

NOTICE OF PUBLICATION



AQUACULTURE & FISHERIES INNOVATION LAB

RESEARCH REPORTS

Sustainable Aquaculture for a Secure Future

Title: Control of leptin by metabolic state and its regulatory interactions with pituitary growth hormone and hepatic growth hormone receptors and insulin like growth factors in the tilapia (*Oreochromis mossambicus*)

Author(s): Jonathan D. Douros¹, David A. Baltzegar¹, Jamie Mankiewicz¹, Jordan Taylor¹, Yoko Yamaguchi², Darren T. Lerner², Andre P. Seale⁴, E. Gordon Grau², Jason P. Breves³, and Russell J. Borski¹

1. Department of Biological Sciences, North Carolina State University, Raleigh, NC 27695-7617, United States

2. Hawaii Institute of Marine Biology, University of Hawaii, Kaneohe, HI 96744, United States

3. Department of Biology, Skidmore College, Saratoga Springs, NY 12866, United States

4. Department of Human Nutrition, Food and Animal Sciences, College of Tropical Agriculture and Human Resources, University of Hawaii at Manoa, Honolulu, HI 96822, United States

Date: 19 July 2016

Publication Number: AquaFish Research Report 16-361

AquaFish will not be distributing this publication. Copies may be obtained by writing to the authors.

Abstract: Leptin is an important cytokine for regulating energy homeostasis, however, relatively little is known about its function and control in teleost fishes or other ectotherms, particularly with regard to interactions with the growth hormone (GH)/insulin-like growth factors (IGFs) growth regulatory axis. Here we assessed the regulation of LepA, the dominant paralog in tilapia (*Oreochromis mossambicus*) and other teleosts under altered nutritional state, and evaluated how LepA might alter pituitary growth hormone (GH) and hepatic insulin-like growth factors (IGFs) that are known to be disparately regulated by metabolic state. Circulating LepA, and *lepa* and *lepr* gene expression increased after 3-weeks fasting and declined to control levels 10 days following refeeding. This pattern of leptin regulation by metabolic state is similar to that previously observed for pituitary GH and opposite that of hepatic GHR and/or IGF dynamics in tilapia and other fishes. We therefore evaluated if LepA might differentially regulate pituitary GH, and hepatic GH receptors (GHRs) and IGFs. Recombinant tilapia LepA (rtLepA) increased hepatic gene expression of *igf-1*, *igf-2*, *ghr-1*, and *ghr-2* from isolated hepatocytes following 24 h incubation. Intraperitoneal

AQUAFISH RESEARCH REPORTS are published as occasional papers by the Management Entity, AquaFish Innovation Lab, Oregon State University, Corvallis, Oregon 97331-1643 USA. The AquaFish Innovation Lab is supported by the US Agency for International Development under Grant No. EPP-A-00-06-00012-00. See the website at <aquafishcrsp.oregonstate.edu>.

Continued...

rtLepA injection, on the other hand, stimulated hepatic igf-1, but had little effect on hepatic igf-2, ghr1, or ghr2 mRNA abundance. LepA suppressed GH accumulation and gh mRNA in pituitaries in vitro, but had no effect on GH release. We next sought to test if abolition of pituitary GH via hypophysectomy (Hx) affects the expression of hepatic lepa and lepr. Hypophysectomy significantly increases hepatic lepa mRNA abundance, while GH replacement in Hx fish restores lepa mRNA levels to that of sham controls. Leptin receptor (lepr) mRNA was unchanged by Hx. In in vitro hepatocyte incubations, GH inhibits lepa and lepr mRNA expression at low concentrations, while higher concentration stimulates lepa expression. Taken together, these findings indicate LepA gene expression and secretion increases with fasting, consistent with the hormones function in promoting energy expenditure during catabolic stress. It would also appear that LepA might play an important role in stimulating GHR and IGFs to potentially spare declines in these factors during catabolism. Evidence also suggests for the first time in teleosts that GH may exert important regulatory effects on hepatic LepA production, insofar as physiological levels (0.05–1 nM) suppress lepa mRNA accumulation. Leptin A, may in turn exert negative feedback effects on basal GH mRNA abundance, but not secretion.

This abstract was excerpted from the original paper, which was published in *General and Comparative Endocrinology* (2016). DOI: 10.1016/j.ygcen.2016.07.017.

AQUAFISH RESEARCH REPORTS are published as occasional papers by the Management Entity, AquaFish Innovation Lab, Oregon State University, Corvallis, Oregon 97331-1643 USA. AquaFish is supported by the US Agency for International Development under CRSP Grant No. EPP-A-00-06-00012-00. See the website at <aquafishcrsp.oregonstate.edu>.