Available online at www.sciencedirect.com

SCIENCE DIRECT®

General and Comparative Endocrinology 142 (2005) 20–24

GENERAL AND COMPARATIVE ENDOCRINOLOGY

www.elsevier.com/locate/ygcen

Minireview

Growth hormone and insulin-like growth factors in fish: Where we are and where to go

Manfred Reinecke [a,*], Björn Thrandur Björnsson [b], Walton W. Dickhoff [c], Stephen D. McCormick [d], Isabel Navarro [e], Deborah M. Power [f], Joaquim Gutiérrez [e]

[a] *Division of Neuroendocrinology, Institute of Anatomy, University of Zürich, CH-8057 Zurich, Switzerland*
[b] *Department of Zoology/Zoophysiology, Göteborg University, Sweden*
[c] *School of Aquatic and Fishery Sciences, University of Washington, Seattle, USA*
[d] *Conte Anadromous Fish Research Center, USGS, Turners Falls, MA, USA*
[e] *Departamenta de Fisiologia, Facultat de Biologia, Universitat de Barcelona, Barcelona, Spain*
[f] *Centre of Marine Sciences, University of Algarve, Campus de Gambelas, Faro, Portugal*

Received 7 December 2004; revised 24 January 2005; accepted 31 January 2005

Abstract

This communication summarizes viewpoints, discussion, perspectives, and questions, put forward at a workshop on “Growth hormone and insulin-like growth factors in fish” held on September 7th, 2004, at the 5th International Symposium on Fish Endocrinology in Castellón, Spain.

Keywords: Growth Hormone and insulin -like growth factors in fish

---

1. Growth hormone

Growth hormone (GH) is a pluripotent hormone produced by the pituitary gland in teleosts as in other vertebrates. GH brings about its action by binding to a single pass-transmembrane receptor, the GH receptor (GHR), in target tissue. Ligand binding induces receptor dimerization producing an active trimeric complex (for review, see Pérez-Sánchez et al., 2002). GH has been sequenced and/or the protein isolated from scores of teleosts, various immunoassays established, and a number of GH-transgenic fish strains established. Over the last two decades, many aspects of GH physiology have been the subject of intense research in fish such as the salmonids, cyprinids, and sparids. In fish, GH participates in almost all major physiological processes in the body including the regulation of ionic and osmotic balance, lipid, protein, and carbohydrate metabolism, skeletal and soft tissue growth, reproduction and immune function. Recent studies have indicated that GH affects several aspects of behaviour, including appetite, foraging behaviour, aggression, and predator avoidance, which in turn has ecological consequences (for reviews, see Björnsson, 1997; Björnsson et al., 2004; Pérez-Sanchez, 2000; Peter and Marchant, 1995).

Despite the vast body of knowledge which exists documenting GH action in teleost fish, the mode of GH action remains a major discussion topic (for review, see Björnsson et al., 2004). Generalized claims have been made that most/all GH effects are indirect, based on an outdated mammalian view where the pituitary/hepatic GH/IGF-I system was seen as an “axis” with IGF-I mediating the physiological action of GH (for review, see Björnsson et al., 2004; Butler and Le Roith, 2001).

---

[*] Corresponding author. Fax: +41 1 635 57 02.
E-mail address: reinecke@anatom.unizh.ch (M. Reinecke).

0016-6480/$ - see front matter
doi:10.1016/j.ygcen.2005.01.016

The wide tissue distribution of IGF-I producing cells (Reinecke et al., 1997) and IGF-I receptors (IGF-1R) (Radaelli et al., 2003a), together with the extensive tissue distribution of GH-receptors (Pérez-Sánchez et al., 2002) makes it a truly challenging task to provide unequivocal data on how GH mediates its actions at the cellular level. In this context, the cloning of the teleostean GH-receptors has been a major break-through. Since 2001 when the GHR was first cloned in goldfish (Lee et al., 2001) and turbot (Calduch-Giner et al., 2001), it has been cloned in a rapidly growing number of teleost species, 15 at the latest count. This promises to accelerate research into the mode of action of GH at the cellular level. Such research into the temporal and spatial distribution of the receptor, receptor sub-types and intracellular signaling pathways will hopefully help explain how the pluripotent actions of GH are mediated, but at the moment, very little is known about the signaling mechanisms of the various forms of fish GH-Rs. Further fields of research would include aspects such as hormone–receptor interaction, receptor-mediated turn-over of the hormone affecting the GH clearance rate, as well as the likely dual role of the receptor molecule to also act as a GH-binding protein in plasma.

2. Insulin-like growth factor I

During the last decade, most studies of IGF-I in fish have focused on identification of the fish IGF, developing assays to measure blood or tissue levels of the IGF-I peptide or mRNA, measuring changes in IGF-I in blood and tissue IGF-I expression in response to varying nutritional conditions and season, and assessing control of IGF-I production by growth hormone (see above) and other endocrine factors, such thyroid hormone (Schmid et al., 2003) or estrogen (Riley et al., 2004). Results of these studies have shown that IGF-I structure, regulation, and function appear similar in fish and mammals (for review, see: Reinecke and Collet, 1998). In many fish species, blood levels of IGF-I or tissue levels of its mRNA positively correlate with dietary ration, dietary protein content, and body growth rate (Beckman et al., 2004; Duan, 1998; Pérez-Sánchez et al., 1995). IGF-I increases in blood during the growing season in temperate fishes showing seasonal growth (Mingarro et al., 2002), and is stimulated by increased temperature (Beckman et al., 1998) and day length (McCormick et al., 2000). Furthermore, treatment of fish with IGF-I implants stimulates growth (McCormick et al., 1992). IGF-I in fish has been associated not only with growth, but also with metabolism (Castillo et al., 2004), development (Greene and Chen, 1999b; Pozios et al., 2001), reproduction (Maestro et al., 1997; Weber and Sullivan, 2000), and osmoregulation in seawater (McCormick, 2001). IGF-I exerts its effects on cells through binding to the IGF-I receptor (IGF-1R), which binds IGF-II in a similar manner in zebrafish (Mendez et al., 2001; Pozios et al., 2001) but not so well in rainbow trout (Loir and Le Gac, 1994).

The wide range of tissue distribution of the IGF-I hormone and the IGF-1R in fish, coupled with the varied functions associated with IGF-I, make fish attractive subjects for future study. Unique functions of IGF-I in fish, such as its role in osmoregulation, raise intriguing questions regarding its action on gills and whether intracellular signaling pathways resemble those involved in mitogenesis. Does IGF-I have an osmoregulatory role in all fish species, or only anadromous or euryhaline species? The relative importance of local vs systemic production of IGF-I, still controversial in mammalian endocrinology, has not been directly addressed in fish species.

Interestingly, fish muscle has a substantially greater abundance of IGF-1R than insulin receptors (IR) (Parrizas et al., 1995). This indicates that IGF-I contributes more to the regulation of muscle function than insulin in trout, in contrast to the situation in mammals. Both zebrafish and salmonid fish have at least two forms of the IGF-I receptor: IGF-1Ra and IGF-1Rb (e.g., Chan et al., 1997; Greene and Chen, 1999a). During zebrafish development, the levels of IGF-1Ra and IGF-1Rb show different patterns of expression (Maures et al., 2002). Furthermore, IGF-1R increases with differentiation of cultured trout muscle cells (Castillo et al., 2002). Fasting of trout increases IGF-1Ra, and refeeding causes a decline in IGF-1Ra, but no change in IGF-1Rb (Chauvigne et al., 2003). In addition to nutrition, environmental factors as temperature affect tissue IGF-1R (Gabillard et al., 2003). More work on IGF receptor regulation in other fish species is needed. What neuroendocrine factors are responsible for the environmental regulation of the IGF-1R? An interesting, yet unresolved, question is whether multiple forms of IGF-1R in salmonids and zebrafish are associated with different functions. Are multiple isoforms of the IGF-1R a primitive vertebrate condition, or are they associated with the genome duplication that has apparently occurred during early teleost evolution?

A critical element in studies of specific actions of IGF and their receptors is the role of IGF binding proteins (IGFBP). The zebrafish genome contains sequences homologous to human IGFBP-1 (Maures and Duan, 2002), IGFBP-2 (Duan et al., 1999), IGFBP-3 (Chen et al., 2004), and IGFBP-5 (Ding, J., Duan, C., unpublished, GenBank Accession #AY100478), and studies of various fish species have shown IFGFBP levels in blood fluctuate in anabolic and catabolic states (for review, see Kelley et al., 2001). It is well known in mammals that IGFBPs influence IGF function by targeting IGF delivery to specific tissues and enhancing or inhibiting IGF effects. Although over 99% of total circulating IGF-I are bound to IGFBPs in salmonids (Shimizu et al., 1999), little work has been done on how IGFBPs regulate IGF function in fish. At present, we don't know whether IGFBPs exert any direct effects on cells, as the mammalian IGFBPs 3 and 5 probably do? Recent work by Duan and colleagues (unpublished) have shown that IGFBP knockdown in zebrafish has profound effects on development. More work on the role of fish IGFBPs is crucial to a full understanding of IGF function in specific tissues.

In summary, IGF-I function in fish is controlled variously by regulation of IGF-I production, IGF receptor function, signaling pathways and cross-talk, and modulation by systemic and local production of IGFBPs. A full understanding of IGF-I function in fish requires more work in all of these areas, in a variety of physiological processes, such as growth, metabolism, reproduction, osmoregulation, and in fish species with various life history and ecological types. The diversity of fish species and habitats, their ancient phylogeny, and their economic and cultural importance will undoubtedly make them useful targets for further exploration of IGF function.

3. Insulin-like growth factor II

In bony fish, not only IGF-I mRNA, but also IGF-II mRNA have been detected both in liver and in numerous other organs, such as brain, eye, gills, heart, gastrointestinal tract, pancreatic islets, kidney, skeletal muscle, spleen, and male and female gonads (e.g., Ayson et al., 2002; Caelers et al., 2004; Vong et al., 2003). The widespread presence of the IGF-II gene in both juvenile and adult fish as shown by RT-PCR contrasts the situation in mammals (for review, see Reinecke and Collet, 1998). Unfortunately, in contrast to IGF-I the precise localization of the IGF-II peptide and/or mRNA in extrahepatic sites has been analyzed only in few studies (Caelers et al., 2003; Radaelli et al., 2003b; Schmid et al., 1999). Knowledge on the cellular production sites of a hormone, however, gives first hints to its potential functions. Thus, we need more information about the organ-specific cells which synthesize IGF-II.

Previously, the IGF type 2 receptor was found only in mammals and it was generally believed to be absent from non-mammalian vertebrates (for review, see Reinecke and Collet, 1998). The presence of an IGF type 2 receptor has been indicated for trout larvae at five weeks postfertilization (Mendez et al., 2001). However, further research on the role of this molecule in fish larvae and adults is needed. As a first step, attempts must be taken to clone the IGF-II receptor.

It has been shown that IGF-II regulates metabolism in trout muscle cells (Codina et al., 2004), indicating that IGF-II, like IGF-I, could act not only as a growth factor but also as a metabolic hormone. Although preliminary evidence indicates that IGF-II and IGF-I potently activate cell proliferation and DNA synthesis in zebrafish embryonic cells via mitogen-activated protein kinase (MAPK) and phosphatidylinositol 3-kinase (PI3 kinase) (Pozios et al., 2001) we are far from understanding the intracellular signaling pathways by which the IGFs exert their effects on the different target cells, and future research should develop this interesting field.

As outlined above, to date four different fish IGFBPs have been cloned, sequenced and shown to be well conserved with their mammalian counterparts. A peculiar mammalian IGFBP is IGFBP-6 that in contrast to the other IGFBPs has a markedly higher affinity for IGF-II than for IGF-I and likely serves as potent inhibitor of IGF-II actions (Headley et al., 2004). However, whether a fish analogon to IGFBP-6 is present also in fish is a matter of future research.

There is evidence that in bony fish both the IGF-I gene and IGF-II gene are controlled by GH (Shamblott et al., 1995; Tse et al., 2002; Vong et al., 2003) in all organs. This makes bony fish quite unique because in other vertebrate classes, GH most likely regulates only the expression of the IGF-I gene (for review, see Reinecke and Collet, 1998). Whether the above results indicate a particular impact of IGF-II in fish remains to be clarified. Thus, an important topic to deal with in future is the determination of IGF-II plasma levels in different fish species, as has recently been done in Atlantic salmon and rainbow trout (Gentil et al., 1996; Wilkinson et al., 2004). Subsequently, the potential changes in circulating IGF-II during development or under different physiological conditions, including nutritional status, smoltification, and temperature, and varying GH levels should be investigated and correlated to alterations in the expression of the IGF-II gene. Otherwise, the "hormone" IGF-II may be left as enigmatic as it has been since its detection some 30 years ago.

References

Ayson, F.G., de Jesus, E.G., Moriyama, S., Hyodo, S., Funkenstein, B., Gertlerm, A., Kawauchi, H., 2002. Differential expression of insulin-like growth factor I and II mRNAs during embryogenesis and early larval development in rabbitfish, *Siganus guttatus*. Gen. Comp. Endocrinol. 126, 165–174.

Beckman, B.R., Larsen, D.A., Moriyama, S., Leepawlak, B., Dickhoff, W.W., 1998. Insulin-like growth factor-1 and environmental modulation of growth during smoltification of spring chinook salmon (*Oncorhynchus tshawytscha*). Gen. Comp. Endocrinol. 109, 325–335.

Beckman, B.R., Shimizu, M., Gadberry, B.A., Cooper, K.A., 2004. Response of the somatotropic axis of juvenile coho salmon to alterations in plane of nutrition with an analysis of the relationships among growth rate and circulating IGF-I and 41 kDa IGFBP. Gen. Comp. Endocrinol. 135, 334–344.

Björnsson, B.Th., 1997. The biology of salmon growth hormone: from daylight to dominance. Fish Physiol. Biochem. 17, 9–24.

Björnsson B.Th., Johansson, V., Benedet, S., Einarsdottir, I.E., Hildahl, J., Agustsson, T., Jönsson, E., 2004. Growth hormone endocrinology of salmonids: regulatory mechanisms and mode of action. Fish Physiol. Biochem. In: Plisetskaya, E.M. (Ed.), Special Issue: Fish Growth and Metabolism. Environmental, Nutritional and Hormonal regulation (published in 2004). 27, 227–242.

Butler, A.A., Le Roith, D., 2001. Control of growth by the somatotrophic axis: growth hormone and the insulin-like growth factors have related and independent roles. Ann. Rev. Physiol. 63, 141–164.

Caelers, A., Schmid, A.C., Hrusovsky, A., Reinecke, M., 2003. Insulin-like growth factor II mRNA is expressed in neurones of the brain of the bony fish *Oreochromis mossambicus*, the tilapia. Eur. J. Neurosci. 18, 355–363.

Caelers, A., Berishvili, G., Meli, M.L., Eppler, E., Reinecke, M., 2004. Establishment of a real-time RT-PCR for the determination of absolute amounts of IGF-I and IGF-II gene expression in liver and extrahepatic sites of the tilapia. Gen. Comp. Endocrinol. 137, 196–204.

Calduch-Giner, J.A., Duval, H., Chesnel, F., Boeuf, G., Pérez-Sánchez, J., Boujard, D., 2001. Fish growth hormone receptor: molecular characterization of two membrane anchored forms. Endocrinology 142, 3269–3273.

Castillo, J., Le Bail, P.-Y., Paboeuf, G., Navarro, I., Weil, C., Fauconneau, B., Gutiérrez, J., 2002. IGF-I binding in primary culture of muscle cells of rainbow trout: changes during in vitro development. Am. J. Physiol. Regul. Integr. Comp. Physiol. 283, R647–R652.

Castillo, J., Codina, M., Martínez, M.L., Navarro, I., Gutiérrez, J., 2004. Metabolic and mitogenic effects of IGF-I and insulin on muscle cells of rainbow trout. Am. J. Physiol. Regul. Integr. Comp. Physiol. 283, R647–R652.

Codina, M., Castillo, J., Gutiérrez, J., Navarro, I., 2004. Role of IGF-II in the metabolism and proliferation of rainbow trout muscle cells. Gen. Comp. Endocrinol. (Abstract of 5th ISFE, O41).

Chan, S.J., Plisetskaya, E.M., Urbinati, E., Jin, Y., Steiner, D.F., 1997. Expression of multiple insulin and insulin-like growth factor receptor genes in salmon gill cartilage. Proc. Natl. Acad. Sci. USA 94, 12446–12451.

Chauvigne, F., Gabillard, J.C., Weil, C., Rescan, P.Y., 2003. Effect of refeeding on IGFI, IGFII, IGF receptors, FGF2, FGF6, and myostatin mRNA expression in rainbow trout myotomal muscle. Gen. Comp. Endocrinol. 132, 209–215.

Chen, J.Y., Chen, J.C., Huang, W.T., Liu, C.W., Hui, C.F., Chen, T.T., Wu, J.L., 2004. Molecular cloning and tissue-specific, developmental-stage-specific, and hormonal regulation of IGFBP3 gene in zebrafish. Mar. Biotechnol. 6, 1–7.

Duan, C., 1998. Nutritional and developmental regulation of insulin-like growth factors in fish. J. Nutr. 128, 306S–314S.

Duan, C., Ding, J., Li, Q., Tsai, W., Pozios, K., 1999. Insulin-like growth factor binding protein 2 is a growth inhibitory protein conserved in zebrafish. Proc. Natl. Acad. Sci. USA 96, 15274–15279.

Gabillard, J.-C., Weil, C., Rescan, P.-Y., Navarro, I., Gutiérrez, J., Le Bail, P.-Y., 2003. Effects of environmental temperature on IGF1, IGF2, and IGF type I receptor expression in rainbow trout (*Oncorhynchus mykiss*). Gen. Comp. Endocrinol. 133, 233–242.

Gentil, V., Martin, P., Smal, J., Le Bail, P.Y., 1996. Production of recombinant insulin-like growth factor-II in the development of a radioimmunoassay in rainbow trout (*Oncorhynchus mykiss*). Gen. Comp. Endocrinol. 104, 156–167.

Greene, M.W., Chen, T.T., 1999a. Characterization of teleost insulin receptor family members. Gen. Comp. Endocrinol. 115, 254–269.

Greene, M.W., Chen, T.T., 1999b. Quantitation of IGF-I, IGF-II, and multiple insulin receptor family member messenger RNAs during embryonic development in rainbow trout. Mol. Reprod. Dev. 54, 348–361.

Headley, S.J., Keizer, D.W., Yao, S., Wallace, J.C., Bach, L.A., Norton, R.S., 2004. Binding site for the C-domain of insulin-like growth factor (IGF) binding protein-6 on IGF-II: implications for inhibition of IGF actions. FEBS Lett. 568, 19–22.

Kelley, K.M., Haigwood, J.T., Perez, M., Galima, M.M., 2001. Serum insulin-like growth factor binding proteins (IGFBPs) as markers for anabolic/catabolic condition in fishes. Comp. Biochem. Physiol. B 129, 229–236.

Lee, L.T.O., Nong, G., Chan, Y.H., Tse, D.L.Y., Cheng, C.H.K., 2001. Molecular cloning of a teleost growth hormone receptor and its functional interaction with human growth hormone. Gene 270, 121–129.

Loir, M., Le Gac, F., 1994. Insulin-like growth factor-I and -II binding and action on DNA synthesis in rainbow trout spermatogonia and spermatocytes. Biol. Reprod. 51, 1154–1163.

Maestro, M.A., Planas, J.V., Moriyama, S., Gutierrez, J., Planas, J., Swanson, P., 1997. Ovarian receptors for insulin and insulin-like growth factor I (IGF-I) and effects of IGF-I on steroid production by isolated follicular layers of the preovulatory coho salmon ovarian follicle. Gen. Comp. Endocrinol. 106, 189–201.

Maures, T.J., Duan, C., 2002. Structure, developmental expression, and physiological regulation of zebrafish IGF binding protein-1. Endocrinology 143, 2722–2731.

Maures, T., Chan, S.J., Xu, B., Sun, H., Ding, J., Duan, C., 2002. Structural, biochemical and expression analysis of two distinct insulin-like growth factor I receptors and their ligands in zebrafish. Endocrinology 143, 1858–1871.

McCormick, S.D., Kelley, K.M., Young, G., Nishioka, R.S., Bern, H.A., 1992. Stimulation of coho salmon growth by insulin-like growth factor-I. Gen. Comp. Endocrinol. 86, 398–406.

McCormick, S.D., Moriyama, S., Björnsson, B.Th., 2000. Low temperature limits photoperiod control of smolting in Atlantic salmon through endocrine mechanisms. Am. J. Physiol. Regul. Integr. Comp. Physiol. 278, R1352–R1361.

McCormick, S.D., 2001. Endocrine control of osmoregulation in teleost fish. Am. Zool. 41, 781–794.

Mendez, E., Planas, J.V., Castillo, J., Navarro, I., Gutiérrez, J., 2001. Identification of a type II insulin-like growth factor receptor in fish embryos. Endocrinology 142, 1090–1097.

Mingarro, M., Vega-Rubin de Celis, S., Astola, A., Pendon, C., Valdivia, M.M., Perez-Sanchez, J., 2002. Endocrine mediators of seasonal growth in gilthead sea bream (*Sparus aurata*): the growth hormone and somatolactin paradigm. Gen. Comp. Endocrinol. 128, 102–111.

Parrizas, M., Maestro, M.A., Banos, N., Navarro, I., Planas, J., Gutiérrez, J., 1995. Insulin/IGF-I binding ratio in skeletal and cardiac muscles of vertebrates: a phylogenetic approach. Am. J. Physiol. Regul. Integr. Comp. Physiol. 269, R1370–R1377.

Pérez-Sanchez, J., 2000. The involvement of growth hormone in growth regulation, energy homeostasis and immune function in the gilthead sea bream (*Sparus aurata*): a short review. Fish Physiol. Biochem. 22, 135–144.

Pérez-Sánchez, J., Marti-Palanca, H., Kaushik, S.J., 1995. Ration size and protein intake affect circulating growth hormone concentration, hepatic growth hormone binding and plasma insulin-like growth factor-I immunoreactivity in a marine teleost, the gilthead sea bream (*Sparus aurata*). J. Nutr. 125, 546–552.

Pérez-Sánchez, J., Calduch-Giner, J.A., Mingarro, M., Vega-Rubín de Celis, S., Gómez-Requeni, P., Saera-Vila, A., Astola, A., Valdivia, M.M., 2002. Overview of fish growth hormone family. New insights in genomic organization and heterogeneity of growth hormone receptors. Fish Physiol. Biochem. 27, 243–258.

Peter, R.E., Marchant, T.A., 1995. The endocrinology of growth in carp and related species. Aquaculture 129, 299–321.

Pozios, K.C., Ding, J., Degger, B., Upton, Z., Duan, C., 2001. IGFs stimulate zebrafish cell proliferation by activating MAP kinase and PI3-kinase-signaling pathways. Am. J. Physiol. Regul. Integr. Comp. Physiol. 280, R1230–R1239.

Radaelli, G., Domeneghini, C., Arrighi, S., Bosi, G., Patruno, M., Funkenstein, B., 2003a. Localization of IGF-I, IGF-I receptor, and IGFBP-2 in developing *Umbrina cirrosa* (Pisces: Osteichthyes). Gen. Comp. Endocrinol. 130, 232–244.

Radaelli, G., Patruno, M., Maccatrozzo, L., Funkenstein, B., 2003b. Expression and cellular localization of insulin-like growth factor-II protein and mRNA in *Sparus aurata* during development. J. Endocrinol. 178, 285–299.

Reinecke, M., Schmid, A., Ermatinger, R., Loffing-Cueni, D., 1997. Insulin-like growth factor I in the teleost *Oreochromis mossambicus*, the tilapia: gene sequence, tissue expression, and cellular localization. Endocrinology 138, 3613–3619.

Reinecke, M., Collet, C., 1998. The phylogeny of the insulin-like growth factors. Int. Rev. Cytol. 183, 1–94.

Riley, L.G., Hirano, T., Grau, E.G., 2004. Estradiol-17beta and dihydrotestosterone differentially regulate vitellogenin and insulin-like growth factor-I production in primary hepatocytes of the tilapia *Oreochromis mossambicus*. Comp. Biochem. Physiol. C Toxicol. Pharmacol. 138, 177–186.

Schmid, A.C., Naf, E., Kloas, W., Reinecke, M., 1999. Insulin-like growth factor-I and -II in the ovary of a bony fish, *Oreochromis mossambicus*, the tilapia: in situ hybridisation, immunohistochemical localisation, Northern blot and cDNA sequences. Mol. Cell. Endocrinol. 156, 141–149.

Schmid, A.C., Lutz, I., Kloas, W., Reinecke, M., 2003. Thyroid hormone stimulates hepatic IGF-I mRNA expression in a bony fish, the tilapia *Oreochromis mossambicus*, in vitro and in vivo. Gen. Comp. Endocrinol. 130, 129–134.

Shamblott, M.J., Cheng, C.M., Bolt, D., Chen, T.T., 1995. Appearance of insulin-like growth factor mRNA in the liver and pyloric ceca of a teleost in response to exogenous growth hormone. Proc. Natl. Acad. Sci. USA 92, 6943–6946.

Shimizu, M., Swanson, P., Dickhoff, W.W., 1999. Free and protein-bound insulin-like growth factor-I (IGF-I) and IGF-binding proteins in plasma of coho salmon, *Oncorhynchus kisutch*. Gen. Comp. Endocrinol. 115, 398–405.

Tse, M.C., Vong, Q.P., Cheng, C.H., Chan, K.M., 2002. PCR-cloning and gene expression studies in common carp (*Cyprinus carpio*) insulin-like growth factor-II. Biochim. Biophys. Acta 1575, 63–74.

Vong, Q.P., Chan, K.M., Cheng, C.H., 2003. Quantification of common carp (*Cyprinus carpio*) IGF-I and IGF-II mRNA by real-time PCR: differential regulation of expression by GH. J. Endocrinol. 178, 513–521.

Weber, G., Sullivan, C.V., 2000. Effects of insulin-like growth factor-I on in vitro final oocyte maturation and ovarian steroidogenesis in striped bass, *Morone saxatilis*. Biol. Reprod. 63, 1049–1057.

Wilkinson, R.J., Elliott, P., Hohmann, A., Francis, G., Carragher, J., 2004. Development and characterization of a competitive polyclonal antibody enzyme-immunoassay for salmon insulin-like growth factor-II. Comp. Biochem. Physiol. B Biochem. Mol. Biol. 139, 193–201.