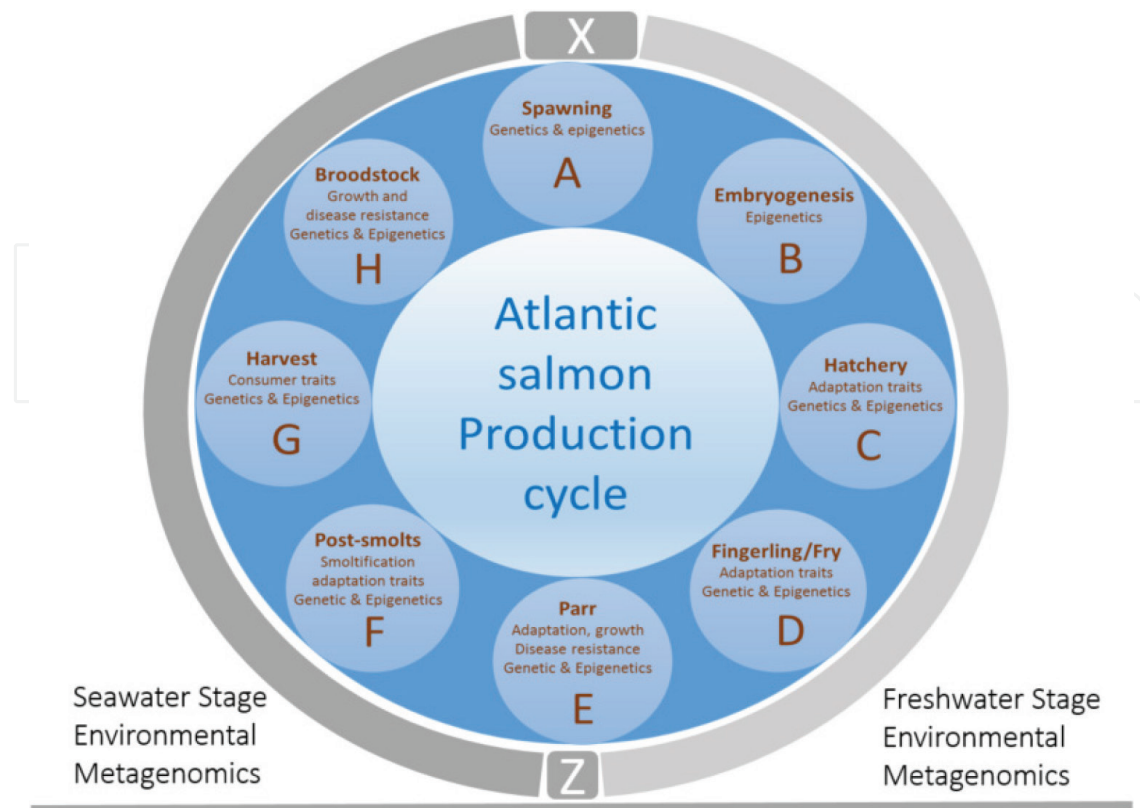


Figure 2. The cycle shows the use of different aspects of functional genomics to improve the production of Atlantic salmon at different stages of the production-cycle. Note that genetics and epigenetics studies are focused on identifying important traits in fish while metagenomics studies are mostly focused on environmental identification of infectious pathogens. Fish from different growth stages are also evaluated for the mucosal microbiota investigations using metagenomics analyses. Nutrigenomics is mostly applied at the outgrower stage. Growth stages are depicted from spawning (A), embryogenesis (B), hatching (C), fingerlings and fry stage (D), Parr stage (E), post-smolts (F), outgrower stage (G) and broodstock (H). Nutrigenomics are after through the feeding stages while the timing of most vaccinations is the parr (D) stage in order to enable fish develop protective antibodies by the post-smolt (E) stage and outgrower stage when they are most vulnerable to stress-related infectious diseases. (X): Depicts the migration of adult fish from seawater into freshwater for spawning. (Z): depicts migration from freshwater to seawater at the parr stage.

parr and mature fish. However, epigenetic analysis showed significant single-locus variations in the gonads followed by the brain and liver between parr and mature fish suggesting that early maturation in Atlantic salmon parr was mediated by epigenetic processes and not genetic differences. As for disease resistance, Shang et al. [221] showed that CpA/CpG methylation of grass carp *Ctenopharyngodon idella* melanoma differentiation associated gene 5 (MDA5) (CiMDA5) was tightly associated with resistance against GCRV. In their findings, they found CpA/CpG methylation sites in the CiMDA5 genome that consisted of putative densely methylated elements (DMEs) that were significantly higher in GCRV susceptible fish than in the resistant fish. In terms of muscle growth, Giannetto et al. [228] found a correlation between DNA (cytosine-5)-methyltransferases (DNMTs) increase in fast muscle with prolonged exposure to light indicating that photoperiod influence may be involved in the DNMTs regulation of muscle growth in Atlantic cod. Similarly, Nagasawa et al. [229] found high histone methyltransferases levels of the mixed-lineage leukaemia (MLL) gene in fast muscle of Atlantic cod subjected to prolonged light exposure, which corresponded with

increase in mRNA expression of myogenic regulatory factors (*Myog* and *Myf-5*) and *Pax7* in fast muscle. Overall, these studies show that DNA methylation and histone modification of chromosomal DNA play an important role in regulating muscle growth, disease resistance and sex maturation in fish.

6.3. Adaption epigenetic traits

Epigenetic factors shown to induce adaptation changes in cultured aquatic organisms include nutrition, migration, salinity and photoperiod exposure. Several nutritional studies have shown that rainbow trout displays persistent hyperglycaemia when fed high carbohydrate (HighCHO) diets. To underpin the underlying causes, Marandel et al. [230] examined the liver of rainbow trout fed HighCHO diets and found global DNA hypomethylation and hypoacetylation of histone H3K9 resembling hyperglycaemic and diabetes conditions in zebrafish and mammals. They also showed that *g6pcb2* ohnologs that encode the glucose-6-phosphatase (G6pc) enzyme involved in gluconeogenesis catalysis were hypomethylated at specific CpG sites indicating that the hepatic epigenetic landscape of rainbow trout can be affected by dietary carbohydrates. As for migration traits, Baerwald et al. [212] identified several DMRs between migratory smolts and resident rainbow trout juveniles in which most DMRs encoded proteins associated with migration showing that epigenetic variations were linked to migration traits in anadromous fish. Their findings were in concordance with Morán et al. [17] who found genome-wide methylation differences between hatchery reared and seawater brown trout. In addition, Morán et al. [17] showed that salt diets used during the seawater phase triggered genome-wide methylation changes when administered in freshwater reared trout indicating that DNA methylation could play a vital role in enabling anadromous fish acclimatize to seawater after transfer from freshwater. DNA methylation and histone modification have also been associated with adaptation changes induced by adverse environmental conditions as shown in Nile tilapia exposed to industrial pollutions [231], eels to cadmium exposure [232], sea urchin (*G. crenularis*) exposure to perfluorooctane sulfonate (PFOS) [216] and the three-spine stickleback (*G. aculeatus*) hexabromocyclododecane (HBCD) exposed to 17- β oestradiol (E_2) and 5-aza 2' deoxycytidine (5AdC) pollutants [233]. In summary, these studies demonstrate that DNA methylation and histone modification contribute to nutritional, environmental and photoperiod adaptation in different aquatic organisms and that these factors could have an influence on improving production in aquaculture.

7. Whole genome sequencing of aquatic organisms

Although teleost fish are the largest known vertebrate group with more than 27,000 species [8], they account for a small proportion of vertebrate species whose whole genomes have been fully sequenced and characterized. The pufferfish genome is one of the earliest fish genome to be sequenced and characterized by 2002 [234], which raised interests to sequence the genomes of other fish species. The zebrafish (*Danio rerio*) whole genome sequencing project was started by Wellcome Trust Sanger Institute in 2001 [235] while the Medaka genome was sequenced in 2007 [236]. Thus, Zebrafish and medaka are not only among the earliest

fish species to have their genomes sequenced and characterized, but they have attracted the highest research in genomic studies among teleost species. Their genomes have been widely used for comparative analyses as model species [235, 237–239]. Sequence analyses of the Atlantic cod genome in 2011 using the whole genome shotgun 454 pyrosequencing technology showed that this fish species lacks the major histocompatibility (MHC) II genes, which are compensated with expansion of the MHC-I and specific adaption of toll-like receptor genes demonstrating that whole genome sequencing can be used to elucidate evolutionary differences in the vertebrate taxa [240]. As shown in **Table 4**, there has been a spontaneous increase in the number of fish species whose genomes have characterized since the discovery of HTS technologies in recent years. Sequencing of other aquatic organism genomes is going on and it is anticipated that as HTS becomes cheaper, more sequences of aquatic organisms will become readily available for more advanced functional genomics research in aquaculture.

Common name	Scientific name	Year Published	Reference
Atlantic salmon	<i>Salmon salar</i> L.	2016	[264]
Atlantic cod	<i>Gadus morhua</i>	2011	[240]
Asian arowana	<i>Scleropages formosus</i>	2015	[8]
Medaka	<i>Oryzias latipes</i>	2007	[236]
Nile tilapia	<i>Oreochromis niloticus</i>	2015	[7]
Platyfish	<i>Xiphophorus maculatus</i>	2013	[265, 266]
Puffer fish	<i>Takifugu rubripes</i>	2002	[234]
Puffer fish	<i>Tetraodon nigroviridis</i>	2004	[267]
Three-spined stickleback	<i>Gasterosteus aculeatus</i>	2012	[268]
Rainbow trout	<i>Oncorhynchus mykiss</i>	2014/2016	[269, 270]
Killifish	<i>Nothobranchius furzeri</i>	2015	[271, 272]
Pearl oyster	<i>Pinctada fucata</i>	2012	[273]

Table 4. Whole genome sequencing of aquatic organisms.

8. Conclusions

In this chapter, we have shown that HTS has contributed to the rapid discovery of novel pathogens in aquaculture using metagenomics, which has significantly contributed in enhancing our ability to develop rationale disease control strategies unlike in the past when it took long from the first report of a clinical disease to identification of a novel pathogen. Moreover, metagenomics enable us to identify and monitor microbial communities found in different ecosystems

used in aquaculture. It has also proved to be an important tool able to map mucosal microbiota of different aquatic organisms. In vaccine production, genomics studies are being used to identify cross-neutralizing antigens able to confer protection across variant strains of the same pathogens. In genetics and epigenetics, several genomics traits have been identified that currently contributing to the improvement of production in aquaculture. Nutrigenomics have not only enhanced our understanding of the genetic markers for enteropathy and other nutritional diseases, but they have also highlighted our ability to formulate diets able to maintain stable GALT homeostasis in the gut. And as shown from the example of the Atlantic salmon production cycle in **Figure 2**, it is evident that functional genomics are used at different production stages of aquatic organisms to improve the overall production in aquaculture. Hence, genomics studies are not only useful at elucidating host-pathogen interactions [13-15], but they also serve as optimization tools for improving the quality and quantity of aquaculture products.

9. Future perspective

As HTS technologies become cheaper, it is anticipated that more genomes for different aquatic organisms will be characterized and that this shall pave the way to a better understanding of the genome duplication seen in some fish species. The use of HTS technologies in pathogen discovery and microbiota inhabiting mucosal surfaces of different aquatic organisms is expected to pave the way into timely design of rational disease control strategies. Hence, in future generations, we shall not only sequence whole genomes of all aquatic organisms, but we expect to provide a better understanding of the evolutionary aspects of the vertebrate taxa as well as providing new insight into host-pathogen interaction mechanisms at protein-protein level. It is our perception that current HTS studies are building a strong foundation for more advanced functional genomics developments in the future.

Author details

Hetron M. Munang'andu* and Øystein Evensen

*Address all correspondence to: hetroney.mweemba.munangandu@nmbu.no

Department of Basic Sciences and Aquatic Medicine, Section of Aquatic Medicine and Nutrition, Faculty of Veterinary Medicine and Biosciences, Norwegian University of Life Sciences, Ullevålsveien, Oslo, Norway

References

- [1] Gibbs RA. DNA amplification by the polymerase chain reaction. *Analytical Chemistry*. 1990;62(13):1202-1214

- [2] Mullis K, Faloona F, Scharf S, Saiki R, Horn G, Erlich H. Specific enzymatic amplification of DNA in vitro: The polymerase chain reaction. In: Cold Spring Harbor Symposia on Quantitative Biology. Edited by Michael A. Innis, David H. Gelfand, John J. Sninsky. Cold Spring Harbor Laboratory Press; Academic Press, San Diego, USA. 1986. pp. 263-273
- [3] Munang'andu HM, Fredriksen BN, Mutoloki S, Dalmo RA, Evensen Ø. The kinetics of CD4+ and CD8+ T-cell gene expression correlate with protection in Atlantic salmon (*Salmo salar* L.) vaccinated against infectious pancreatic necrosis. *Vaccine*. 2013;**31**(15):1956-1963
- [4] Rhodes SD. Quantitative Real-time Polymerase Chain Reaction. In: Encyclopedia of Systems Biology. Dubitzky W., Wolkenhauer O., Yokota H., Cho K.-H. (Eds.) Springer, New York, USA; 2013. pp. 1807-1807
- [5] Yamaguchi S, Kaji N, Munang'andu H, Kojima C, Mase M, Tsukamoto K. Quantification of chicken anaemia virus by competitive polymerase chain reaction. *Avian Pathology*. 2000;**29**(4):305-310
- [6] Tsofack JEK, Zamostiano R, Watted S, Berkowitz A, Rosenbluth E, Mishra N, Briese T, Lipkin WI, Kabuusu RM, Ferguson H. Detection of Tilapia Lake virus in clinical samples by culturing and nested reverse Transcription-PCR. *Journal of Clinical Microbiology*. 2017;**55**(3):759-767
- [7] Xia JH, Bai Z, Meng Z, Zhang Y, Wang L, Liu F, Jing W, Wan ZY, Li J, Lin H. Signatures of selection in tilapia revealed by whole genome resequencing. *Scientific Reports*. 2015;**5**:14168. doi: 10.1038/srep14168.
- [8] Austin CM, Tan MH, Croft LJ, Hammer MP, Gan HM. Whole genome sequencing of the Asian arowana (*Scleropages formosus*) provides insights into the evolution of ray-finned fishes. *Genome Biology and Evolution*. 2015 Oct 6;**7**(10):2885-95. doi: 10.1093/gbe/evv186.
- [9] Munang'andu HM, Mugimba KK, Byarugaba DK, Mutoloki S, Evensen Ø. Current advances on virus discovery and diagnostic role of viral metagenomics in aquatic organisms. *Frontiers in Microbiology*. 2017;**8**:406. doi: 10.3389/fmicb.2017.00406.
- [10] Munang'andu HM. Environmental viral metagenomics analyses in aquaculture: Applications in epidemiology and disease control. *Frontiers in Microbiology*. 2016;**7**:1986
- [11] Gajardo K, Jaramillo-Torres A, Kortner TM, Merrifield DL, Tinsley J, Bakke AM, Krogdahl Å. Alternative protein sources in the diet modulate microbiota and functionality in the distal intestine of Atlantic salmon (*Salmo salar*). *Applied and Environmental Microbiology*. 2016:02615-02616
- [12] Gajardo K, Rodiles A, Kortner TM, Krogdahl Å, Bakke AM, Merrifield DL, Sørum H. A high-resolution map of the gut microbiota in Atlantic salmon (*Salmo salar*): A basis for comparative gut microbial research. *Scientific Reports*. 2016;**6**:30893. doi: 10.1038/srep30893.
- [13] Xu C, Evensen O, Munang'andu HM. A de novo transcriptome analysis shows that modulation of the JAK-STAT signaling pathway by salmonid alphavirus subtype 3 favors virus replication in macrophage/dendritic-like TO-cells. *BMC Genomics*. 2016;**17**:390

- [14] Xu C, Evensen O, Munang'andu HM. De Novo transcriptome analysis shows that SAV-3 infection upregulates pattern recognition receptors of the endosomal Toll-Like and RIG-I-Like receptor signaling pathways in Macrophage/Dendritic like TO-Cells. *Viruses*. 2016;**8**(4):114
- [15] Xu C, Evensen Ø, Munang'andu HM. De novo assembly and transcriptome analysis of Atlantic salmon macrophage/dendritic-like TO cells following type I IFN treatment and Salmonid alphavirus subtype-3 infection. *BMC Genomics*. 2015;**16**(1):96
- [16] Morais S, Silva T, Cordeiro O, Rodrigues P, Guy DR, Bron JE, Taggart JB, Bell JG, Tocher DR. Effects of genotype and dietary fish oil replacement with vegetable oil on the intestinal transcriptome and proteome of Atlantic salmon (*Salmo salar*). *BMC Genomics*. 2012;**13**(1):448
- [17] Morán P, Marco-Rius F, Megías M, Covelo-Soto L, Pérez-Figueroa A. Environmental induced methylation changes associated with seawater adaptation in brown trout. *Aquaculture*. 2013;**392**:77-83
- [18] Morán P, Pérez-Figueroa A. Methylation changes associated with early maturation stages in the Atlantic salmon. *BMC Genetics*. 2011;**12**(1):86
- [19] Moffitt CM, Cajas-Cano L. Blue growth: The 2014 FAO state of world fisheries and aquaculture. *Fisheries*. 2014;**39**(11):552-553
- [20] Bibby K. Metagenomic identification of viral pathogens. *Trends in Biotechnology*. 2013;**31**(5):275-279
- [21] Alavandi S, Poornima M. Viral metagenomics: A tool for virus discovery and diversity in aquaculture. *Indian Journal of Virology*. 2012;**23**(2):88-98
- [22] McGonigle R. Acute catarrhal enteritis of salmonid fingerling. *Journal Transactions of the American Fisheries Society*. 1941;**70**(7)
- [23] Wolf K, Snieszko S, Dunbar C, Pyle E. Virus nature of infectious pancreatic necrosis in trout. *Proceedings of the Society for Experimental Biology and Medicine*. 1960;**104**(1):105-108
- [24] Jensen MH. Research on the virus of Egtved disease. *Annals of the New York Academy of Sciences*. 1965;**126**:422-426
- [25] Amin A, Trasti J. Endomyocarditis in Atlantic salmon in Norwegian seafarms. *Bulletin-European Association of Fish Pathologists*. 1988;**8**:70-71
- [26] Boucher P, Castric J, Laurencin FB. Observation of virus-like particles in rainbow trout *Oncorhynchus mykiss* infected with sleeping disease virulent material. *Bulletin of the European Association of Fish Pathologists (United Kingdom)*. 1995;**14**:215-216
- [27] Castric J, Baudin Laurencin F, Bremont M, Jeffroy J, Ven AI, Bearzotti M. Isolation of the virus responsible for sleeping disease in experimentally infected rainbow trout

- (*Oncorhynchus mykiss*). Bulletin of the European Association of Fish Pathologists. 1997;**17**(1):27-30
- [28] Wingfield W, Fryer J, Pilcher K. Properties of the sockeye salmon virus (Oregon strain). *Experimental Biology and Medicine*. 1969;**130**(4):1055-1059
- [29] Glazebrook J, Heasman M, Beer S. Picorna-like viral particles associated with mass mortalities in larval barramundi, *Lates calcarifer* Bloch. *Journal of Fish Diseases*. 1990;**13**(3):245-249
- [30] Munday B, Kwang J, Moody N. Betanodavirus infections of teleost fish: A review. *Journal of Fish Diseases*. 2002;**25**(3):127-142
- [31] Haugland Ø, Mikalsen AB, Nilsen P, Lindmo K, Thu BJ, Eliassen TM, Roos N, Rode M, Evensen Ø. Cardiomyopathy syndrome of Atlantic salmon (*Salmo salar* L.) is caused by a double-stranded RNA virus of the Totiviridae family. *Journal of Virology*. 2011;**85**(11):5275-5286
- [32] Kongtorp R, Kjerstad A, Taksdal T, Guttvik A, Falk K. Heart and skeletal muscle inflammation in Atlantic salmon, *Salmo salar* L.: A new infectious disease. *Journal of Fish Diseases*. 2004;**27**(6):351-358
- [33] Palacios G, Lovoll M, Tengs T, Hornig M, Hutchison S, Hui J, Kongtorp R-T, Savji N, Bussetti AV, Solovyov A. Heart and skeletal muscle inflammation of farmed salmon is associated with infection with a novel reovirus. *PLoS one*. 2010;**5**(7):e11487
- [34] Tarján Z, Péntzes J, Tóth R, Benko M. First detection of circovirus-like sequences in amphibians and novel putative circoviruses in fishes. *Acta Veterinaria Hungarica*. 2013;**62**(1):134-144
- [35] Fichtner D, Philipps A, Groth M, Schmidt-Posthaus H, Granzow H, Dauber M, Platzer M, Bergmann SM, Schrudde D, Sauerbrei A. Characterization of a novel picornavirus isolate from a diseased European eel (*Anguilla anguilla*). *Journal of Virology*. 2013;**87**(19):10895-10899
- [36] Reuter G, Pankovics P, Delwart E, Boros Á. A novel posavirus-related single-stranded RNA virus from fish (*Cyprinus carpio*). *Archives of Virology*. 2015;**160**(2):565-568
- [37] Reuter G, Boros Á, Delwart E, Pankovics P. Novel seadornavirus (family Reoviridae) related to Banna virus in Europe. *Archives of Virology*. 2013;**158**(10):2163-2167
- [38] Lotz J. Viruses, biosecurity and specific pathogen-free stocks in shrimp aquaculture. *World Journal of Microbiology and Biotechnology*. 1997;**13**(4):405-413
- [39] van Hulten MC, Witteveldt J, Peters S, Kloosterboer N, Tarchini R, Fiers M, Sandbrink H, Lankhorst RK, Vlak JM. The white spot syndrome virus DNA genome sequence. *Virology*. 2001;**286**(1):7-22
- [40] Yang F, He J, Lin X, Li Q, Pan D, Zhang X, Xu X. Complete genome sequence of the shrimp white spot bacilliform virus. *Journal of Virology*. 2001;**75**(23):11811-11820

- [41] Jimenez R. Síndrome de taura (Resumen). *Acuicultura del Ecuador*. 1992;1:1-16
- [42] Hasson K, Lightner DV, Poulos B, Redman R, White B, Brock J, Bonami J. Taura syndrome in *Penaeus vannamei*: Demonstration of a viral etiology. *Diseases of Aquatic Organisms*. 1995;23(2):115-126
- [43] Limsuwan C. Handbook for Cultivation of Black Tiger Prawns. Bangkok: Tansetakit Co Ltd; 1991
- [44] Tang KF-J, Lightner DV. A yellow head virus gene probe: Nucleotide sequence and application for in situ hybridization. *Diseases of Aquatic Organisms*. 1999;35(3):165-173
- [45] Brock J, Lightner D, Bell T. A review of four virus (BP, MBV, BMN and IHHNV) diseases of penaeid shrimp with particular reference to clinical significance, diagnosis and control in shrimp aquaculture. Proceedings of the 71st International Council for the Exploration of the Sea, CM. 1983:1-18.
- [46] Lightner D, Pantoja C, Poulos B, Tang K, Redman R, Andreas T, Bonami J. Infectious myonecrosis (IMN): A new virus disease of *Litopenaeus vannamei*. *Aquaculture*. 2004;242:353
- [47] Lightner DV, Redman R. A parvo-like virus disease of penaeid shrimp. *Journal of Invertebrate Pathology*. 1985;45(1):47-53
- [48] Nunes AJ, Martins P, Gesteira TCV. Carcinicultura ameaçada. *Rev Panoram Aquic*. 2004;83:37-51
- [49] Poulos BT, Tang KF, Pantoja CR, Bonami JR, Lightner DV. Purification and characterization of infectious myonecrosis virus of penaeid shrimp. *Journal of General Virology*. 2006;87(4):987-996
- [50] Tang KF, Pantoja CR, Redman RM, Lightner DV. Development of in situ hybridization and RT-PCR assay for the detection of a nodavirus (PvNV) that causes muscle necrosis in *Penaeus vannamei*. *Diseases of Aquatic Organisms*. 2007;75(3):183-190
- [51] Gadan K, Sandtro A, Marjara IS, Santi N, Munang'andu HM, Evensen O. Stress-induced reversion to virulence of infectious pancreatic necrosis virus in naive fry of Atlantic Salmon (*Salmo salar* L.). *Plos One*. 2013;8(2)
- [52] Angly FE, Felts B, Breitbart M, Salamon P, Edwards RA, Carlson C, Chan AM, Haynes M, Kelley S, Liu H. The marine viromes of four oceanic regions. *PLoS Biology*. 2006;4(11):e368
- [53] Dinsdale EA, Pantos O, Smriga S, Edwards RA, Angly F, Wegley L, Hatay M, Hall D, Brown E, Haynes M. Microbial ecology of four coral atolls in the Northern Line Islands. *PloS One*. 2008;3(2):e1584
- [54] Programme UNE. Marine and coastal ecosystems and human well-being: A synthesis report based on the findings of the Millennium Ecosystem Assessment. UNEP. 2006:76
- [55] Nogales B, Lanfranconi MP, Piña-Villalonga JM, Bosch R. Anthropogenic perturbations in marine microbial communities. *FEMS Microbiology Reviews*. 2011;35(2):275-298

- [56] Roux S, Enault F, Robin A, Ravet V, Personnic S, Theil S, Colombet J, Sime-Ngando T, Debroas D. Assessing the diversity and specificity of two freshwater viral communities through metagenomics. *PLoS One*. 2012;7(3):e33641
- [57] Tseng C-H, Chiang P-W, Shiah F-K, Chen Y-L, Liou J-R, Hsu T-C, Maheswararajah S, Saeed I, Halgamuge S, Tang S-L. Microbial and viral metagenomes of a subtropical freshwater reservoir subject to climatic disturbances. *The ISME Journal*. 2013;7(12):2374-2386
- [58] Islam MS, Tanaka M. Impacts of pollution on coastal and marine ecosystems including coastal and marine fisheries and approach for management: A review and synthesis. *Marine Pollution Bulletin*. 2004;48(7):624-649
- [59] Halpern BS, Walbridge S, Selkoe KA, Kappel CV, Micheli F, D'agrosa C, Bruno JF, Casey KS, Ebert C, Fox HE. A global map of human impact on marine ecosystems. *Science*. 2008;319(5865):948-952
- [60] Port JA, Wallace JC, Griffith WC, Faustman EM. Metagenomic profiling of microbial composition and antibiotic resistance determinants in Puget Sound. *PLoS One*. 2012;7(10):e48000
- [61] Morán AC, Hengst MB, De la Iglesia R, Andrade S, Correa JA, González B. Changes in bacterial community structure associated with coastal copper enrichment. *Environmental Toxicology and Chemistry*. 2008;27(11):2239-2245
- [62] Sugita H, Nakamura H, Shimada T. Microbial communities associated with filter materials in recirculating aquaculture systems of freshwater fish. *Aquaculture*. 2005;243(1):403-409
- [63] Itoi S, Niki A, Sugita H. Changes in microbial communities associated with the conditioning of filter material in recirculating aquaculture systems of the pufferfish *Takifugu rubripes*. *Aquaculture*. 2006;256(1):287-295
- [64] Schneider O, Chabrillon-Popelka M, Smidt H, Haenen O, Sereti V, Eding EH, Verreth JA. HRT and nutrients affect bacterial communities grown on recirculation aquaculture system effluents. *FEMS Microbiology Ecology*. 2007;60(2):207-219
- [65] Itoi S, Ebihara N, Washio S, Sugita H. Nitrite-oxidizing bacteria, *Nitrospira*, distribution in the outer layer of the biofilm from filter materials of a recirculating water system for the goldfish *Carassius auratus*. *Aquaculture*. 2007;264(1):297-308
- [66] Fox BK, Tamaru CS, Hollyer J, Castro LF, Fonseca JM, Jay-Russell M, Low T. A preliminary study of microbial water quality related to food safety in recirculating aquaponic fish and vegetable production systems. College of Tropical Agriculture and Human Resources, University of Hawaii at Manoa Food Safety and Technology. 2012
- [67] Munguia-Fragozo P, Alatorre-Jacome O, Rico-Garcia E, Torres-Pacheco I, Cruz-Hernandez A, Ocampo-Velazquez RV, Garcia-Trejo JF, Guevara-Gonzalez RG. Perspective for aquaponic systems: "Omic" technologies for microbial community analysis. *BioMed Research International*. 2015;2015:480386. doi: 10.1155/2015/480386.

- [68] Larsen A, Tao Z, Bullard SA, Arias CR. Diversity of the skin microbiota of fishes: Evidence for host species specificity. *FEMS Microbiology Ecology*. 2013;**85**(3):483-494
- [69] Lokesh J, Kiron V. Transition from freshwater to seawater reshapes the skin-associated microbiota of Atlantic salmon. *Scientific Reports*. 2016;**6**:19707. doi: 10.1038/srep19707.
- [70] Wilson B, Danilowicz BS, Meijer WG. The diversity of bacterial communities associated with Atlantic cod *Gadus morhua*. *Microbiology Ecology*. 2008;**55**(3):425-434
- [71] Boutin S, Sauvage C, Bernatchez L, Audet C, Derome N. Inter individual variations of the fish skin microbiota: Host genetics basis of mutualism? *PLoS One*. 2014;**9**(7):e102649
- [72] Lyons PP, Turnbull JF, Dawson KA, Crumlish M. Phylogenetic and functional characterization of the distal intestinal microbiome of rainbow trout *Oncorhynchus mykiss* from both farm and aquarium settings. *Journal of Applied Microbiology*. 2016. **2017**;122(2):347-363. doi: 10.1111/jam.13347.
- [73] Mouchet MA, Bouvier C, Bouvier T, Troussellier M, Escalas A, Mouillot D. Genetic difference but functional similarity among fish gut bacterial communities through molecular and biochemical fingerprints. *FEMS Microbiology Ecology*. 2012;**79**(3):568-580
- [74] Desai AR, Links MG, Collins SA, Mansfield GS, Drew MD, Van Kessel AG, Hill JE. Effects of plant-based diets on the distal gut microbiome of rainbow trout (*Oncorhynchus mykiss*). *Aquaculture*. 2012;**350**:134-142
- [75] Star B, Haverkamp TH, Jentoft S, Jakobsen KS. Next generation sequencing shows high variation of the intestinal microbial species composition in Atlantic cod caught at a single location. *BMC Microbiology*. 2013;**13**(1):248
- [76] Navarrete P, Magne F, Araneda C, Fuentes P, Barros L, Opazo R, Espejo R, Romero J. PCR-TTGE analysis of 16S rRNA from rainbow trout (*Oncorhynchus mykiss*) gut microbiota reveals host-specific communities of active bacteria. *PloS One*. 2012;**7**(2):e31335
- [77] Boutin S, Audet C, Derome N. Probiotic treatment by indigenous bacteria decreases mortality without disturbing the natural microbiota of *Salvelinus fontinalis*. *Canadian Journal of Microbiology*. 2013;**59**(10):662-670
- [78] Skrodenyte-Arbaciauskiene V, Sruoga A, Butkauskas D. Assessment of microbial diversity in the river trout *Salmo trutta fario* L. intestinal tract identified by partial 16S rRNA gene sequence analysis. *Fisheries Science*. 2006;**72**(3):597-602
- [79] Semova I, Carten JD, Stombaugh J, Mackey LC, Knight R, Farber SA, Rawls JF. Microbiota regulate intestinal absorption and metabolism of fatty acids in the zebrafish. *Cell Host & Microbe*. 2012;**12**(3):277-288
- [80] Ye L, Amberg J, Chapman D, Gaikowski M, Liu W-T. Fish gut microbiota analysis differentiates physiology and behavior of invasive Asian carp and indigenous American fish. *The ISME Journal*. 2014;**8**(3):541-551
- [81] Li X, Yu Y, Feng W, Yan Q, Gong Y. Host species as a strong determinant of the intestinal microbiota of fish larvae. *The Journal of Microbiology*. 2012;**50**(1):29-37

- [82] Li X, Yan Q, Xie S, Hu W, Yu Y, Hu Z. Gut microbiota contributes to the growth of fast-growing transgenic common carp (*Cyprinus carpio* L.). *PLoS One*. 2013;**8**(5):e64577
- [83] Wu S, Wang G, Angert ER, Wang W, Li W, Zou H. Composition, diversity, and origin of the bacterial community in grass carp intestine. *PLoS One*. 2012;**7**(2):e30440
- [84] Sun Y, Yang H, Ling Z, Chang J, Ye J. Gut microbiota of fast and slow growing grouper *Epinephelus coioides*. *African Journal of Microbiology Research*. 2009;**3**(11):637-640
- [85] Tapia-Paniagua ST, Chabrillón M, Díaz-Rosales P, de la Banda IG, Lobo C, Balebona MC, Moriñigo MA. Intestinal microbiota diversity of the flat fish *Solea senegalensis* (Kaup, 1858) following probiotic administration. *Microbial Ecology*. 2010;**60**(2):310-319
- [86] Xia JH, Lin G, Fu GH, Wan ZY, Lee M, Wang L, Liu XJ, Yue GH. The intestinal microbiome of fish under starvation. *BMC Genomics*. 2014;**15**(1):266
- [87] Liu H, Guo X, Gooneratne R, Lai R, Zeng C, Zhan F, Wang W. The gut microbiome and degradation enzyme activity of wild freshwater fishes influenced by their trophic levels. *Scientific Reports*. 2016;**6**:24340. doi: 10.1038/srep24340.
- [88] Lyons PP, Turnbull JF, Dawson KA, Crumlish M. Phylogenetic and functional characterization of the distal intestinal microbiome of rainbow trout *Oncorhynchus mykiss* from both farm and aquarium settings. *Journal of Applied Microbiology*. 2017;**122**(2):347-363
- [89] Wong S, Waldrop T, Summerfelt S, Davidson J, Barrows F, Kenney PB, Welch T, Wiens GD, Snekvik K, Rawls JF. Aquacultured rainbow trout (*Oncorhynchus mykiss*) possess a large core intestinal microbiota that is resistant to variation in diet and rearing density. *Applied and Environmental Microbiology*. 2013;**79**(16):4974-4984
- [90] Xing M, Hou Z, Yuan J, Liu Y, Qu Y, Liu B. Taxonomic and functional metagenomic profiling of gastrointestinal tract microbiome of the farmed adult turbot (*Scophthalmus maximus*). *FEMS Microbiology Ecology*. 2013;**86**(3):432-443
- [91] Li Y, Xie W, Li Q. Characterisation of the bacterial community structures in the intestine of *Lampetra morii*. *Antonie van Leeuwenhoek*. 2016;**109**(7):979-986
- [92] Sanders JG, Beichman AC, Roman J, Scott JJ, Emerson D, McCarthy JJ, Girguis PR. Baleen whales host a unique gut microbiome with similarities to both carnivores and herbivores. *Nature Communications*. 2015;**6**:8285. doi: 10.1038/ncomms9285.
- [93] Etyemez M, Balcázar JL. Bacterial community structure in the intestinal ecosystem of rainbow trout (*Oncorhynchus mykiss*) as revealed by pyrosequencing-based analysis of 16S rRNA genes. *Research in Veterinary Science*. 2015;**100**:8-11
- [94] Jan C, Petersen JM, Werner J, Teeling H, Huang S, Glöckner FO, Golyshina OV, Dubilier N, Golyshin PN, Jebbar M. The gill chamber epibiosis of deep-sea shrimp *Rimicaris exoculata*: An in-depth metagenomic investigation and discovery of Zetaproteobacteria. *Environmental Microbiology*. 2014;**16**(9):2723-2738
- [95] Prakash T, Taylor TD. Functional assignment of metagenomic data: Challenges and applications. *Briefings in Bioinformatics*. 2012;**13**(6):711-727

- [96] Quinn NL, Levenkova N, Chow W, Bouffard P, Boroevich KA, Knight JR, Jarvie TP, Lubieniecki KP, Desany BA, Koop BF. Assessing the feasibility of GSFLX Pyrosequencing for sequencing the Atlantic salmon genome. *BMC Genomics*. 2008;**9**(1):404
- [97] Edwards RA, Rohwer F. Viral metagenomics. *Nature Reviews Microbiology*. 2005;**3**(6): 504-510
- [98] Hunter S, Jones P, Mitchell A, Apweiler R, Attwood TK, Bateman A, Bernard T, Binns D, Bork P, Burge S. InterPro in 2011: New developments in the family and domain prediction database. *Nucleic Acids Research*. 2011:(**Database** issue):D306-12. doi: 10.1093/nar/gkr948.
- [99] Attwood TK, Bradley P, Flower DR, Gaulton A, Maudling N, Mitchell AL, Moulton G, Nordle A, Paine K, Taylor P. PRINTS and its automatic supplement, prePRINTS. *Nucleic Acids Research*. 2003;**31**(1):400-402
- [100] Pellegrini M, Marcotte EM, Thompson MJ, Eisenberg D, Yeates TO. Assigning protein functions by comparative genome analysis: Protein phylogenetic profiles. *Proceedings of the National Academy of Sciences*. 1999;**96**(8):4285-4288
- [101] Dandekar T, Snel B, Huynen M, Bork P. Conservation of gene order: A fingerprint of proteins that physically interact. *Trends in Biochemical Sciences*. 1998;**23**(9):324-328
- [102] Overbeek R, Fonstein M, D'souza M, Pusch GD, Maltsev N. The use of gene clusters to infer functional coupling. *Proceedings of the National Academy of Sciences*. 1999;**96**(6):2896-2901
- [103] Calduch-Giner JA, Sitjà-Bobadilla A, Pérez-Sánchez J. Gene expression profiling reveals functional specialization along the intestinal tract of a carnivorous teleostean fish (*Dicentrarchus labrax*). *Frontiers in Physiology*. 2016;**7**:359. doi: 10.3389/fphys.2016.00359.
- [104] Ezeasor D, Stokoe W. Light and electron microscopic studies on the absorptive cells of the intestine, caeca and rectum of the adult rainbow trout, *Salmo gairdneri*, Rich. *Journal of Fish Biology*. 1981;**18**(5):527-544
- [105] Nasruddin NS, Azmai MNA, Ismail A, Saad MZ, Daud HM, Zulkifli SZ. Histological features of the gastrointestinal tract of wild Indonesian shortfin eel, *Anguilla bicolor bicolor* (McClelland, 1844), captured in Peninsular Malaysia. *The Scientific World Journal*. 2014;**2014**:312670. doi: 10.1155/2014/312670.
- [106] Munang'andu HM, Mutoloki S, Evensen Ø. A review of the immunological mechanisms following mucosal vaccination of finfish. *Frontiers in Immunology*. 2015;**6**:427
- [107] Mutoloki S, Munang'andu HM, Evensen Ø. Oral vaccination of fish—antigen preparations, uptake, and immune induction. *Frontiers in Immunology*. 2015;**6**:519
- [108] Salinas I. The mucosal immune system of teleost fish. *Biology*. 2015;**4**(3):525-539
- [109] Munang'andu HM, Mutoloki S, Evensen Ø. An overview of challenges limiting the design of protective mucosal vaccines for finfish. *Frontiers in Immunology*. 2015;**6**:542

- [110] Król E, Douglas A, Tocher DR, Crampton VO, Speakman JR, Secombes CJ, Martin SA. Differential responses of the gut transcriptome to plant protein diets in farmed Atlantic salmon. *BMC Genomics*. 2016;**17**(1):156
- [111] Torrecillas S, Montero D, Caballero MJ, Pittman KA, Custódio M, Campo A, Sweetman J, Izquierdo M. Dietary mannan oligosaccharides: Counteracting the side effects of soybean meal oil inclusion on european sea bass (*Dicentrarchus labrax*) gut health and skin mucosa mucus production? *Frontiers in Immunology*. 2015;**6**:397. doi: 10.3389/fimmu.2015.00397.
- [112] Azeredo R, Pérez-Sánchez J, Sitjà-Bobadilla A, Fouz B, Tort L, Aragão C, Oliva-Teles A, Costas B. European sea bass (*Dicentrarchus labrax*) immune status and disease resistance are impaired by arginine dietary supplementation. *PLoS One*. 2015;**10**(10):e0139967
- [113] Estensoro I, Ballester-Lozano G, Benedito-Palos L, Grammes F, Martos-Sitcha JA, Mydland L-T, Caldutch-Giner JA, Fuentes J, Karalazos V, Ortiz Á. Dietary butyrate helps to restore the intestinal status of a marine teleost (*Sparus aurata*) fed extreme diets low in fish meal and fish oil. *PLoS One*. 2016;**11**(11):e0166564
- [114] Núñez-Acuña G, Gonçalves AT, Valenzuela-Muñoz V, Pino-Marambio J, Wadsworth S, Gallardo-Escárate C. Transcriptome immunomodulation of in-feed additives in Atlantic salmon *Salmo salar* infested with sea lice *Caligus rogercresseyi*. *Fish & Shellfish Immunology*. 2015;**47**(1):450-460
- [115] Olsvik PA, Hemre G-I, Waagbø R. Correction: Exploring early micronutrient deficiencies in rainbow trout (*Oncorhynchus mykiss*) by Next-Generation sequencing Technology-From black box to functional genomics. *PLoS One*. 2016;**11**(5):e0156668
- [116] Zhao H, Li C, Beck BH, Zhang R, Thongda W, Davis DA, Peatman E. Impact of feed additives on surface mucosal health and columnaris susceptibility in channel catfish fingerlings, *Ictalurus punctatus*. *Fish & Shellfish Immunology*. 2015;**46**(2):624-637
- [117] Li C, Beck BH, Peatman E. Nutritional impacts on gene expression in the surface mucosa of blue catfish (*Ictalurus furcatus*). *Developmental & Comparative Immunology*. 2014;**44**(1):226-234
- [118] Rurangwa E, Sipkema D, Kals J, ter Veld M, Forlenza M, Bacanu GM, Smidt H, Palstra AP. Impact of a novel protein meal on the gastrointestinal microbiota and the host transcriptome of larval zebrafish *Danio rerio*. *Frontiers in Physiology*. 2015;**6**:133. doi: 10.3389/fphys.2015.00133.
- [119] Corthésy-Theulaz I, den Dunnen JT, Ferré P, Geurts JM, Müller M, van Belzen N, van Ommen B. Nutrigenomics: The impact of biomics technology on nutrition research. *Annals of Nutrition and Metabolism*. 2005;**49**(6):355-365
- [120] Poirion OB, Zhu X, Ching T, Garmire L. Single-Cell transcriptomics bioinformatics and computational challenges. *Frontiers in Genetics*. 2016;**7**:163.
- [121] Stegle O, Teichmann SA, Marioni JC. Computational and analytical challenges in single-cell transcriptomics. *Nature Reviews Genetics*. 2015;**16**(3):133-145

- [122] Wang Z, Gerstein M, Snyder M. RNA-Seq: A revolutionary tool for transcriptomics. *Nature Reviews Genetics*. 2009;**10**(1):57-63
- [123] Neeha V, Kint P. Nutrigenomics research: A review. *Journal of Food Science and Technology*. 2013;**50**(3):415-428
- [124] Müller M, Kersten S. Nutrigenomics: Goals and strategies. *Nature Reviews Genetics*. 2003;**4**(4):315-322
- [125] Munang'andu HM, Mutoloki S, Evensen O. Acquired immunity and vaccination against infectious pancreatic necrosis virus of salmon. *Developmental & Comparative Immunology*. 2014;**43**(2):184-196
- [126] Munang'andu HM, Sandtro A, Mutoloki S, Brudeseth BE, Santi N, Evensen O. Immunogenicity and cross protective ability of the central VP2 amino acids of infectious pancreatic necrosis virus in Atlantic salmon (*Salmo salar* L.). *PLoS One*;2013;**8**(1):e54263
- [127] Christie K. Immunization with viral antigens: Infectious pancreatic necrosis. *Developments in Biological Standardization*. 1996;**90**:191-199
- [128] Costa J, Adams A, Bron J, Thompson K, Starkey W, Richards R. Identification of B-cell epitopes on the betanodavirus capsid protein. *Journal of Fish Diseases*. 2007;**30**(7):419-426
- [129] Ou-yang Z, Wang P, Huang Y, Huang X, Wan Q, Zhou S, Wei J, Zhou Y, Qin Q. Selection and identification of Singapore grouper iridovirus vaccine candidate antigens using bioinformatics and DNA vaccination. *Veterinary Immunology and Immunopathology*. 2012;**149**(1):38-45
- [130] Munang'andu HM, Mutoloki S, Evensen Ø. Non-replicating Vaccines. *Fish Vaccination*. 22-32
- [131] Munang'andu HM, Evensen Ø. A review of intra-and extracellular antigen delivery systems for virus vaccines of finfish. *Journal of Immunology Research*. 2015;**2015**
- [132] Munang'andu HM, Paul J, Evensen Ø. An overview of vaccination strategies and antigen delivery systems for streptococcus agalactiae vaccines in Nile Tilapia (*Oreochromis niloticus*). *Vaccines*. 2016;**4**(4):48
- [133] Handfield M, Brady LJ, Progulske-Fox A, Hillman JD. IVIAT: A novel method to identify microbial genes expressed specifically during human infections. *Trends in Microbiology*. 2000;**8**(7):336-339
- [134] Sun Y, Hu Y-H, Liu C-S, Sun L. Construction and analysis of an experimental *Streptococcus iniae* DNA vaccine. *Vaccine*. 2010;**28**(23):3905-3912
- [135] Zou YX, Mo ZL, Hao B, Ye XH, Guo DS, Zhang PJ. Screening of genes expressed in vivo after infection by *Vibrio anguillarum* M3. *Letters in Applied Microbiology*. 2010;**51**(5):564-569
- [136] Menanteau-Ledouble S, El-Matbouli M. Antigens of *Aeromonas salmonicida* subsp. *salmonicida* specifically induced in vivo in *Oncorhynchus mykiss*. *Journal of Fish Diseases*. 2015;**39**(8):1015-9. doi: 10.1111/jfd.12430.

- [137] Menanteau-Ledouble S, Soliman H, Kumar G, El-Matbouli M. Use of in vivo induced antigen technology to identify genes from *Aeromonas salmonicida* subsp. *salmonicida* that are specifically expressed during infection of the rainbow trout *Oncorhynchus mykiss*. BMC Veterinary Research. 2014;**10**(1):298
- [138] Jiao X-D, Dang W, Hu Y-H, Sun L. Identification and immunoprotective analysis of an in vivo-induced *Edwardsiella tarda* antigen. Fish & Shellfish Immunology. 2009;**27**(5):633-638
- [139] Nho SW, Hikima J-i, Cha IS, Park SB, Jang HB, del Castillo CS, Kondo H, Hirono I, Aoki T, Jung TS. Complete genome sequence and immunoproteomic analyses of the fish bacterial pathogen *Streptococcus parauberis*. Journal of Bacteriology. 2011: 00182-00111
- [140] Sun Y, Liu C-S, Sun L. Construction and analysis of the immune effect of an *Edwardsiella tarda* DNA vaccine encoding a D15-like surface antigen. Fish & Shellfish Immunology. 2011;**30**(1):273-279
- [141] Board BA. Norwegian breeding strategies—a success story of Long-term benefits
- [142] Lester LJ. Developing a selective breeding program for penaeid shrimp mariculture. Aquaculture. 1983;**33**(1-4):41-50
- [143] Argue BJ, Arce SM, Lotz JM, Moss SM. Selective breeding of Pacific white shrimp (*Litopenaeus vannamei*) for growth and resistance to Taura Syndrome Virus. Aquaculture. 2002;**204**(3):447-460
- [144] López ME, Neira R, Yáñez JM. Applications in the search for genomic selection signatures in fish. Frontiers in Genetics. 2014;**5**
- [145] McAndrew B, Napier J. Application of genetics and genomics to aquaculture development: Current and future directions. The Journal of Agricultural Science. 2011;**149**(S1):143-151
- [146] Andriantahina F, Liu X, Huang H. Genetic map construction and quantitative trait locus (QTL) detection of growth-related traits in *Litopenaeus vannamei* for selective breeding applications. PloS One. 2013;**8**(9):e75206
- [147] Li Y, Byrne K, Miggiano E, Whan V, Moore S, Keys S, Crocos P, Preston N, Lehnert S. Genetic mapping of the kuruma prawn *Penaeus japonicus* using AFLP markers. Aquaculture. 2003;**219**(1):143-156
- [148] Geldermann, H. Investigations on inheritance of quantitative characters in animals by gene markers I. Methods. TAG Theoretical and Applied Genetics. 1975;**46**(7):319-330
- [149] Tsai H-Y, Hamilton A, Tinch AE, Guy DR, Gharbi K, Stear MJ, Matika O, Bishop SC, Houston RD. Genome wide association and genomic prediction for growth traits in juvenile farmed Atlantic salmon using a high density SNP array. BMC Genomics. 2015;**16**(1):969
- [150] Salem M, Vallejo RL, Leeds TD, Palti Y, Liu S, Sabbagh A, Rexroad III CE, Yao J. RNA-Seq identifies SNP markers for growth traits in rainbow trout. PLoS One. 2012;**7**(5):e36264

- [151] Liu H, Fu B, Pang M, Feng X, Wang X, Yu X, Tong J. QTL fine mapping and identification of candidate genes for growth-related traits in bighead carp (*Hypophthalmichthys nobilis*). *Aquaculture*. 2016;**465**:134-143
- [152] Lv W, Zheng X, Kuang Y, Cao D, Yan Y, Sun X. QTL variations for growth-related traits in eight distinct families of common carp (*Cyprinus carpio*). *BMC Genetics*. 2016;**17**(1):65
- [153] Laghari M, Lashari P, Zhang X, Xu P, Xin B, Zhang Y, Narejo N, Sun X. Mapping quantitative trait loci (QTL) for body weight, length and condition factor traits in back-cross (BC1) family of Common carp (*Cyprinus carpio* L.). *Molecular Biology Reports*. 2014;**41**(2):721-731
- [154] Huang C, Li Y, Hu S, Chi J, Lin G, Lin C, Gong H, Chen J, Chen R, Chang S. Differential expression patterns of growth-related microRNAs in the skeletal muscle of Nile tilapia. *Journal of Animal Science*. 2012;**90**(12):4266-4279
- [155] Laine VN, Shikano T, Herczeg G, Vilkki J, Merilä J. Quantitative trait loci for growth and body size in the nine-spined stickleback *Pungitius pungitius* L. *Molecular Ecology*. 2013;**22**(23):5861-5876
- [156] Moghadam HK, Poissant J, Fotherby H, Haidle L, Ferguson MM, Danzmann RG. Quantitative trait loci for body weight, condition factor and age at sexual maturation in Arctic charr (*Salvelinus alpinus*): Comparative analysis with rainbow trout (*Oncorhynchus mykiss*) and Atlantic salmon (*Salmo salar*). *Molecular Genetics and Genomics*. 2007;**277**(6):647-661
- [157] Lu X, Luan S, Hu LY, Mao Y, Tao Y, Zhong SP, Kong J. High-resolution genetic linkage mapping, high-temperature tolerance and growth-related quantitative trait locus (QTL) identification in *Marsupenaesus japonicus*. *Molecular Genetics and Genomics*. 2016;**291**(3):1391-1405
- [158] Lyons R, Dierens L, Tan S, Preston N, Li Y. Characterization of AFLP markers associated with growth in the Kuruma prawn, *Marsupenaesus japonicus*, and identification of a candidate gene. *Marine Biotechnology*. 2007;**9**(6):712-721
- [159] Wang W, Tian Y, Kong J, Li X, Liu X, Yang C. Integration genetic linkage map construction and several potential QTLs mapping of Chinese shrimp (*Fenneropenaeus chinensis*) based on three types of molecular markers. *Russian Journal of Genetics*. 2012;**48**(4):422-434
- [160] Jung H, Lyons RE, Li Y, Thanh NM, Dinh H, Hurwood DA, Salin KR, Mather PB. A candidate gene association study for growth performance in an improved giant freshwater prawn (*Macrobrachium rosenbergii*) culture line. *Marine Biotechnology*. 2014;**16**(2):161-180
- [161] Li J, Li J, Chen P, Liu P, He Y. Transcriptome analysis of eyestalk and hemocytes in the ridgetail white prawn *Exopalaemon carinicauda*: Assembly, Annotation and Marker Discovery. *Molecular Biology Reports*. 2015;**42**(1):135-147

- [162] Ma K, Qiu G, Feng J, Li J. Transcriptome analysis of the oriental river prawn, *Macrobrachium nipponense* using 454 pyrosequencing for discovery of genes and markers. *PLoS One*. 2012;7(6):e39727
- [163] Sun X, Liang L. A genetic linkage map of common carp (*Cyprinus carpio* L.) and mapping of a locus associated with cold tolerance. *Aquaculture*. 2004;238(1):165-172
- [164] Eshel O, Shirak A, Weller J, Hulata G, Ron M. Linkage and physical mapping of sex region on LG23 of Nile tilapia (*Oreochromis niloticus*). *G3: Genes | Genomes | Genetics*. 2012;2(1):35-42
- [165] Zhang Y, Xu P, Lu C, Kuang Y, Zhang X, Cao D, Li C, Chang Y, Hou N, Li H. Genetic linkage mapping and analysis of muscle fiber-related QTLs in common carp (*Cyprinus carpio* L.). *Marine Biotechnology*. 2011;13(3):376-392
- [166] Gjedrem T, Baranski M. *Selective Breeding in Aquaculture: An Introduction*. Vol. 10. Springer Science & Business Media; 2010
- [167] Araneda C, Neira R, Iturra P. Identification of a dominant SCAR marker associated with colour traits in Coho salmon (*Oncorhynchus kisutch*). *Aquaculture*. 2005;247(1):67-73
- [168] McAndrew B, Roubal FR, Roberts RJ, Bullock AM, McEwen I. The genetics and histology of red, blond and associated colour variants in *Oreochromis niloticus*. *Genetica*. 1988;76(2):127-137
- [169] Kaese A, Ritola O, Paananen T, Eskelinen U, Mäntysaari E. Big and beautiful? Quantitative genetic parameters for appearance of large rainbow trout. *Journal of Fish Biology*. 2003;62(3):610-622
- [170] Nakamura K, Ozaki A, Akutsu T, Iwai K, Sakamoto T, Yoshizaki G, Okamoto N. Genetic mapping of the dominant albino locus in rainbow trout (*Oncorhynchus mykiss*). *Molecular Genetics and Genomics*. 2001;265(4):687-693
- [171] Greenwood AK, Jones FC, Chan YF, Brady SD, Absher DM, Grimwood J, Schmutz J, Myers RM, Kingsley DM, Peichel CL. The genetic basis of divergent pigment patterns in juvenile threespine sticklebacks. *Heredity*. 2011;107(2):155-166
- [172] Xuan-Peng W, Xiao-Feng Z, Wen-Sheng L, Tian-Qi Z, Xiao-Wen LCAS. Mapping and genetic effect analysis on quantitative trait loci related to feed conversion ratio of common carp (*Cyprinus carpio* L.). *Acta Hydrobiologica Sinica*. 2012;2:002
- [173] Köbis JM, Rebl A, Kühn C, Goldammer T. Comparison of splenic transcriptome activity of two rainbow trout strains differing in robustness under regional aquaculture conditions. *Molecular Biology Reports*. 2013;40(2):1955-1966
- [174] Shimada Y, Shikano T, Kuparinen A, Gonda A, Leinonen T, Merilä J. Quantitative genetics of body size and timing of maturation in two nine-spined stickleback (*Pungitius pungitius*) populations. *PLoS One*. 2011;6(12):e28859
- [175] Cnaani A, Hallerman EM, Ron M, Weller JI, Indelman M, Kashi Y, Gall GA, Hulata G. Detection of a chromosomal region with two quantitative trait loci, affecting cold tolerance and fish size, in an F₂ tilapia hybrid. *Aquaculture*. 2003;223(1):117-128

- [176] Somorjai IM, Danzmann RG, Ferguson MM. Distribution of temperature tolerance quantitative trait loci in Arctic charr (*Salvelinus alpinus*) and inferred homologies in rainbow trout (*Oncorhynchus mykiss*). *Genetics*. 2003;**165**(3):1443-1456
- [177] Seear PJ, Carmichael SN, Talbot R, Taggart JB, Bron JE, Sweeney GE. Differential gene expression during smoltification of Atlantic salmon (*Salmo salar* L.): A first large-scale microarray study. *Marine Biotechnology*. 2010;**12**(2):126-140
- [178] Sakamoto T, Danzmann RG, Okamoto N, Ferguson MM, Ihssen PE. Linkage analysis of quantitative trait loci associated with spawning time in rainbow trout (*Oncorhynchus mykiss*). *Aquaculture*. 1999;**173**(1):33-43
- [179] Huang R, Sun J, Luo Q, He L, Liao L, Li Y, Guo F, Zhu Z, Wang Y. Genetic variations of body weight and GCRV resistance in a random mating population of grass carp. *Oncotarget*. 2015;**6**(34):35433
- [180] Liu P, Wang L, Wan ZY, Ye BQ, Huang S, Wong S-M, Yue GH. Mapping QTL for resistance against viral nervous necrosis disease in Asian seabass. *Marine Biotechnology*. 2016;**18**(1):107-116
- [181] Rodríguez-Ramilo ST, De La Herrán R, Ruiz-Rejón C, Hermida M, Fernández C, Pereiro P, Figueras A, Bouza C, Toro MA, Martínez P. Identification of quantitative trait loci associated with resistance to viral haemorrhagic septicaemia (VHS) in turbot (*Scophthalmus maximus*): A comparison between bacterium, parasite and virus diseases. *Marine Biotechnology*. 2014;**16**(3):265-276
- [182] Verrier ER, Dorson M, Mauger S, Torhy C, Ciobotaru C, Hervet C, Dechamp N, Genet C, Boudinot P, Quillet E. Resistance to a rhabdovirus (VHSV) in rainbow trout: Identification of a major QTL related to innate mechanisms. *PLoS One*. 2013;**8**(2):e55302
- [183] Fuji K, Kobayashi K, Hasegawa O, Coimbra MRM, Sakamoto T, Okamoto N. Identification of a single major genetic locus controlling the resistance to lymphocystis disease in Japanese flounder (*Paralichthys olivaceus*). *Aquaculture*. 2006;**254**(1):203-210
- [184] Gheyas A, Houston R, Mota-Velasco J, Guy D, Tinch A, Haley C, Woolliams J. Segregation of infectious pancreatic necrosis resistance QTL in the early life cycle of Atlantic Salmon (*Salmo salar*). *Animal Genetics*. 2010;**41**(5):531-536
- [185] Gheyas A, Haley C, Guy D, Hamilton A, Tinch A, Mota-Velasco J, Woolliams J. Effect of a major QTL affecting IPN resistance on production traits in Atlantic salmon. *Animal Genetics*. 2010;**41**(6):666-668
- [186] Hjeltnes BWC, Bang Jensen B, Haukaas A. A: Fish health report 3B—2016. Fiskehelserapporten, 2015. The Norwegian Veterinary Institute; 2016
- [187] Wiens GD, Vallejo RL, Leeds TD, Palti Y, Hadidi S, Liu S, Evenhuis JP, Welch TJ, Rexroad III CE. Assessment of genetic correlation between bacterial cold water disease resistance and spleen index in a domesticated population of rainbow trout: Identification of QTL on chromosome Omy19. *PLoS One*. 2013;**8**(10):e75749

- [188] Robinson N, Baranski M, Mahapatra KD, Saha JN, Das S, Mishra J, Das P, Kent M, Arnyasi M, Sahoo PK. A linkage map of transcribed single nucleotide polymorphisms in rohu (*Labeo rohita*) and QTL associated with resistance to *Aeromonas hydrophila*. BMC Genomics. 2014;**15**(1):541
- [189] Shao C, Niu Y, Rastas P, Liu Y, Xie Z, Li H, Wang L, Jiang Y, Tai S, Tian Y. Genome-wide SNP identification for the construction of a high-resolution genetic map of Japanese flounder (*Paralichthys olivaceus*): Applications to QTL mapping of *Vibrio anguillarum* disease resistance and comparative genomic analysis. DNA Research. 2015;**22**(2):161-70. doi: 10.1093/dnares/dsv001.
- [190] Vallejo RL, Palti Y, Liu S, Evenhuis JP, Gao G, Rexroad III CE, Wiens GD. Detection of QTL in rainbow trout affecting survival when challenged with *Flavobacterium psychrophilum*. Marine Biotechnology. 2014;**16**(3):349-360
- [191] Massault C, Franch R, Haley C, De Koning D, Bovenhuis H, Pellizzari C, Patarnello T, Bargelloni L. Quantitative trait loci for resistance to fish pasteurellosis in gilthead sea bream (*Sparus aurata*). Animal Genetics. 2011;**42**(2):191-203
- [192] Gilbey J, Verspoor E, Mo TA, Sterud E, Olstad K, Hytterød S, Jones C, Noble L. Identification of genetic markers associated with *Gyrodactylus salaris* resistance in Atlantic salmon *Salmo salar*. Diseases of Aquatic Organisms. 2006;**71**(2):119-129
- [193] Ozaki A, Yoshida K, Fuji K, Kubota S, Kai W, Aoki J-y, Kawabata Y, Suzuki J, Akita K, Koyama T. Quantitative trait loci (QTL) associated with resistance to a monogenean parasite (*Benedenia seriola*) in yellowtail (*Seriola quinqueradiata*) through genome wide analysis. PloS One. 2013;**8**(6):e64987
- [194] Wilson K, Li Y, Whan V, Lehnert S, Byrne K, Moore S, Pongsomboon S, Tassanakajon A, Rosenberg G, Ballment E. Genetic mapping of the black tiger shrimp *Penaeus monodon* with amplified fragment length polymorphism. Aquaculture. 2002;**204**(3):297-309
- [195] Mukherjee K, Mandal N. A microsatellite DNA marker developed for identifying Disease-resistant population of Giant Black Tiger Shrimp, *Penaeus monodon*. Journal of the World Aquaculture Society. 2009;**40**(2):274-280
- [196] Hizer SE, Dhar AK, Klimpel KR, Garcia DK. RAPD markers as predictors of infectious hypodermal and hematopoietic necrosis virus (IHHNV) resistance in shrimp (*Litopenaeus stylirostris*). Genome. 2002;**45**(1):1-7
- [197] Ødegård J, Gitterle T, Madsen P, Meuwissen TH, Yazdi MH, Gjerde B, Pulgarin C, Rye M. Quantitative genetics of taura syndrome resistance in pacific white shrimp (*Penaeus vannamei*): A cure model approach. Genetics Selection Evolution. 2011;**43**(1):14
- [198] Waddington CH. Canalization of development and the inheritance of acquired characters. Nature. 1942;**150**(3811):563-565
- [199] Waddington CH. The epigenotype. Endeavour. 1942;**1**:18-20
- [200] Hotchkiss RD. The quantitative separation of purines, pyrimidines, and nucleosides by paper chromatography. Journal of Biological Chemistry. 1948;**175**(1):315-332

- [201] Holliday R, Pugh JE. DNA modification mechanisms and gene activity during development. Cold Spring Harbor Monograph Series. 1996;**32**:639-645
- [202] Razin A, Riggs AD. DNA methylation and gene function. Science. 1980;**210**(4470):604-610
- [203] Taylor SM, Jones PA. Multiple new phenotypes induced in 10T12 and 3T3 cells treated with 5-azacytidine. Cell. 1979;**17**(4):771-779
- [204] Goldberg AD, Allis CD, Bernstein E. Epigenetics: A landscape takes shape. Cell. 2007;**128**(4):635-638
- [205] Bernstein BE, Meissner A, Lander ES. The mammalian epigenome. Cell. 2007;**128**(4):669-681
- [206] Martín-Subero J. How epigenomics brings phenotype into being. Pediatric Endocrinology Reviews: PER. 2011;**9**:506-510
- [207] Wang Y, 王源. Hypoxia causes epigenetic changes and transgenerational reproductive impairments in marine medaka (*Oryzias melastigma*). HKU Theses Online (HKUTO). 2016
- [208] Wan ZY, Xia JH, Lin G, Wang L, Lin VC, Yue GH. Genome-wide methylation analysis identified sexually dimorphic methylated regions in hybrid tilapia. Scientific Reports. 2016;**6**:35903. doi: 10.1038/srep35903.
- [209] Sun L-X, Wang Y-Y, Zhao Y, Wang H, Li N, Ji XS. Global DNA methylation changes in Nile tilapia gonads during high temperature-induced masculinization. PLoS One. 2016;**11**(8):e0158483
- [210] Shao C, Li Q, Chen S, Zhang P, Lian J, Hu Q, Sun B, Jin L, Liu S, Wang Z. Epigenetic modification and inheritance in sexual reversal of fish. Genome Research. 2014;**24**(4):604-615
- [211] Zhang G. Epigenetic modification and inheritance in sexual reversal of tongue-sole fish. In: Proceeding of Plant and Animal Genome Asia (PAG), Grand Copthorn Waterfront Hotel. China, 2013.
- [212] Baerwald MR, Meek MH, Stephens MR, Nagarajan RP, Goodbla AM, Tomalty KM, Thorgaard GH, May B, Nichols KM. Migration-related phenotypic divergence is associated with epigenetic modifications in rainbow trout. Molecular Ecology. 2015
- [213] Kimura T, Yoshida K, Shimada A, Jindo T, Sakaizumi M, Mitani H, Naruse K, Takeda H, Inoko H, Tamiya G. Genetic linkage map of medaka with polymerase chain reaction length polymorphisms. Gene. 2005;**363**:24-31
- [214] Taneda Y, Konno S, Makino S, Morioka M, Fukuda K, Imai Y, Kudo A, Kawakami A. Epigenetic control of cardiomyocyte production in response to a stress during the medaka heart development. Developmental Biology. 2010;**340**(1):30-40
- [215] Cao Z, Ding W, Yu J, Cao L, Wu T. Differences in methylated loci among different grass carp individuals from one pair of parents. 2007: 1083-1088.
- [216] Ding G, Wang L, Zhang J, Wei Y, Wei L, Li Y, Shao M, Xiong D. Toxicity and DNA methylation changes induced by perfluorooctane sulfonate (PFOS) in sea urchin *Glyptocidaris crenularis*. Chemosphere. 2015;**128**:225-230

- [217] Zhao Y, Chen M, Storey KB, Sun L, Yang H. DNA methylation levels analysis in four tissues of sea cucumber *Apostichopus japonicus* based on fluorescence-labeled methylation-sensitive amplified polymorphism (F-MSAP) during aestivation. *Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology*. 2015;**181**:26-32
- [218] Covelo-Soto L, Morán P, Pasantes JJ, Pérez-García C. Cytogenetic evidences of genome rearrangement and differential epigenetic chromatin modification in the sea lamprey (*Petromyzon marinus*). *Genetica*. 2014;**142**(6):545-554
- [219] Mhanni A, McGowan R. Global changes in genomic methylation levels during early development of the zebrafish embryo. *Development Genes and Evolution*. 2004; **214**(8): 412-417
- [220] Gavery MR, Roberts SB. DNA methylation patterns provide insight into epigenetic regulation in the Pacific oyster (*Crassostrea gigas*). *BMC Genomics*. 2010;**11**(1):483
- [221] Shang X, Su J, Wan Q, Su J. CpA/CpG methylation of CiMDA5 possesses tight association with the resistance against GCRV and negatively regulates mRNA expression in grass carp, *Ctenopharyngodon idella*. *Developmental & Comparative Immunology*. 2015;**48**(1):86-94
- [222] Navarro-Martín L, Viñas J, Ribas L, Díaz N, Gutiérrez A, Di Croce L, Piferrer F. Epigenetics and fish sex ratios: The case of the sea bass. II Jornada de Cromatina i Epigenètica. 2011. <http://hdl.handle.net/10261/81182>.
- [223] Navarro-Martín L, Viñas J, Ribas L, Díaz N, Gutiérrez A, Di Croce L, Piferrer F. DNA methylation of the gonadal aromatase (*cyp19a*) promoter is involved in temperature-dependent sex ratio shifts in the European sea bass. *PLoS Genetics*. 2011;**7**(12):e1002447
- [224] Santos F, Hendrich B, Reik W, Dean W. Dynamic reprogramming of DNA methylation in the early mouse embryo. *Developmental Biology*. 2002;**241**(1):172-182
- [225] Contractor RG, Foran CM, Li S, Willett KL. Evidence of gender-and tissue-specific promoter methylation and the potential for ethinylestradiol-induced changes in Japanese medaka (*Oryzias latipes*) estrogen receptor and aromatase genes. *Journal of Toxicology and Environmental Health, Part A*. 2004;**67**(1):1-22
- [226] Wen A, You F, Sun P, Li J, Xu D, Wu Z, Ma D, Zhang P. CpG methylation of *dmrt1* and *cyp19a* promoters in relation to their sexual dimorphic expression in the Japanese flounder *Paralichthys olivaceus*. *Journal of Fish Biology*. 2014;**84**(1):193-205
- [227] Gómez R, Van Damme K, Gosálvez J, Morán ES, Colbourne JK. Male meiosis in Crustacea: Synapsis, recombination, epigenetics and fertility in *Daphnia magna*. *Chromosoma*. 2016; **125**(4):769-787
- [228] Giannetto A, Nagasawa K, Fasulo S, Fernandes JM. Influence of photoperiod on expression of DNA (cytosine-5) methyltransferases in Atlantic cod. *Gene*. 2013;**519**(2):222-230
- [229] Nagasawa K, Giannetto A, Fernandes JM. Photoperiod influences growth and *mll* (mixed-lineage leukaemia) expression in Atlantic cod. *PLoS One*. 2012;**7**(5):e36908

- [230] Marandel L, Lepais O, Arbenoits E, Véron V, Dias K, Zion M, Panserat S. Remodelling of the hepatic epigenetic landscape of glucose-intolerant rainbow trout (*Oncorhynchus mykiss*) by nutritional status and dietary carbohydrates. *Scientific Reports*. 2016;**6**
- [231] Flohr L, Fuzinatto CF, Melegari SP, Matias WG. Effects of exposure to soluble fraction of industrial solid waste on lipid peroxidation and DNA methylation in erythrocytes of *Oreochromis niloticus*, as assessed by quantification of MDA and m 5 dC rates. *Ecotoxicology and Environmental Safety*. 2012;**76**:63-70
- [232] Pierron F, Baillon L, Sow M, Gotreau S, Gonzalez P Effect of low-dose cadmium exposure on DNA methylation in the endangered European eel. *Environmental Science & Technology*. 2013;**48**(1):797-803
- [233] Aniagu SO, Williams TD, Allen Y, Katsiadaki I, Chipman JK. Global genomic methylation levels in the liver and gonads of the three-spine stickleback (*Gasterosteus aculeatus*) after exposure to hexabromocyclododecane and 17- β oestradiol. *Environment International*. 2008;**34**(3):310-317
- [234] Aparicio S, Chapman J, Stupka E, Putnam N, Chia J-m, Dehal P, Christoffels A, Rash S, Hoon S, Smit A. Whole-genome shotgun assembly and analysis of the genome of *Fugu rubripes*. *Science*. 2002;**297**(5585):1301-1310
- [235] Howe K, Clark MD, Torroja CF, Torrance J, Berthelot C, Muffato M, Collins JE, Humphray S, McLaren K, Matthews L. The zebrafish reference genome sequence and its relationship to the human genome. *Nature*. 2013;**496**(7446):498-503
- [236] Kasahara M, Naruse K, Sasaki S, Nakatani Y, Qu W, Ahsan B, Yamada T, Nagayasu Y, Doi K, Kasai Y. The medaka draft genome and insights into vertebrate genome evolution. *Nature*. 2007;**447**(7145):714-719
- [237] Wittbrodt J, Shima A, Scharl M. Medaka—a model organism from the far East. *Nature Reviews Genetics*. 2002;**3**(1):53-64
- [238] Hill AJ, Teraoka H, Heideman W, Peterson RE. Zebrafish as a model vertebrate for investigating chemical toxicity. *Toxicological Sciences*. 2005;**86**(1):6-19
- [239] Chen X, Li L, Wong CKC, Cheng SH. Rapid adaptation of molecular resources from zebrafish and medaka to develop an estuarine/marine model. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*. 2009;**149**(4):647-655
- [240] Star B, Nederbragt AJ, Jentoft S, Grimholt U, Malmstrøm M, Gregers TF, Rounge TB, Paulsen J, Solbakken MH, Sharma A. The genome sequence of Atlantic cod reveals a unique immune system. *Nature*. 2011;**477**(7363):207-210
- [241] Rastorguev S, Nedoluzhko A, Levina M, Prokhorchuk E, Skryabin K, Levin B. Pleiotropic effect of thyroid hormones on gene expression in fish as exemplified from the blue bream *Ballerus ballerus* (Cyprinidae): Results of transcriptomic analysis. In: *Doklady Biochemistry and Biophysics*: 2016. Springer; 2016. pp. 124-127

- [242] Li F-G, Chen J, Jiang X-Y, Zou S-M. Transcriptome analysis of blunt snout bream (*Megalobrama amblycephala*) reveals putative differential expression genes related to growth and hypoxia. *PloS One*. 2015;**10**(11):e0142801
- [243] Robledo D, Fernández C, Hermida M, Sciara A, Álvarez-Dios JA, Cabaleiro S, Caamaño R, Martínez P, Bouza C. Integrative transcriptome, genome and quantitative trait loci resources identify single nucleotide polymorphisms in candidate genes for growth traits in turbot. *International Journal of Molecular Sciences*. 2016;**17**(2):243
- [244] Sun Y, Guo C-Y, Wang D-D, Li XF, Xiao L, Zhang X, You X, Shi Q, Hu G-J, Fang C. Transcriptome analysis reveals the molecular mechanisms underlying growth superiority in a novel grouper hybrid (*Epinephelus fuscogutatus*♀× *E. lanceolatus*♂). *BMC Genetics*. 2016;**17**(1):24
- [245] Sun L, Li J, Liang X, Yi T, Fang L, Sun J, He Y, Luo X, Dou Y, Yang M. Microsatellite DNA markers and their correlation with growth traits in mandarin fish (*Siniperca chuatsi*). *Genetics and Molecular Research*. 2015;**14**(4):19128-19135
- [246] Estévez A, Andree K, Johnston IA. Fast skeletal muscle transcriptome of the Gilthead sea bream (*Sparus aurata*) determined by next generation sequencing. *BMC Genomics*. 2012;**13**(1):181
- [247] Sánchez CC, Weber GM, Gao G, Cleveland BM, Yao J, Rexroad CE. Generation of a reference transcriptome for evaluating rainbow trout responses to various stressors. *BMC Genomics*. 2011;**12**(1):626
- [248] Hemmer-Hansen J, Nielsen EE, Meldrup D, Mittelholzer C. Identification of single nucleotide polymorphisms in candidate genes for growth and reproduction in a nonmodel organism; the Atlantic cod, *Gadus morhua*. *Molecular Ecology Resources*. 2011;**11**(s1):71-80
- [249] Renaut S, Bernatchez L. Transcriptome-wide signature of hybrid breakdown associated with intrinsic reproductive isolation in lake whitefish species pairs (*Coregonus* spp. Salmonidae). *Heredity*. 2011;**106**(6):1003-1011
- [250] Whiteley AR, Derome N, Rogers SM, St-Cyr J, Laroche J, Labbe A, Nolte A, Renaut S, Jeukens J, Bernatchez L. The phenomics and expression quantitative trait locus mapping of brain transcriptomes regulating adaptive divergence in lake whitefish species pairs (*Coregonus* sp.). *Genetics*. 2008;**180**(1):147-164
- [251] Tao W, Boulding E. Associations between single nucleotide polymorphisms in candidate genes and growth rate in Arctic charr (*Salvelinus alpinus* L.). *Heredity*. 2003;**91**(1):60-69
- [252] Perry GM, Danzmann RG, Ferguson MM, Gibson JP. Quantitative trait loci for upper thermal tolerance in outbred strains of rainbow trout (*Oncorhynchus mykiss*). *Heredity*. 2001;**86**(3):333-341
- [253] Kawahara-Miki R, Wada K, Azuma N, Chiba S. Expression profiling without genome sequence information in a non-model species, Pandalid shrimp (*Pandalus latirostris*), by next-generation sequencing. *PLoS One*. 2011;**6**(10):e26043

- [254] Li Y, Dierens L, Byrne K, Miggiano E, Lehnert S, Preston N, Lyons R. QTL detection of production traits for the Kuruma prawn *Penaeus japonicus* (Bate) using AFLP markers. *Aquaculture*. 2006;**258**(1):198-210
- [255] Robinson NA, Gopikrishna G, Baranski M, Katneni VK, Shekhar MS, Shanmugakarthish J, Jothivel S, Gopal C, Ravichandran P, Gitterle T. QTL for white spot syndrome virus resistance and the sex-determining locus in the Indian black tiger shrimp (*Penaeus monodon*). *BMC Genomics*. 2014;**15**(1):731
- [256] Zhang L, Yang C, Zhang Y, Li L, Zhang X, Zhang Q, Xiang J. A genetic linkage map of Pacific white shrimp (*Litopenaeus vannamei*): Sex-linked microsatellite markers and high recombination rates. *Genetica*. 2007;**131**(1):37-49
- [257] Yu Y, Zhang X, Yuan J, Li F, Chen X, Zhao Y, Huang L, Zheng H, Xiang J. Genome survey and high-density genetic map construction provide genomic and genetic resources for the Pacific White Shrimp *Litopenaeus vannamei*. *Scientific Reports*. 2015;**5**:15612
- [258] Anelli V, Santoriello C, Distel M, Köster RW, Ciccarelli FD, Mione M. Global repression of cancer gene expression in a zebrafish model of melanoma is linked to epigenetic regulation. *Zebrafish*. 2009;**6**(4):417-424
- [259] Hove JR, Köster RW, Forouhar AS, Acevedo-Bolton G, Fraser SE, Gharib M. Intracardiac fluid forces are an essential epigenetic factor for embryonic cardiogenesis. *Nature*. 2003;**421**(6919):172-177
- [260] Bhandari RK. Medaka as a model for studying environmentally induced epigenetic trans-generational inheritance of phenotypes. *Environmental Epigenetics*. 2016;**2**(1):dvv010
- [261] Dos Santos Campos MCM. Thermal epigenetic regulation of muscle growth and development in the Senegalese sole (*Solea senegalensis* Kaup, 1858) [thesis]. Instituto de Ciências Biomédicas, Abel Salazar da Universidade do Porto; 2013
- [262] Pierron F, Bureau du Colombier S, Moffett A, Caron A, Peluhet L, Daffe G, Lambert P, Elie P, Labadie P, Budzinski Hln. Abnormal ovarian DNA methylation programming during gonad maturation in wild contaminated fish. *Environmental Science & Technology*. 2014;**48**(19):11688-11695
- [263] Matsumoto Y, Buemio A, Chu R, Vafae M, Crews D. Epigenetic control of gonadal aromatase (*cyp19a1*) in temperature-dependent sex determination of red-eared slider turtles. *PLoS One*. 2013;**8**(6):e63599
- [264] Lien S, Koop BF, Sandve SR, Miller JR, Kent MP, Nome T, Hvidsten TR, Leong JS, Minkley DR, Zimin A. The Atlantic salmon genome provides insights into rediploidization. *Nature*. 2016;**533**(7602):200-5. doi: 10.1038/nature17164.
- [265] Schartl M, Walter RB, Shen Y, Garcia T, Catchen J, Amores A, Braasch I, Chalopin D, Volff J-N, Lesch K-P. The genome of the platyfish, *Xiphophorus maculatus*, provides insights into evolutionary adaptation and several complex traits. *Nature Genetics*. 2013;**45**(5):567-572

- [266] Walter RB, Shen Y, Garcia T, Catchen J, Amores A, Braasch I, Chalopin D, Volff J-N, Lesch K-P, Bisazza A. The Genome of the Platyfish, *Xiphophorus Maculatus*, Provides Insights into Evolutionary Adaptation and Several Complex Traits [Internet]. 2013. Available from: <http://www.nature.com/ng/index.html>.
- [267] Jaillon O, Aury J-M, Brunet F, Petit J-L, Stange-Thomann N, Mauceli E, Bouneau L, Fischer C, Ozouf-Costaz C, Bernot A. Genome duplication in the teleost fish *Tetraodon nigroviridis* reveals the early vertebrate proto-karyotype. *Nature*. 2004;**431**(7011):946-957
- [268] Jones FC, Grabherr MG, Chan YF, Russell P, Mauceli E, Johnson J, Swofford R, Pirun M, Zody MC, White S. The genomic basis of adaptive evolution in threespine sticklebacks. *Nature*. 2012;**484**(7392):55-61
- [269] Berthelot C, Brunet F, Chalopin D, Juanchich A, Bernard M, Noël B, Bento P, Da Silva C, Labadie K, Alberti A. The rainbow trout genome provides novel insights into evolution after whole-genome duplication in vertebrates. *Nature Communications*. 2014;**5**:3657. doi: 10.1038/ncomms4657.
- [270] Guiguen Y. The rainbow trout genome provides novel insights into evolution after Whole-Genome duplication in vertebrates. In: *Plant and Animal Genome XXIV Conference: 2016: Plant and Animal Genome; 2016*
- [271] Harel I, Benayoun BA, Machado B, Singh PP, Hu C-K, Pech MF, Valenzano DR, Zhang E, Sharp SC, Artandi SE. A platform for rapid exploration of aging and diseases in a naturally short-lived vertebrate. *Cell*. 2015;**160**(5):1013-1026
- [272] Valenzano DR, Benayoun BA, Singh PP, Zhang E, Etter PD, Hu C-K, Clément-Ziza M, Willemsen D, Cui R, Harel I. The African turquoise killifish genome provides insights into evolution and genetic architecture of lifespan. *Cell*. 2015;**163**(6):1539-1554
- [273] Takeuchi T, Kawashima T, Koyanagi R, Gyoja F, Tanaka M, Ikuta T, Shoguchi E, Fujiwara M, Shinzato C, Hisata K. Draft genome of the pearl oyster *Pinctada fucata*: A platform for understanding bivalve biology. *DNA Research*. 2012;dss005

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