Prolactin Influences Different Aspects of Fish Biology

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ABSTRACT
Prolactin (PRL) is a 198 amino acid long polypeptide hormone, structurally similar to growth hormone, secreted by adenohypophysis in the vertebrates. The full-length amino acid sequence of PRL has been determined from a variety of teleost and non-teleost fish. Teleost PRL genes are shorter than mammalian. PRL exists in two forms, namely, PRL-1 commonly found in all vertebrates and PRL-2 found in several non-mammalian vertebrates including fish. This hormone binds to transmembrane Prolactin receptor (PRLR) which is a member of the class 1 cytokine receptor superfamily. We know that PRL has over 300 different functions in vertebrates. In fish, PRL plays an important role in migration, osmoregulation, parental behaviour, reproduction and development along with other hormones. Recent studies show prolactin has a role in cell proliferation in the gills of teleost fish. This review highlights diversified role of PRL in fish which may serve as avenues for further researches in near future.

Key words: Prolactin, Osmoregulation, Fish, Migration, Reproduction.

INTRODUCTION
Prolactin (PRL) is a well-known regulatory molecule with diverse physiological functions (Freeman et al. 2000). It has been expressed in a variety of different organs and is highest in the pituitary. In fish, it is maximally expressed in specific cells of the adenohypophysis, from which it is released into the bloodstream. PRL gene structure was first discovered in the chum salmon fish (Oncorhynchus keta) and is similar to the human PRL gene.[1] In 1930, Oscar Riddle first found out PRL from the pigeon. Prolactin plays an important role in fish, which is a peptide hormone found in all vertebrates except the jawless fish. In the human body, this hormone helps in milk production.[2] Prolactin hormone belongs to the same hormone family of Growth Hormone (GH) and Placental Lactogen (PL).[3] PRL is 277 amino acid long with 28 amino acid long chain of signal peptide.[4] Different types of PRL sequence are found in several species of fish like Fugu, European eel and rainbow trout.[5-7] Most of the teleost and non-teleost fish can be identified by the length of the PRL sequence. Pars distalis of pituitary gland is made by a definitive mass of PRL secreting cells which are found in all teleost fishes.[8] Researchers suggested that extra pituitary PRL gene expression has been exhibited in the spleen and gonad of goldfish[9] as well as in the liver and intestine of the seabream.[10] Here the review highlights the current state of knowledge on the role of prolactin in fish reproduction, osmoregulation, regulation of calcium secretion, migration, cell proliferation and parental behaviour. This review tries to provide knowledge about the multidimensional effects of prolactin, which can be taken up for researches to explore more on prolactin and its effect on fish under different experimental or stressed environmental conditions.

Structure of Prolactin Gene
Prolactin (PRL) is the part of a larger hormone family that includes other hormones like Growth Hormone (GH) and Placental Lactogen (PL).[11] The length of this
gene is approximately 10kb, and is made up of 5 exons and 4 introns. We found different types of prolactin which in most cases are monomeric with a molecular weight of 23kDa and rest with a molecular weight of 50kDa. Molecular weight of macroprolactin is 150kDa is made of a prolactin-Ig complex. From the suggested research papers, the first discovered PRL gene structure was in Chum salmon (Oncorhynchus keta) from the piscine family. About 400 to 800 million years ago, the ancestral gene of PRL produced by duplication, simultaneously borne some similarities with other hormones like growth hormone (GH), placental lactogen (PL) and somatolectin. A difference in the disulphide bond of PRL is found between teleost and other vertebrates. The disulphide was lost from the n-terminal in the common ancestors of teleost where was maintained in the tetrapod and the lobe finned fish. In cases three disulphide bonds are present in PRL-2. Two types of PRL namely PRL-1 is found in all vertebrates and PRL-2 found in fish and non-mammalian vertebrates.

### Prolactin Hormone Receptor

The prolactin receptor (PRLR) belongs to the class one cytokines located on the cell membrane. PRLR was discovered in the Oreochromis niloticus; PRLR is made of 600 amino acid long chain which is as same as to mammalian PRLR. Alternative splicing occurs during the formation of PRLR, therefore different types of PRLR of different lengths can be found. Mainly two types of PRLR are found namely PRLR 1 and PRLR 2 in several teleost fish. The PRLR made of two disulphide bonds and a modified WS motif which is without N-glycosylation between conserved 2 and conserved 3 regions.

### Factors Affecting Prolactin Release

The prolactin is secreted by special cells from the anterior pituitary is called lactotrophs. On the cell membrane G-protein coupled receptors (GPCRs) that induced cellular activities are present. In many fishes PRL secretion is regulated by a neuro hormone (GnRH) that is produced by the hypothalamus. Reproductive period and osmolality are the other factors that control the secretion of PRL. In the Mozambique tilapia (Oreochromis mossambicus) the secretion of PRL is controlled by GnRH. Another substance, the leptin regulates the secretion of PRL that comes from the liver. A high level of GnRH increases signalling by phospholipase - c and inositol triphosphate, leading to intracellular calcium movement. In Masu salmon (Oncorhynchus masou) the GnR enhances the mRNA expression in the PRL gene promoter region, which act as a transcription factor. The prolactin binds with the receptor via two binding sites, dimer form of PRLRs initiate Janus Kinase pathway and phosphorylates STAT transcription, where it stimulates PRL genes specific promoter that causes biological response and may also activates MAP kinase pathway for cell proliferation.

### Influences of Prolactin in Fish

#### Regulation of Calcium Secretion

Marine and freshwater fishes face change in calcium concentration in the environment. Calcium is deposited in the bone by the intestine in form of ionized calcium. Calcium is needed for maintaining skeletons of fishes. PRL stimulates the calcium absorption through branchial tissue using ATP. When Oreochromis mossambicus moves from seawater to freshwater unexpectedly plasma levels of prolactin rise to enhance the bone calcium influx and resist the calcium outflow generating a condition known as hypercalcemia. However, PRL secretion increases during high extracellular osmolality, causing the opening of the ion gated channels. Reports show that calcium is deposited in bones and scales of female gold fish (Carassius auratus) with the help of prolactin hormone.

#### Effect on Osmoregulation

It is challenging for fishes to survive in a hypo-osmotic environment. But PRL controls the activities of gills whose main function is ion and water exchange. During freshwater adaptation, prolactin-releasing peptide stimulate prolactin expression in the pituitary and peripheral organs in fish. Several research papers suggested that when PRL concentration is lowered, then osmotic permeability of gills is reduced as well as mucus secretion is increased which contribute in maintaining ion and water balance. Growth Hormone, which is similar to prolactin, promotes acclimation to seawater in several teleost fish through the action of Insulin-like Growth Factor I. It has been reported that in the sea water-type chloride cell the development and differentiation of branchial epithelia (and their underlying biochemistry) is regulated by GH, IGF-I, and cortisol whereas in the freshwater-type chloride cell, prolactin and cortisol help in development and differentiation of the chloride cells. Levels of extracellular osmolality regulate PRL secretion by autocrine feedback. Receptor of PRL found in chloride cells of Oreochromis mossambicus help in the chloride ion balance of fresh water fish. PRL regulates the Na⁺ / K⁺ ATPase activity in Sparus sarba which is closely connected with hypercalcemic action. It has been also reported that the glomerular filtration rate is controlled by PRL concentration decreasing the urine
osmolality. Furthermore, prolactin at a low level can absorb intestinal fluid and salt in Japanese eel and trout.

Role in Migration

The migration between the parental river and the sea, and the homing migration to the maternal stream is one of the most interesting and challenging phenomena in fish biology. PRL plays an important role during migration as its level increases in salmon under the anadromous migration regulated by the GnRH. During the transition from salt water to fresh water during pre-spawning PRL maintains the ion balance in fish. When Anguilla japonica migrates from sea water to fresh water, the PRL mRNA expression is low. These literature surveys suggest that PRL regulate the movement of fish during migration.

Role in Reproductive Cycle

PRL helps in the reproductive cycle and development of the sexual organ in fishes. PRL and GnRH levels are usually high at the time of gonadal development and spawning in the Japanese eel and cat fish (Clarias batrachus). The gonads of various species of fishes like Mozambique tilapia, seabream and gold fish show mRNA of PRL receptor suggesting that prolactin regulates the gonadal growth and development in fishes by binding to its receptors. On the other hand, PRL secretion increases after spawning during vitellogenesis in female tilapia. The production of testosterone hormone in the Mozambique tilapia as well as the oocytes development in the Guppy fish are directly regulated by PRL. It has been found that sex hormones like estradiol increase the PRL synthesis in vitro in the Mozambique tilapia cells whereas GnRH stimulates the PRL release. It has been reported that PRL suppresses progesterone as well as oestradiol expression when it is at its peak after vitellogenesis and before ovulation. Therefore, prolactin along with other sex hormones and neurohormones like GnRH may regulate reproductive cycles in fish.

Development of Parental Behaviour

Researchers suggested that oral egg carrying behaviour is developed by the combined effect of prolactin and estrogen in tilapia. PRL secretion increases at the time of embryogenesis and somitogenesis in the seabream. The hormone can maintain the osmoregulation of eggs through chloride cells which response to changes in salinity by autonomous regulation in embryonic condition. Most of the research papers suggested that PRL secretion and brood care are interrelated with positive feedback but exceptions are found in Neolamprologus puleher. Most fishes develop nest building behaviour, secrete mucous to protect their eggs and hatchlings under influence of prolactin. It also induces fanning in wrasse males Symphodus ocellatus and stickleback males.

Regulation of Cell Proliferation

In seawater-adapted euryhaline fish, the permeability of the gastrointestinal tract is generally greater than that of freshwater-adapted fish. The esophageal epithelium of sea-water fish is simple columnar, whereas that of freshwater fish is stratified. The number of these cells can be increased through three mechanisms: proliferation and differentiation of new cells, differentiation (or transformation) of existing chloride cells from one type to another and a decrease in cell death (necrosis or apoptosis). These mechanisms of cell turnover and differentiation are regulated by the growth hormone, prolactin, and cortisol by governing chloride cells and the acclimating teleost gills. On the goldfish scales, PRL expanded the mucous cell layers, which may restrict efficiently water inflow by the mucous system. However, the control of cell turnover is an important function of PRL in teleost. Furthermore, prolactin specifically inhibited the osteoclastic activities of goldfish scales and promoted osteoblastic activities in vitro.

Regulation of Immunological Functions

The prolactin is capable of inducing the expression of the pro-inflammatory cytokines IL-1β and TNFα, and Reactive Oxygen Species (ROS) in leukocytes and macrophages found in head kidney of gilthead seabream. It has been reported that PRL has immunomodulatory and immunostimulatory effects by targeting the lysozyme activities in the macrophages of the head kidney in Salmon and increasing the expression levels of Toll Like Receptors (TLR) during pathogenic infections.

CONCLUSION

This brief review shows that PRL is a vertebrate-specific hormone whose functions have been studied for a long time. Indeed, immense knowledge been accumulated on prolactin secretion and function in a variety of different species. Thus, prolactin represents an exciting opportunity for evolutionary neuroendocrinology as its functions are compared between the different species and classes of vertebrates. We review the current state of knowledge on the role of prolactin in fish reproduction, migration, reproductive development and cycling, brood care behaviour, pregnancy, and nutrient
provisioning to young and summarized it in Figure 1. We also highlight significant knowledge and specific action of prolactin in fish. It has a wide range of functions in fish physiology. Fish is a diverse group of species and comparative study on different aspects of fishes has clearly identified that PRL is a regulatory hormone for ion and water transport. In bony fish, PRL enhances calcium transport in the gills of both freshwater and euryhaline species, leading to hypercalcemia. Prolactin, a major osmoregulatory hormone in fish has evolved into a hormone that regulates lactation in mammals. In fact, both of these functions require the action of prolactin on epithelial cells and their proliferation. However, an intriguing change in the action of prolactin on parental behaviour in fish becomes prominent in birds and mammals with different brooding and nursing behaviours. The multifaceted role of prolactin in fish may be considered as different avenues for future researches.

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CONFLICT OF INTEREST

There is no conflict of interest between the authors.

Author’s Contribution

Miss Chakraborty and Mr. Das, being undergraduate students, have contributed in literature survey and prepared a draft of the review. Dr. Saha corrected it and made necessary modifications of it and prepared the final manuscript.

ABBREVIATIONS

GH: Growth Hormone; PRL: Prolactin; GnRH: Gonadotropin Releasing Hormone; PL: Placental Lactogen; Ig: immunoglobulin; kDa: kilo dalton; IL: Interleukin; TNF: Tumor Necrosis Factor.

SUMMARY

Prolactin is the well-known regulatory molecule with diverse physiological functions. In fish, it is maximally expressed in specific cells of the adenohypophysis. Prolactin maintains the blood calcium level in fishes
by changing the osmolality of blood that opens the ion
gated channels creating a stable blood calcium level which
is important for maintaining the skeletal structures in
fishes. Prolactin helps in osmoregulation by controlling
the activities of gill. The decrease in prolactin reduces
the osmotic permeability of gills as well as increased
mucus secretion. Prolactin causes migration as the level
increases in salmon under the anadromous migration
regulated by the GnRH. The current review shows a
comprehensive role of prolactin in fish reproduction,
migration, immunomodulation, cell proliferation and
parental care.

REFERENCES

1. Kawauchi H, Abe KI, Takahashi A, Hirano T, Hasegawa S, Naito N, et al.
   Isolation and properties of chum salmon prolactin. Gen Comp Endocrinol.
   1983;49(3):446-58.
2. Freeman ME, Kanyicska B, Lerant A, Nagy G. Prolactin: Structure, function,
   and regulation of secretion. Physiological Reviews. 2000;80(4):1523-631.
3. Ziegler TE, Wegner FH, Carlson AA, Lazaro-Peraes C, Snowdon CT. Prolactin
   levels during the periparturitional period in the biparental cotton-top tamarin
   (Saguinus oedipus): Interactions with gender, androgen levels, and parenting.
   Hormones and Behaviour. 2000;38(2):111-22.
4. Bole-Feyso C, Goffin V, Edery M, Binart N, Kelly PA. Prolactin (PRL) and its
   receptor: Actions, signal transduction pathways and phenotypes observed in
   PRL receptor knockout mice. Endocrine Reviews. 1998;19(3):225-68.
5. Lee KM, Kaneko T, Aida K. Prolactin and prolactin receptor expressions in
   a marine teleost, pufferfish Takifugu rubripes. Gen. Comp. Endocrinol.
   2006;146(3):318-28.
6. Querel B, Cardinaud B, Hardy A, Vitali B, D’Angelo G. Sequence and
   regulation of European eel prolactin mRNA. Mol. Cell Endocrinol. 1994;102(1-
   2):151-60.
7. Degani G, Yom-Din S, Goldberg D, Jackson, K. cDNA cloning of blue gourami
   (Trichogaster trichopterus) prolactin and its expression during the gonadal
   cycles of males and females. Journal of Endocrinological Investigation.
   2010;33(1):7-12.
8. Brown PS, Brown SC. Osmoregulatory actions of prolactin and other
   adenohypophysial hormones. Vertebrate Endocrinology: Fundamentals and
   Biomedical Implications. 1989:2:45-84.
9. Power DM. Developmental ontogeny of prolactin and its receptor in fish. Gen
   Comp Endocrinol. 2005;142(1-2):25-33.
10. Manzon LA. The role of prolactin in fish osmoregulation: A review. Gen
    Endocrinol. 2002;125(20):291-310.
11. Huang X, Hui MN, Liu, Y, Yuen DS, Zhang Y, Chan WY, Lin HR. et al.
    Discovery of a novel prolactin in non-mammalian vertebrates: Evolutionary
    perspectives and its involvement in teleost retina development. PLoS One.
    2009;4(7):e6163.
12. Sandra O, Rouzie PL, Cauty C. Expression of the prolactin receptor (PRL-R)
    gene in tilapia Oreochromis niloticus: Tissue distribution and cellular
    localization in osmoregulatory organs. J Mol Endocrinol. 2000;24(2):215-24.
13. Chen M, Huang X, Yuen DS, Cheng CH. A study on the functional interaction
    between the GH/PRL family of polypeptides with their receptors in zebrafish;
    Evidence against GHRI being the receptor for somatolactin. Mol Cell
    Endocrinol. 2011;337(1-2):114-21.
14. Parhar IS, Soga T, Sakuma Y, Miliar RP. Spatio: temporal expression of
    gonadotropin-releasing hormone receptor subtypes in gonadotropes,
    somatotropes and lactotropes in the cichlid fish. Journal of Neuroendocrinology.
    2002;14(8):657-65.
15. Weber GM, Powell JFF, Park M, Fischer WH, Craig AG, Rivier JE. Evidence
    that gonadotropin-releasing hormone (GnRH) functions as a prolactin-
    releasing factor in a teleost fish (Oreochromis mossambicus) and primary
    structures for three native GnRH molecules. J Endocrinol. 1997;155:121-32.
16. Tipsmark CK, Weber GM, Strom CN, Grau EG, Hirano T, Borski RJ. Involvement
    of phospholipase C and intracellular calcium signaling in the gonadotropin-releasing hormone regulation of prolactin release from
    lactotrophs of tilapia (Oreochromis mossambicus). Gen Comp Endocrinol.
    2005;142(1-2):227-33.
17. Onuma T, Kitahashi T, Taniyama S, Saito D, Ando H, Urano A. Changes in
    expression of genes encoding gonadotropin subunits and growth hormone/
    prolactin/somatolactin family homologues during final maturation and freshwater
    adaptation in pre spawning chum salmon. Endocrine. 2003;20(1-2):23-33.
18. Filg G, Rentier-Detruce F, Bonga WSE. Calcitropic effects of recombinant
    prolactins in Oreochromis mossambicus. American Journal of Physiology-
    Regulatory, Integrative and Comparative Physiology. 1994;266(4):R1302-8.
19. Norris DO. Bioregulation of calcium and phosphate homeostasis. Vertebrate
    Endocrinology, fourth ed., Elsevier Academic Press, London. 2007:486-511.
20. Anderson JM, Itilite CM. Physiology and function of the tight junction. Cold
    Spring Harbor perspectives in biology. 2009;1(2):002584.
21. Seale AP, Richman NH, Hirano T, Cooke I, Grau EG. Evidence that signal
    transduction for osmoreception is mediated by stretch-activated ion channels
    in tilapia. Am J Physiol Cell Physiol. 2009;284(5):C1290-20.
22. Takahashi H, Suzuki N, Takagi C, Ikegame M, Yamamoto T, Takahashi A, et
    al. Prolactin inhibits osteoclastic activity in the goldfish scale: a novel direct
    action of prolactin in teleosts. Zoological Science. 2000;25(7):739-45.
23. Mc Cormick SD. Endocrine control of osmoregulation in teleost fish. American
    Zoologist. 2001;41(4):781-94.
24. Horseman ND. Models of prolactin action in nonmammalian vertebrates. In:
    “Actions of Prolactin on Molecular Processes”. 1st edition: 1987:1-27.
25. Bentley PJ, Comparative Vertebrate Endocrinology. Cambridge University
    Press. 1998.
26. Sakamoto T, McCormick SD. Prolactin and growth hormone in fish
    osmoregulation. Gen Comp Endocrinol. 2006;147(1):24-30.
27. Weng CF, Lee TH, Hwang PP. Immune localization of prolactin receptor in the
    mitochondria-rich cells of the euryhaline teleost (Oreochromis mossambicus)
    gill. FEBS Letters. 1997;405(1):91-4.
28. Kelly SP, Chow IN, Woo NY. Effects of prolactin and growth hormone on
    strategies of hyposmotic adaptation in a marine teleost, Sparus sarba. Gen
    Comp Endocrinol. 1999;113(1):9-22.
29. Clarke WC, Bern HA. Comparative endocrinology of prolactin. Hormonal
    Proteins and Peptides. 2012:8:105-97.
30. Mainoya JR. Water and NaCl absorption by the intestine of the Tilapia
    Sarotherodon mossambicus adapted to fresh water or seawater and the
    possible role of prolactin and cortisol. Journal of Comparative Physiology.
    1982;146(1):1-7.
31. Onuma TA, Ban M, Makino K, Katsumata H, Hu W, Ando H, et al. Changes in
    gene expression for GH/PRL/SL family hormones in the pituitaries of homing
    chum salmon during ocean migration through upstream migration. Gen
    Comp Endocrinol. 2010;166(3):5372-482.
32. Whittington CM, Wilson AB. The role of prolactin in fish reproduction. Gen
    Comp Endocrinol. 2013;191:123-36.
33. Singh SP, Singh TP. Prolactin level in relation to gonadotrophin concentration
    during different phases of annual reproductive cycle in the freshwater catfish,
    Clarias batrachus (Linn.). In Annales d’endocrinologie. 1981;42(2):159-68.
34. Ozaki Y, Ishida K, Saito K, Ura K, Adachi S, Yamauchi K. Immunohistochemical
    changes in production of pituitary hormones during artificial maturation of
    female Japanese eel Anguilla japonica. Fisheries Science. 2007;73(3):574-84.
35. Cavaco JEB, Santos CR, Ingleton PM, Canario AV, Power DM. Quantification
    of prolactin (PRL) and PRL receptor messenger RNA in gilthead seabream
    (Sparus aurata) after treatment with estradiol-17B. Biology of Reproduction.
    2003;68(2):588-94.
36. Tipsmark CK, Weber GM, Strom CN, Grau EG, Hirano T, Borski RJ. Involvement
    of phospholipase C and intracellular calcium signaling in the gonadotropin-releasing hormone regulation of prolactin release from
    lactotrophs of tilapia (Oreochromis mossambicus). Gen Comp Endocrinol.
    1992;87(2):189-96. DOI: 10.1016/0016-6480(92)90022-c
37. Seale AP, Fliess JC, Hirano T, Cooke IM, Grau EG. Disparate release of
    prolactin and growth hormone from the tilapia pituitary in response to osmotic
stimulation. Gen Comp Endocrinol. 2006;145(3):222-31. DOI: 10.1016/j.

39. Galas J, Epler P. Does prolactin affect steroid secretion by isolated rainbow trout ovarian cells? Comparative Biochemistry and Physiology B-Biochemistry and Molecular Biology. 2002;132(1):287-97. doi: 10.1016/
s1096-4959(01)00542-5.

40. Blüm V. Immunological determination of injected mammalian prolactin in cichlid fishes. Gen Comp Endocrinol. 1968;11(3):595-602.

41. Santos CR, Brinca L, Ingleton PM, Power DM. Cloning, expression, and tissue localisation of prolactin in adult sea bream (Sparus aurata). Gen Comp Endocrinol. 1999;114(1):57-66.

42. Kaneko T, Shiraiishi K, Katoh F, Hasegawa S, Hiroi J. Chloride cells during early life stages of fish and their functional differentiation. Fisheries Science. 2002;68(1):1-9.

43. Bender N, Taborsky M, Power DM. The role of prolactin in the regulation of brood care in the cooperatively breeding fish Neolamprologus pulcher. Journal of Experimental Zoology Part A: Ecological Genetics and Physiology. 2008;309(9):515-24.

44. Páll MK, Liljander M, Borg B. Prolactin diminishes courtship behaviour and stimulates fanning in nesting male three-spined sticklebacks, Gasterosteus aculeatus. Behaviour. 2004;141(11):1511-9.

45. McCormick SD, Sundell K, Bjornsson BT, Brown CL, Hiroi J. Influence of salinity on the localization of Na+/K+/2Cl cotransporter (NKCC) and CFTR anion channel in chloride cells of the Hawaiian goby (Stenogobius hawaiensis). J Exp Biol. 2003;206(24):4575-83.

46. Hiroi J, McCormick SD, Ohtani-Kaneko R, Kaneko T. Functional classification of mitochondrion-rich cells in euryhaline Mozambique tilapia (Oreochromis mossambicus) embryos, by means of triple immunofluorescence staining for Na+/K+/ATPase, Na+/K+/2Cl cotransporter and CFTR anion channel. J Exp Biol. 2005;208(11):2023-36.

47. Fujimoto M, Sakamoto T, Kanetoh T, Osaka M, Moriya S. Prolactin-releasing peptide is essential to maintain the prolactin level and osmotic balance in freshwater teleost fish. Peptides. 2006;27(5):1104-9.

48. Suzuki N, Kitamura K, Nemoto T, Shimizu N, Wada S, Kondo T, et al. Effect of vibration on osteoblastic and osteoclastic activities: Analysis of bone metabolism using goldfish scale as a model for bone. Adv Space Res. 2007;40(11):1711-21.

49. Olavarria VH, Fiqueroa J, Mulero V. Prolactin-induced activation of phagocyte NADPH oxidase in the teleost fish gilthead seabream involves the phosphorylation of p47phox by protein kinase C. Developmental and Comparative Immunology. 2011;36(1):216-21.

50. Paredes M, Gonzalez K, Figueroa J, Montiel-Eulefi E. Immunomodulatory effect of prolactin on Atlantic salmon (Salmo salar) macrophage function. Fish Physiol Biochem. 2013;39(5):1215-21.