Is Basic Research on Salmon Endocrinology Relevant to Improving the Fishery?

Howard A. Bern
Department of Integrative Biology
Cancer Research Laboratory and Bodega Marine Laboratory
University of California
Berkeley, California

The answer to the question posed in the title: "Is basic research on salmon endocrinology relevant to improving the fishery?", is a resounding "yes." This brief commentary, in fact an extended abstract, aims at giving some examples of the nature of the contribution, actual and potential, of basic neuroendocrinological research to salmon hatchery practice and aquaculture.

The endocrinology of the parr-smolt transformation has been studied intensively, largely in coho salmon *Oncorhynchus kisutch*. Information on blood hormone levels (thyroid hormones, cortisol, growth hormone, prolactin, insulin, calcitonin) during the smoltification period is now available. These hormones peak at various times, and the levels can in some cases be related to the physiological needs of the fish (Plisetskaya et al., 1988, Aquaculture 72:151: Bjornsson et al., 1989, Gen. Comp. Endocrinol. 74:346; Prunet et al., 1989, Gen. Comp. Endocrinol. 74:355; Young et al., 1989, Gen. Comp. Endocrinol. 74:335). Growth hormone receptor levels have also been determined (E.S. Gray, personal communication). Particular attention has been paid to changes in blood thyroxin concentrations. In northern California, the thyroxin level in coho generally peaks on the new moon closest to the vernal equinox (Grau et al., 1989, Science 211:607) and provides an indicator of the optimum time for release of smolts from hatcheries for downstream migration or potentially for transfer into seapens (Nishioka et al., 1983, Proc. 2nd N. Pac. Aqua. Symp., p. 161; Nishioka et al., 1985, Aquaculture 45:215). The only datum that is needed is the date of the appropriate new moon, which can be derived from an almanac. This is truly a simple criterion upon which a meaningful decision can be based. Nishioka at this meeting discusses aspects of amplification and synchronization of the thyroxin peak in hatchery populations (see also Nishioka et al., 1989, Aquaculture 82:355).

The initial impetus for the Berkeley salmonid research program came from the phenomenon of "stunting" observed when juvenile coho salmon were transferred into seapens prematurely (Bern, 1978, In: Comparative Endocrinology, Gaillard and Boer, eds., p. 97). We have analyzed this phenomenon in detail and, as expected, have concluded that the stunt is basically panhypoendocrine (Nishioka et al., 1982, Aquaculture 28:21; Young et al., 1987, In: Proc. 1st Cong. Asia and Oceania Soc. Comp. Endocrinol., Ohnishi, Nagahama, Ishizaki, eds., p. 363). The startling exception to this generalization is growth hormone, the levels of which prove to be several times higher in the blood and pituitary in the stunt than in the comparable normal seawater smolt (Bolton et al., 1987, J. Exp. Zool. 242:379). There is a comparable human clinical syndrome of dwarfism (Laron dwarfism) associated with elevated growth hormone levels, and coho salmon stunting (which also occurs in the Atlantic salmon (Bjornsson et al., 1989, Aquaculture 73:275) provides a possible model system for understanding the clinical disorder. As in the human, salmon stunting is at least in part a receptor disease (GH receptor levels in the liver are substantially lower in the stunt -- Gray et al., 1990, J. Exp. Zool., in press), resulting in the failure to generate insulin-like growth factor-1 (IGF-1), a necessary mediator for the transformation of cartilage into bone needed for growth.

We have recently become concerned with the role of IGF-1 in coho salmon and have discovered that combinant bovine IGF-1 (provided by Monsanto, St. Louis, MO) will stimulate growth both in vivo and in vitro (increased sulfate uptake by cartilage) (S. McCormick, K.M. Kelly, E.S. Gray, P. Tsai, personal communications). The rbIGF-1 also has an osmoregulatory action in preventing excess blood ion levels in rainbow trout *O. mykiss* after their transfer into water of high salinity (S. McCormick and T. Hirano, personal communication). These actions of a mammalian growth factor in a teleost fish are in themselves noteworthy.

Another area in which basic research has led to new technology with great potential for aquacultural practice results from the discovery of appreciable quantities of thyroid hormones in unfertilized, fertilized, and developing eggs of various salmonids (and other teleosts) including coho, chinook *O. tshawytscha*, and chum *O. keta* salmon (Kobuke et al., 1987, J. Exp. Zool. 242:89; Tagawa and Hirano, 1987, Gen. Comp. Endocrinol. 68:129; 1989, Gen. Comp. Endocrinol. 76:437; Greenblatt et al., 1989, Fish Physiol. Biochem. 6:261; Tagawa et al., 1990, Fish Physiol. Biochem. 8:515). The large quantities of thyroxin and triiodothyronine in salmon eggs make it unlikely that supplementation with thyroid hormones would prove useful in these species. However, in the striped bass *Morone saxatilis*, in which the levels of thyroid hormones in early embryonic and larval development have been analyzed (Brown et al., 1987, Trans. Am. Fish. Soc. Symp. 2:144), supplementation of egg thyroid hormone concentration by injecting the mother with a bolus of triiodothyronine before spawning has had genuinely beneficial effects: the triiodothyronine level of the eggs is significantly increased, as are survival, swimbladder inflation, and returns of juveniles from holding ponds (Brown et al., 1988, J. Exp. Zool. 248:168; 1989, Fish Physiol. Biochem. 7:295). The potential of other hormones and growth factors being transferred as such or as maternal mRNA to the eggs is real; so that in salmonids factors other than thyroid hormones may prove to be significant in playing a role in embryonic differentiation and in enhancing development, thus improving condition and survival of later stages (see Brown and Bern, 1989, In: Development, Maturation, and Senescence of Neuroendocrine Systems: A Comparative Approach, Schreibman and Scanes, eds., p. 289; Bern, 1990, Am. Zool., in press).

There has been considerable interest in the production of transgenic fish, including rainbow trout, with extra genes for growth hormone, in the hope that such fish would grow more rapidly and be better sources of dietary protein. Basic physiological research of the transgenic fish must accompany such efforts, in order to ascertain the pathophysiological consequences of an excess of growth hormone (similar considerations apply to fish treated with exogenous growth hormone, homologous or heterologous, natural or cloned). In addition to stimulating growth, and even this outcome is uncertain owing to possible downregulation of growth hormone receptors by growth hormone itself (Gray et al., 1990, J. Exp. Zool., in press). Growth hormone may have osmoregulatory effects: encouraging ion loss in fresh water, for example, where such an effect would be deleterious (Richman and Zaugg, 1987, Gen. Comp. Endocrinol. 65:189). Growth hormone may also act through the adrenocortical equivalent (the interrenal tissue) to stimulate cortisol secretion (Young, 1988, Gen. Comp. Endocrinol. 71:85), further increasing ion efflux (Richman and Zaugg, 1987, Gen. Comp. Endocrinol. 65:189). Both growth hormone and cortisol are potentially diabetogenic and may influence other aspects of fish physiology as well. To reiterate, basic endocrinological research on salmonids is essential to assess the consequences of the new molecular technology.

There is a two-way road between the basic science laboratory and the practicing salmon hatchery or aquaculture facility. The practitioner needs the results of fundamental research for innovative advances and changes in established technology; the basic researcher needs the observations of the practitioner to understand the phenomenology and the problems meriting investigation. This paper aims to underline the importance of keeping this two-way road open. (Research support for the Bern laboratory has come from the California Sea Grant College Program, the California Department of Fish and Game, and the National Science Foundation).

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Thomas J. Hassler, Editor
California Cooperative Fishery Research Unit
Humboldt State University, Arcata, California 95521