CHAPTER

16

Role of Prolactin, Growth Hormone, Insulin-like Growth Factor I and Cortisol in Teleost Osmoregulation

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INTRODUCTION

Maintenance of constant cellular ion concentrations is a basic requirement of all life forms. The strategy evolved by teleost fish to achieve this requirement is by maintaining nearly constant levels of extracellular ions at approximately one-third the ionic strength of seawater (SW). In freshwater (FW), teleosts must counteract the passive loss of ions and gain of water by actively taking up ions (primarily through the gills), and removing excess water by excreting a dilute urine. In SW, teleosts

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counteract the gain of ions and loss of water by drinking SW, absorbing water and ions through the gut, and secreting excess monovalent ions through the gills and divalent ions through the kidney. Details of these mechanisms can be found in excellent reviews published in the last several years (Marshall, 2002; Evans *et al.*, 2005).

The demands on these ion-regulatory pathways will change as a function of environmental salinity, feeding, activity, injury, reproductive state and a variety of stressors. Therefore, control of ion regulation is critical, and the neuroendocrine system is the major means for regulating these mechanisms. Several excellent reviews on various aspects of the hormonal control of osmoregulation in fish have been published previously (Foskett *et al.*, 1983; Mayer-Gostan *et al.*, 1987; Bern and Madsen, 1992; McCormick, 1995, 2001; Sakamoto *et al.*, 2001; Sakamoto and McCormick, 2006). Here, we will focus on the endocrine mechanisms that control the overall capacity of the ion regulatory mechanisms in teleost fish, focussing on the osmoregulatory actions of prolactin (PRL), the growth hormone (GH)/insulin-like growth factor I (IGF-I) axis and cortisol. We will build on existing reviews and incorporate new data to give an integrative synthesis of the role of these hormones in the osmoregulation of teleost fish.

PROLACTIN (PRL)

PRL is a pleiotropic hormone with a wide spectrum of functions in vertebrates. Many of these functions are related to osmoregulatory processes (Bole-Feysot *et al.*, 1998; Sakamoto *et al.*, 2003; Harris *et al.*, 2004). The first evidence of the hyperosmoregulatory role of PRL in fish came from the studies by Grace Pickford and her collaborators (1959, 1970). Using hypophysectomized FW-adapted killifish, *Fundulus heteroclitus,* they demonstrated that PRL treatment was essential for survival of this species in a hypoosmotic environment. Although pituitary PRL is not necessary for FW survival of all teleosts, subsequent studies have established the hyperosmoregulatory role of PRL using other species, types of studies, and experimental approaches (see Hirano, 1986; McCormick, 1995; Manzon, 2002).

PRL has been shown to regulate several aspects of the ion regulatory mechanisms that are characteristic of FW fish. Water permeability of the gill, gut, and kidney are generally lower in FW- than in SW-acclimated fish, and PRL has been shown to decrease water permeability in these

tissues in several teleost species (Table 16.1; see also Manzon, 2002). To date, the mechanisms and gene products responsible for the actions of PRL on water permeability have not been identified, though they are likely to include regulation of tight junctions, membrane composition, and water channels such as aquaporins.

Treatment with PRL increases the ion uptake capacity of teleosts, and it is likely that this effect is carried out through regulation of gill chloride

Table 16.1 Physiological evidence for a hyperosmoregulatory role of PRL in teleosts.

Action	*References*
Pituitary	
Higher PRL cells activity, synthesis and secretion in FW and BW relative to SW	Nishioka *et al.* (1988) Mancera *et al.* (1993) Martin *et al.* (1999)
Low osmolality stimulates pituitary PRL secretion *in vitro*	Seale *et al.* (2003)
Plasma	
Higher PRL plasma levels in FW and BW relative to SW	Manzon (2002)
Receptors	
PRL receptor mRNA levels show a negative relationship with salinity (i.e., lower in higher salinities)	Shiraishi *et al.* (1999) Sandra *et al.* (2000)
PRL receptors present in gill chloride cells and in kidney	Ng *et al.* (1991) Weng *et al.* (1997) Santos *et al.* (2001)
Gills	
Exogenous PRL reduces gill Na^+,K^+-ATPase activity and mRNA levels	Sakamoto *et al.* (1997) Kelly *et al.* (1999) Mancera *et al.* (2002)
Exogenous PRL stimulates development of chloride cells 'fresh water morphology'	Herndon *et al.* (1991) Pisam *et al.* (1993)
Kidney	
Exogenous PRL increases Na^+ reabsorption and water excretion, through stimulation of glomerular size and urine output	Clarke and Bern (1980) Braun and Dantlzler (1987)
Contradictory effects on renal Na^+,K^+-ATPase activity, with increases or no effects	Pickford *et al.* (1970) Seidelin and Madsen (1997) Kelly *et al.* (1999)
Intestine	
Exogenous PRL decreases permeability to water and ions and Na^+,K^+-ATPase activity	Collie and Hirano (1987) Manzon (2002)
Contradictory effects on intestinal Na^+,K^+-ATPase activity, with increases or no effects	Kelly *et al.* (1999) Seidelin and Madsen (1999)
Skin	
Exogenous PRL increases mucus production by stimulation of differentiation and proliferation of mucous cells	Clarke and Bern (1980) Brown and Brown (1987)

cells. Herndon *et al.* (1991) found that PRL injection in SW-acclimated tilapia resulted in decreased chloride cell size, typical of FW-acclimated tilapia. In the Nile tilapia, Pisam *et al.* (1993) found that treatment with PRL increased the number of 'β-cells' typical of FW-acclimated tilapia and decreased the number of a-cells typical of SW-acclimated tilapia. Kelly *et al.* (1999) have found that the impact of PRL on chloride cells of *Sparus sarba* is dependent on the environmental salinity; in hypoosmotic brackish water PRL reduces chloride cell number and size, whereas in SW this hormone has no effect. Sakamoto and McCormick (2006) have suggested that the control of cell turnover (apoptosis and cell proliferation) in different osmoregulatory epithelia (e.g., gill and gastrointestinal tract) is a critical feature of the control of osmoregulation by PRL.

It is also likely that PRL affects the transporters that are involved in ion uptake. However, there is still some uncertainty regarding the transporters that are most directly involved in ion uptake in teleost fish. To date, the most favored models include a chloride-bicarbonate exchanger through which chloride uptake is driven through production of carbon dioxide. Sodium is thought to be taken up through an apical sodium channel energized by an apical H^+-ATPase. Characterization and localization of these necessary transporters to fully validate these models is ongoing, and no information on the role of PRL in regulating these transporters is currently available. This hormone has variable effects on gill Na^+,K^+-ATPase activity among teleost species (see McCormick, 1995). This may stem, in part, from differences in the relative importance of the Na^+,K^+-ATPase pump in ion uptake among teleosts (in most teleosts gill Na^+,K^+-ATPase activity is higher in SW, but in others it is lower), their relative euryhalinity, and the salinity at which the studies were carried out.

The activity of PRL cells is under hypothalamic and extra-hypothalamic control. Decreases in plasma osmolality result in increased PRL synthesis and release (Seale *et al.*, 2003). In addition, other hormones such as cortisol decrease PRL release (Borski *et al.*, 2002). At the hypothalamic level, dopamine has a clear inhibitory effect on PRL cells (Nishioka *et al.*, 1988). In mammals, a specific prolactin-releasing hormone peptide (Pr-RP) has been described, and in recent years, a Pr-RP has also been identified in teleosts (see Sakamoto *et al.*, 2003, 2005; Fujimoto *et al.*, 2006). This peptide is synthesized in hypothalamic

neurons, with axons ending close to PRL cells in the *rostral pars distalis* of the pituitary (Sakamoto *et al.*, 2003). This peptide can stimulate PRL cells, increasing synthesis and release of this hormone to systemic blood. In addition, in the amphibious, euryhaline mudskipper (*Periophthalmus modestus*) molecular studies have demonstrated a strong relationship between expression of Pr-RP and environmental salinity, with higher Pr-RP expression in fish acclimated to freshwater and terrestrial environments relative to SW conditions (Sakamoto *et al.*, 2005). The presence of Pr-RP in peripheral organs (like gut mucus cells) suggests the possibility of other actions, including effects on hormone expression outside of the pituitary, and even direct actions on osmoregulatory tissues (see Sakamoto and McCormick, 2006).

GROWTH HORMONE (GH)/INSULIN-LIKE GROWTH FACTOR I (IGF-I) AXIS

GH is a member of the GH/PRL family with a role in osmotic acclimation (McCormick, 1995) as well as growth and energy metabolism in fish (Björnsson, 1997). GH causes both local and systemic production of IGF-I, the latter being produced primarily in the liver. IGF-I carries out many of the growth-promoting actions of GH, though GH can also have direct actions on target tissues. Also, in carrying out its osmoregulatory function in fish, GH appears to work—at least in part—by increasing circulating IGF-I and production of IGF-I by the target tissue itself (Sakamoto and Hirano, 1993).

Smith (1956) was the first to demonstrate that GH treatment increased the capacity of trout to move from FW to SW. Later, Bolton *et al.* (1987) demonstrated that these effects were relatively rapid and independent of the growth promoting actions of GH. McCormick *et al.* (1991) demonstrated that IGF-I was as potent as GH in increasing the salinity tolerance of rainbow trout. Increased salinity tolerance in response to GH treatment has also been demonstrated in several non-salmonid teleosts, including tilapia and killifish (Mancera and McCormick, 1998a, 1999).

GH and IGF-I impacts on hypoosmoregulatory tissue are exerted in part through their influence on gill chloride cells. Many studies of salmonids have shown an effect of GH and/or IGF-I treatment on the number, size and specific ultrastructural features of gill chloride cells (see

references in McCormick, 2001). Sakamoto and McCormick (2006) have hypothesized that this impact of GH and IGF-I may be through the control of cell turnover and differentiation in the gill. This effect would be consistent with the known proliferative and anti-apoptotic roles of IGF-I in many vertebrate tissues (Wood *et al.*, 2005). It should be noted, however, that such effects have yet to be demonstrated in osmoregulatory tissues of fish.

GH and IGF-I are also involved in the upregulation of transporters critical to salt secretion by the gill. Both Na^+,K^+-ATPase and the Na^+,K^+,$2Cl^-$ cotransporter (NKCC) are upregulated by GH (Pelis and McCormick, 2001). Although GH has not been shown to have direct (*in vitro*) effects on these transporters, IGF-I has been shown to increase gill Na^+,K^+-ATPase, both *in vivo* and *in vitro* (Madsen and Bern, 1993; Seidelin and Madsen, 1999). These impacts on specific transporters may be part of a proliferation and differentiation pathway for the development of salt secreting chloride cells in the gill. Surprisingly, the impact of GH and IGF-I on osmoregulatory tissues other than the gill has received little attention. To date, what is known suggests that the action of GH and IGF-I on salt secretory capacity is primarily through its impact on gill physiology (Seidelin and Madsen, 1999).

IGF-I binding proteins are known to play a critical role in regulating the interaction of IGF-I with its receptor (Wood *et al.*, 2005). Recently, Shepherd *et al.* (2005) have shown that plasma levels of three IGF binding proteins (21-, 42- and 50-kDa) are higher after salinity acclimation. To our knowledge, this is the only report of the possible role of binding proteins in ion regulation. High-affinity, low-capacity IGF-I binding sites characteristic of receptors have recently been found in Atlantic salmon gill, and are most abundant in gill chloride cells (McCormick, unpublished results). Reinecke *et al.* (1997) present evidence that local production of IGF-I in the gill occurs primarily in chloride cells (Tables 16.2-16.4).

CORTISOL

Cortisol is the major corticosteroid produced by the interrenal tissue of teleost fish. This hormone has several established physiological roles related to osmoregulation, intermediary metabolism, growth, stress and immune function (Wendelaar Bonga, 1997; Mommsen *et al.*, 1999). Evidence for the osmoregulatory role of cortisol in fish has been compiled in excellent reviews (McCormick, 1995, 2001; Sakamoto *et al.*, 2001;

Table 16.2 Physiological evidence for a hyperosmoregulatory role of GH in salmonids.

Action	*References*
Pituitary	
Higher GH cell activity, synthesis and secretion in SW relative to FW	Nishioka *et al.* (1988) Sakamoto *et al.* (1993) Björnsson (1997)
Plasma	
Higher plasma GH levels and metabolic clearance rate of GH during smolting and after transfer from FW to SW	Sakamoto *et al.* (1990) Björnsson (1997)
Receptors	
GH receptors present at high levels in gill, kidney and intestine	Sakamoto and Hirano (1991)
Gills	
Exogenous GH increases gill Na^+,K^+-ATPase activity and mRNA levels	Boeuf *et al.* (1994) Madsen *et al.* (1995) McCormick (1995) Seidelin and Madsen (1999)
Exogenous GH stimulated proliferation of chloride cells with "seawater morphology"	See McCormick (1995) Sakamoto and McCormick (2006)
Exogenous GH increased abundance of Na^+-K^+-$2Cl^-$ cotransporter	Pelis and McCormick (2001)
Kidney	
GH treatment has not effect on kidney Na^+-K^+-ATPase activity	Madsen *et al.* (1995)
Intestine	
Exogenous GH induces 'seawater morphology' in the mucosa of the middle intestine of *Salmo salar* previous to smoltification	Nonnotte *et al.* (1995)
Exogenous GH increases the drinking response in *S. salar* pre-smolts after transfer to SW	Fuentes and Eddy (1997)

Evans, 2002). However, in recent years, new aspects of the physiology of cortisol in fish have arisen, and it is on these that we will focus our attention.

This hormone is considered a classical SW-promoting hormone, and evidence has shown a hypoosmoregulatory role of cortisol in several teleosts. Cortisol decreased plasma ion levels and osmolality in SW-adapted teleosts and enhanced salinity tolerance after transfer from low-salinity water to high-salinity water. This effect is due to increases in gill chloride cell size and density induced by cortisol treatment (McCormick, 1995, 2001). In addition, this hormone enhanced expression of gill Na^+,K^+-ATPase α-subunit and gill Na^+,K^+-ATPase activity in salmonid and no-salmonid species (Madsen *et al.*, 1995; Seidelin *et al.*, 1999;

Table 16.3 Physiological evidence for an osmoregulatory role of GH in non-salmonids.

Action	*References*
Pituitary	
GH cells activation is depending on the species studied and the environmental salinity	Nishioka *et al.* (1988) Mancera and McCormick (1998b)
Plasma	
GH levels behave differently depending on the species studied and the environmental salinity	Nishioka *et al.* (1988) Mancera and McCormick (1998b)
Receptors	
GH binding found in renal tubule of gilthead sea bream	Munoz-Cueto *et al.* (1996)
Gill and operculum	
Exogenous GH increases salinity tolerance, opercular chloride cell number and gill Na^+,K^+-ATPase activity in tilapia (*O. mossambicus*) and mummichog (*Fundulus heteroclitus)*	Flik *et al.* (1993) Xu *et al.* (1998) Mancera and McCormick (1998a)
Exogenous GH did not cause any significant changes in gill Na^+,K^+-ATPase activity or α- and β-subunit mRNA levels in silver sea bream (*Sparus sarba*)	Deane *et al.* (1999) Kelly *et al.* (1999)
Exogenous GH increases gill Na^+,K^+-ATPase activity in gilthead seabream (*Sparus aurata*)	Sangiao-Alvarellos *et al.* (2006)
Kidney	
Exogenous GH reduces Na^+,K^+-ATPase activity in SW- and BW-acclimated silver seabream (*Sparus sarba*)	Kelly *et al.* (1999)

Mancera *et al.*, 2002; Laiz-Carrión *et al.*, 2003). Finally, cortisol stimulated expression and abundance of Na^+-K^+-$2Cl^-$ cotransporter in the gills of FW-acclimated *S. salar* (Pelis and McCormick, 2001).

At the intestinal level, cortisol stimulated Na^+,K^+-ATPase activity, together with ion and water absorption, thus helping adaptation to high environmental salinity (Veillette and Young, 2005). Also, an improved drinking response after transfer to SW has been observed in *Oncorhynchus mykiss* and *S. salar* treated with this hormone (Fuentes *et al.*, 1996).

In addition to the classical hypoosmoregulatory role of cortisol, and according to several evidences (see Table 16.5), a new role of this hormone either in ion uptake in FW- or BW-adapted fish has been suggested. McCormick (2001), in his excellent revision of this topic, proposed a 'dual osmoregulatory' role for cortisol: (1) a stimulatory action on ion secretion in cooperation with GH/IGF-I axis in hyperosmotic environments; and (2) an increase of ion uptake in cooperation with PRL in hypoosmotic environments.

Table 16.4 Physiological evidence for an osmoregulatory role of IGF-I in salmonids and non-salmonids.

Action	*References*
Plasma	
IGF-I levels increased during smolting and SW acclimation	Sakamoto and Hirano (1993)
IGF-I binding proteins levels are altered after SW exposure of rainbow trout	Shepherd *et al.* (2005)
Receptors	
High affinity, low capacity IGF-I binding in salmon gill	McCormick (unpublished)
IGF-I receptor immunoreactivity present in chloride cells	McCormick (unpublished)
Gill	
IGF-I mRNA levels increase after exogenous GH and transfer to SW in salmonids and tilapia (*O. mossambicus*)	Sakamoto and Hirano (1993) Weng *et al.* (2000)
Exogenous IGF-I increases salinity tolerance, gill Na^+,K^+-ATPase activity and development of chloride cells	McCormick (1995) Mancera and McCormick (1998a) Seidelin and Madsen (1999)
IGF-I immunoreactivity present in chloride cells	Reinecke *et al.* (1997)

A large number of binding studies in fish have found evidence for a single class of corticosteroid receptors (CR) (see references in Prunet *et al.*, 2006). However, in the last several years, molecular techniques have demonstrated the presence of genes in several teleost species related to the mammalian glucocorticoid (GR) and mineralcorticoid receptors (MR). Fish GR has been characterized in several species (*Oreochromis mossambicus*, *Paralichthys olivaceus*), with a second isoform present in some species (*O. mykiss*, *Haplochromis burtoni*). In addition, MR has been molecularly characterized in *O. mykiss* and *H. burtoni*. Using a transfected cell line, Sturm *et al.* (2005) found that the rainbow trout MR (rtMR) has high transactivation efficiency for both aldosterone and 11-deoxycorticosterone (DOC), similar to the mammalian MR. Prunet *et al.* (2006) suggest that DOC, present in the plasma of some teleosts at levels that could activate the rtMR, might be a mineralocorticoid in fish. It may be possible that the teleost MR is involved in the 'dual osmoregulatory' role (ion secretion and uptake) of cortisol in teleost fish. However, the physiological function of the MR in fish and the possible physiological relevance of DOC remains to be established.

Table 16.5 Physiological evidence for a hyperosmoregulatory role of cortisol.

Action	*References*
Plasma	
Transfer from SW to FW transiently increases plasma cortisol levels	Mancera *et al.* (1994) McCormick (2001)
Effects of cortisol treatment	
Restored plasma osmolality and ion levels in hypophysectomized eels, goldfish and bowfin	McCormick (2001)
Increased surface area of gill chloride cells and the influx of sodium and chloride in FW rainbow trout, tilapia, eel and catfish	Laurent and Perry (1990) Perry *et al.* (1992)
Stimulated whole-body calcium uptake and the branchial calcium pump in freshwater rainbow trout	Flik and Perry (1989)
Enhanced H^+-ATPase activity in gills of salmonids, possibly involved in sodium uptake in hypo-osmotic environments	Lin and Randall (1995) Marshall (2002)
Increased ion regulatory capacity after transfer of *Sparus aurata* to low salinity environments	Mancera *et al.* (1994)
Stimulated gill Na^+,K^+-ATPase activity, plasma osmolality and ion levels in BW-adapted *S. aurata*	Mancera *et al.* (2002)
Interactions with other hormones	
A positive interaction of cortisol with PRL for maintenance of ion balance in FW-acclimated channel catfish *Ictalurus punctatus* and stinging catfish *Heteropneustes fossilis*	Parwez and Goswami (1985) Eckert *et al.* (2001)
A positive interaction of cortisol with PRL for promoting the transepithelial resistance and potential of cultured branchial epithelia from FW rainbow trout	Zhou *et al.* (2003)

HORMONE INTERACTIONS

In addition to the independent osmoregulatory actions of PRL, GH/IGF-I axis and cortisol, there is substantial evidence indicating the existence of synergy and antagonism of these hormones with one another.

PRL and Cortisol

Consistent with its role in promoting acclimation to low environmental salinities, PRL antagonizes the salt-secretory actions of both cortisol and GH (*O. mykiss*: Madsen and Bern, 1992; *S. salar*: Boeuf *et al.*, 1994; *S. trutta*: Seidelin and Madsen, 1997). Seidelin and Madsen (1997) found that PRL could reverse all of the increases in hypoosmoregulatory ability induced by cortisol, but did not affect the capacity of cortisol to increase gill Na^+,K^+-ATPase activity. They suggested that an interaction of PRL and cortisol on salt secretory capacity may occur in non-branchial tissue

such as the intestine. Cortisol has been shown to rapidly decrease the release of PRL from the tilapia pituitary (Borski *et al.*, 1991).

As outlined above, cortisol also has an apparent role in ion uptake, and there is evidence for a positive interaction of exogenous treatment with cortisol and PRL for maintenance of ion balance in FW fish (Parwez and Goswami, 1985; Eckert *et al.*, 2001). In *S. aurata*, a greater activation of pituitary PRL and ACTH cells have been shown to occur in BW-acclimated fish relative to SW-acclimated fish, suggesting a possible cooperation of PRL and cortisol in the control of osmoregulation at low salinities has also been suggested (Mancera *et al.*, 1993, 2002). Using an *in vitro* gill cell preparation, it has been demonstrated that PRL and cortisol act synergistically in order to promote transepithelial resistance and potential (Zhou *et al.*, 2003).

PRL and GH/IGF-I Axis

It has also been demonstrated that treatment with PRL can antagonize the hyperosmoregulatory actions of GH and IGF-I in salmonids (*O. mykiss*: Madsen and Bern, 1992; *S. salar*: Boeuf *et al.*, 1994; *S. trutta*: Seidelin and Madsen, 1997, 1999). This effect has been shown to occur at the level of specific ion transporters (gill Na^+,K^+-ATPase), and chloride cell number and morphology, resulting in differences in decreased whole animal performance (higher plasma ions) in SW. This antagonistic action of PRL, along with the lower PRL levels seen in BW, may explain the greater efficacy of GH treatment on salt-secretory capacity in BW relative to FW (Bolton *et al.*, 1987; McCormick, 1996). Currently, it is thought that this antagonism occurs primarily at target tissues, as we are not aware of any studies indicating that GH and PRL affect one another's synthesis or secretion.

GH/IGF-I Axis and Cortisol

An important synergy of the GH axis and cortisol to improve salinity tolerance and salt-secretory capacity has been demonstrated in salmonid and non-salmonid species. This cooperation is mediated by increased expression of gill Na^+,K^+-ATPase subunits, gill Na^+,K^+-ATPase activity, and abundance of Na^+-K^+-$2Cl^-$ cotransporter in gill chloride cells (Madsen, 1990; McCormick, 1996; Mancera and McCormick, 1999; Pelis and McCormick, 2001; McCormick, 2001). GH has been shown to

increase the abundance of gill cortisol receptors in two species of salmonids (*O. kisutch* and *S. salar*) (Shrimpton *et al.*, 1995; Shrimpton and McCormick, 1998), and this may explain a substantial part of the interaction between GH and cortisol. Seidelin *et al.* (1999) found an additive effect of IGF-I and cortisol on gill chloride cell number and Na^+,K^+-ATPase activity, but to date, no one has examined whether IGF-I can increase the number of gill cortisol receptors. Another possible mechanism of IGF-I and cortisol interaction is through a possible anti-apoptotic action of IGF-I on gill chloride cells, permitting cortisol to affect a greater number of partially or fully differentiated chloride cells.

In addition to interactions at target tissues, GH, IGF-I and cortisol are likely to interact so as to affect one another's synthesis and secretion, though surprisingly little research has been done in this area. GH has been shown to increase the sensitivity of the interrenal tissue to adrenocorticotropic hormone (ACTH) *in vitro* and *in vivo*, thus enhancing cortisol release (Young, 1988). Exogenous cortisol has been shown to decrease the circulating levels of IGF-I (Peterson and Small, 2005; McCormick, unpublished results). It is important to remember that these hormones have active roles in growth and energy mobilization, and thus their feedback mechanisms may reflect their involvement in processes other that just osmoregulation.

CONCLUSION

The control of the osmoregulatory system of teleosts involves several hypophysial and extra hypophysial hormones (PRL, GH and cortisol), which play an important role in osmotic acclimation (McCormick, 1995, 2001; McCormick and Sakamoto, 2006). It is a well-established fact that PRL has an important role in the FW acclimation of many teleosts, though the mechanisms of ion regulation controlled by this hormone have not been fully elucidated. In contrast, the osmoregulatory role of the GH/IGF-I axis appears to be more highly species-dependent. In salmonids this axis has a hypoosmoregulatory role acting clearly as a SW-adapting hormone. However, in non-salmonid species, the evidence is contradictory, with GH exhibiting an apparent hypoosmoregulatory role in some species, and no clear osmoregulatory role in others. Finally, cortisol has been shown to have a role in SW acclimation in both primitive and advanced teleost fish. However, in recent years, evidence also suggests a role for cortisol in ion uptake in low-salinity water-adapted fish. This new evidence suggests a

'dual osmoregulatory' role for cortisol, with the classic role of stimulation of ion secretion in hyperosmotic media (in cooperation with GH and IGF-I), and an additional role of increasing ion uptake in hypoosmotic environments (in cooperation with PRL).

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