

The Role of Non-Coding RNAs (miRNAs & lncRNAs) in the Muscles of Rainbow Trout *Oncorhynchus mykiss*

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Abstract - The vital goal of aquaculture genomics, genetics and genomic editing is to enhance production efficiency in aquaculture sector. Rainbow trout (RBT) *Oncorhynchus mykiss* is a native species from the northwest coast of North America and it belongs to *salmonid* family. Rainbow trout is an important species in, wild stock fisheries and recreational sport fisheries in Aquaculture sector and RBT is valued for superior growth. Muscle is a molecular motor and muscle mass of livestock is crucial in food industry. Some studies reported the non-coding RNAs gene expression in muscle tissues of healthy and unhealthy (affected by muscle deterioration and muscle atrophy) fishes. During vitellogenesis, significant loss of muscle mass and sufficient muscle proteins accumulate in developing ova. This change throws a glimpse on general pattern of muscle wastage supporting RBT as an ideal model to illuminate muscle catabolism molecular mechanism. This review reports the differentially expression of microRNAs and lncRNAs of rainbow trout muscle tissues in the healthy and unhealthy fishes.

Keywords: Rainbow trout, miRNA, lncRNA, Degradome, Quantitative trait loci.

Background

Apart from the protein coding genes, there are other types of genes which code for the many small RNAs known as Non-coding RNAs. These include microRNAs, long non coding RNAs (lncRNAs), small non coding RNAs, small interfering RNAs and PIWI-interacting RNAs (JS and JL 2015). lncRNAs are one of the most studied non coding RNAs with size of above 200 nucleotides. Most of the lncRNAs do not contain any open reading frame (ORF) or with small ORF with an unknown coding potential (Ruiz-Orera et al. 2014). Additionally, there are several sub categories of long non coding RNAs which include long intergenicncRNAs, antisense or pseudogene RNAs, and long intronicncRNAs etc. (Mattick and Rinn 2015).

Micro RNA's are a class of small non-coding RNA bind to 3' untranslated region of its target messenger RNA and inhibit the translation or induce the target mRNA degradation. The major role of micro RNA's is regulation of gene

expression at post-transcriptional level. Post transcriptional regulation of target mRNA by miRNA is evolutionarily conserved mechanism and also found in all plants and animals (Mehta and Baltimore 2016; Garc et.al 2018).

Rainbow trout (*Oncorhynchus mykiss*) is a native species belongs to northwest coast of North America and it is a member of *Salmonid* family. Rainbow trout culture is introduced into approximately 99 countries worldwide.

Such a global success can be ascribed to a combination of factors which includes valued game fish in western culture, tolerance to extreme temperatures, selective breeding, rapid growth, suitability for hatchery cultivation and its economic importance in food sector.

Muscle yield and its quality traits are important for cultivating aquaculture organisms, wild stock fisheries and recreational sport fisheries. Apart from that skeletal muscle, the most abundant and edible tissue of other muscles of fish and typically makes up to more than 50% of the fish weight. Differentially expressed mRNAs and small non coding RNAs (nc RNAs) include micro RNAs and long non coding RNAs (lncRNAs) etc. which are found in muscle tissues during differentiation, growth, sexual maturation, starvation, muscle deterioration and muscle atrophy conditions in rainbow trout (Jian Wang et.al 2017). Small non coding RNAs also regulate the expression of different hormones and growth factors by inhibiting them at post transcriptional or translational stages (Jian Wang et.al 2017).

Genetic maps and genetic marker tools have been developed and used for a wide range of species including fish. These tools are useful to discover the allelic variation affecting traits with an ultimate goal of identifying DNA sequences underlying phenotypes. Genomic selection (GS) tools have been developed to increase the efficiency of genetic improvement in livestock. Single nucleotide polymorphisms (SNPs) located within or near coding sequences (cSNPs) is useful as genetic markers with large effect on phenotypes as they have the potential to alter the protein function. The ability to use genomic selection or marker associated selection (MAS) will allow further within family selection for the muscle yield traits (Salem et.al 2019).

Microarray chip and proteomic technologies revealed that muscle deterioration is caused as a result of nutrient mobilization in response to homeostatic and energy demands during later stages of egg/ ovarian development and spawning. Muscle atrophy triggers muscle deterioration through specific cellular mechanisms (Ali et al. 2018)

This review reports the expression of various non-coding RNA molecules that includes miRNAs and lncRNA markers during muscle differentiation, muscle atrophy and sexual maturation. Variation of these ncRNAs in muscle growth and fillet quality traits, sexual maturation and QTL (Quantitative Trait Loci) affecting fillet firmness and protein content, and muscle atrophy in response to vitellogenesis are also analyzed.

lncRNAs and miRNAs expression in skeletal muscle exposed to estradiol:

Estradiol is a steroidal hormone (E2) and its maturation related signal negatively affects the muscle growth in rainbow trout. Estradiol also affects the myogenic precursor cells (MPC) proliferation and protein turnover. Expressions of 226 lncRNAs in rainbow trout skeletal muscles are found and have catabolic effect on E2. These lncRNAs are subjected to co-expression analysis and revealed that co expression network contained total 104 differentially expressed lncRNAs and 201 differentially expressed mRNAs. Apart from that 65 lncRNAs linked with 20 significantly enriched metabolic pathways.

During sexual maturation of salmonids, muscles direct the nutrients towards the gonadal development. This energy intensive process compromises the muscle quality. Differently expressed lncRNAs and miRNAs in skeletal muscle exposed to E2 create a network of the miRNAs and lncRNAs involved in this process (Jian Wang et al. 2017).

Focal adhesion (FA) is an integrin containing, multi protein structure that regulates the cell in response to extra cellular matrix (ECM) adhesion and degradation. Most of the lncRNAs linked to the FA protein. In rainbow trout, it was found that there is a reduced expression of ECM and FA genes during muscle atrophy condition. Additionally, lncRNAs regulated by E2 in skeletal muscle have functional roles in nutrient metabolism as well as protein degradation (Jian Wang et al. 2018).

lncRNAs, microRNAs and mRNAs in the muscle 'degradome':

Studies has showed that approximately 200 protein coding genes, microRNAs and long noncoding RNAs (lncRNAs) that were differentially expressed during sexual maturation and are associated with muscle atrophy in trout (Salem et al. 2018).

Bam paneru et al. 2016 stated that fish muscle atrophy is regulated by ubiquitin – proteasome system which similar are in mechanism to the mammalian muscle atrophy

The expression pattern of genes in atrophying muscle correlated with muscle atrophy phenotype such as muscle mass, protein content and muscle shear force (Bam paneru et al. 2016)

RNA –seq approach has identified large number of candidate genes involved in muscle proteolysis or degradation. lncRNA-mRNA, lncRNA – MicroRNA and mRNA-microRNA interaction that potentially regulates the muscle atrophy. Bam paneru et al. revealed that various types of differentially expressed genes and RNAs in muscle during sexual maturation triggers skeletal muscle atrophy in fish.

Expression variation of lncRNAs in muscle growth and fillet quality traits in Rainbow trout:

Fillet is the most nutritional and economically important part of the fish. It is high in protein and, depends on the species, relatively low in fat content. Muscle yield and flesh quality greatly affect fish processing profitability (Rora et al. 2017).

Genome-wide studies identified lncRNAs exhibiting differential expression during skeletal muscle differentiation. Some lncRNAs are experimentally validated as participants in regulation of myogenesis including H19, malat1, MyoD upstream ncRNA (MUNC), lncMyoD, developmental pluripotency-associated 2 (Dppa2), Upstream binding Muscle lncRNA (DUM), and Linc-MD. lncRNAs showed higher variability in terms of expression between divergent families (Salem M et al. 2019).

Ali et al. 2019 study revealed complex microRNA sponge effects for lncRNA that may contribute to fast and efficient growth rates by controlling genes belonging to protein catabolic/anabolic pathways also revealed that possible regulatory interactions that is exerted by noncoding RNAs to control expression of protein-coding genes which impact muscle quality traits. These regulatory pathways add additional layers of complexity helps in understanding the molecular network of muscle development in RBT.

Growth, development and quality traits of muscle are governed by organized expression of genes encoding contractile and regulatory proteins. Marker assisted selection (MAS) can be used to improve breeding for phenotypes with long effect QTL's. 57K and 50K SNP chip array are used mostly for quantitative loci (Gernard and Grant 2003).

Han-Yuan Zhang et.al 2018 revealed that 57K rainbow trout SNP array was utilized to explore the genetic diversity population. This type of study has been potentially used for genomic selection in *salmonid* family breeding.

GWA (Genome Wide Analysis) which is useful for identification of large effect QTL for muscle yield in *salmonid* population. Body weight, muscle yield, muscle fat content, shear force and whiteness are five traits controlled by various SNPs (Salem et.al 2018).

Conclusion

MicroRNAs and long non coding RNAs are two classes of non-coding RNAs which plays a role in the regulation of gene expression. The expression of these ncRNAs varies from healthy to disease affected individuals. Differentially expressed lncRNAs and MicroRNAs are found in muscle tissues of rainbow trout in various studies. By editing genomes of various aquatic cultivated organisms potentially increase the growth and productivity. High productivity leads to good yield. Muscle deterioration and muscle atrophy are the major pathological conditions observed usually during sexual maturation. Studying these gene expressions will be useful to alter the genomes using genome editing techniques which helps in the increase the production of rainbow trout.

Declarations

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