Relationship of Igf1 signaling to growth rate variation in California yellowtail

Nola Weston[1], Olivia Martin[1], Victoria Miller[1], Greg Schwartz[2], Sean Lema[1]

[1] Biological Sciences Department, Center for Coastal Marine Sciences, California Polytechnic State University, San Luis Obispo, CA

[2] BioResource and Agricultural Engineering Department, Center for Coastal Marine Sciences, California Polytechnic State University, San Luis Obispo, CA

Cal Poly Center *for* Coastal Marine Sciences

Introduction

Growth in fish is regulated by the growth hormone (Gh)/insulin-like growth factor-1 (Igf1) hormone axis, and shifts in Gh/Igf1 signaling are an important endocrine mechanism underlying growth variation (**Fig. 1**).[1,2] In most vertebrates, Gh secreted from the anterior pituitary binds liver Gh receptors to stimulate hepatic production of insulin-like growth factor-1 (Igf1), which regulates somatic tissue growth by binding Igf1 receptors in target tissues.[3]

In fish experiencing differing rates of somatic growth, changes in the production of both Igf1 and Igf binding proteins (Igfbps) can contributing to variation in somatic growth.[4] In this study, we examined how Igf1 signaling related to somatic growth rate variation in California yellowtail (*Seriola dorsalis*), a carangid fish under development for aquaculture. We also characterized Igfbp diversity in this species. The aim was to develop endocrine tools to better assess the impacts of captive culture conditions on somatic growth physiology in this species.

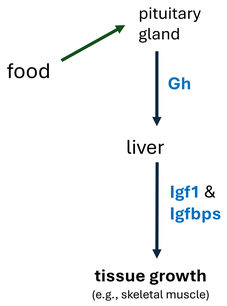


Fig. 1. *Food consumption triggers the pituitary to produce growth hormone (Gh) which stimulates the liver to produce somatomedins including Igf1 that regulate somatic growth.*

Objectives

① Evaluate how individual variation in somatic growth rate relates to Igf1 endocrine signaling pathways in California yellowtail.

② Characterize the diversity of Igf binding proteins (Igfbps) in California yellowtail and assess any relationships between liver *igfbp* mRNA levels and somatic growth rate.

Methods

Juvenile California yellowtail (*Seriola dorsalis*) were provided by the Sustainable Seafood program, Hubbs Sea World Research Institute (San Diego, California). Fish were reared at ~22°C in a Recirculating Aquaculture System (RAS) containing a total volume of 3,500 liters.

Fish were reared under captive conditions of either **low density** (29.9 kg fish / m^3 on day of sampling) or **high density** (49.5 kg fish/m^3) in 1,000 liter closed-system tanks (**Fig. 2**). Fish were fed a high protein (48% content) commercial diet at the same mass per wet fish mass in both density conditions. We measured individual growth rates by weighing and measuring individually PIT tagged fish (**Fig. 3**). Fish were tracked for 216 d. Fish were measured on day 188 and 216 to allow for calculation of somatic growth rates during that 28 d period prior to sampling.

Fig. 2. *Closed-system experimental tank system.*

Fig. 3. *Tagging and scanning a PIT-tagged California yellowtail fish.*

On day 216, a subset of fish (N = 35) from each density condition was netted, euthanized, and then weighed and measured. Blood was collected, and liver tissue was dissected and flash frozen in liquid N_2 for later RNA extraction. To determine if individual variation in somatic growth rate linked to gene expression (mRNA) in the Igf1 system, total RNA was extracted from the liver and relative mRNA levels for select Igf pathway genes (*igf1* and 11 *igfbp* genes) were measured using SYBR Green quantitative real-time reverse transcription PCR (qPCR). *Beta-actin* and *ribosomal protein L8* were used as reference genes for qPCR analyses.

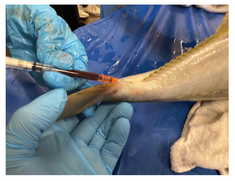


Fig. 4. *Blood collection from California yellowtail fish.*

Results

Fig. 5. *Growth profiles of fish from day 0 to day 216, the time period under when fish were maintained under the two density conditions.*

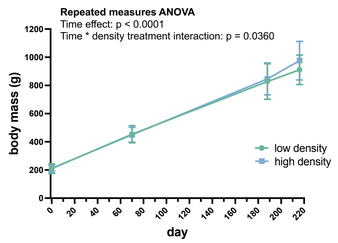


Fig. 6. *Fish sampled on day 216 showed no differences in mean body mass, length, or body condition factor (K).*

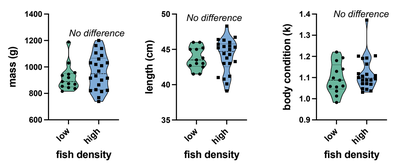
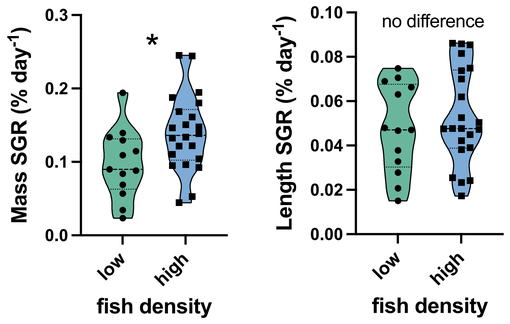


Fig. 7. *Sampled fish showed differences in specific growth rate (SGR) in the last 28 d prior to sampling on day 216. Fish sampled from the* **high density** *treatment had higher mass SGRs, on average, than fish from the* **low density** *treatment. Fish from these treatments did not, however, differ in SRG calculated by change in length (length SGR).*



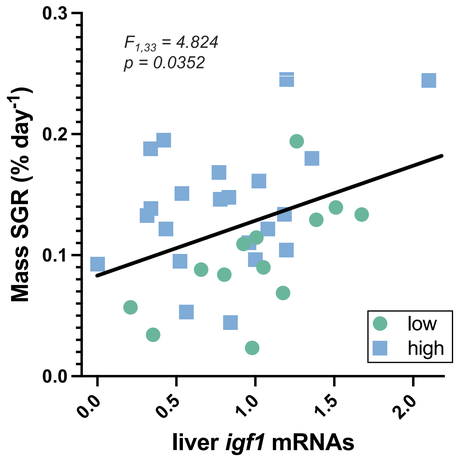


Fig. 8. *Mass specific growth rate (SGR) variation among individual fish related positively to individual variation in relative abundance of liver insulin-like growth factor 1 (igf1) mRNAs. Different color points refer to* **low density** *and* **high density** *treatments.*

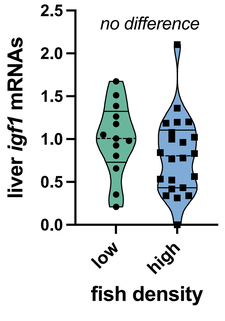


Fig. 9. *Liver insulin-like growth factor 1 (igf1) mRNAs did not vary between the two density tanks (p = 0.2238).*

Results (cont.)

Fig. 9. *Phylogenetic analysis of 11 Igf binding protein (Igfbp) genes identified in California yellowtail. Igfbp proteins identified in the genome of California yellowtail (GenBank reference sequence genome* ***PRJNA423295****) are indicated by the* ***red*** *boxes. Evolutionary relationships among Igfbp deduced amino acid sequences were inferred using the Maximum Parsimony (MP) method. The MP tree was obtained using the Subtree-Pruning-Regrafting algorithm, with bootstapping (1000 replicates).*

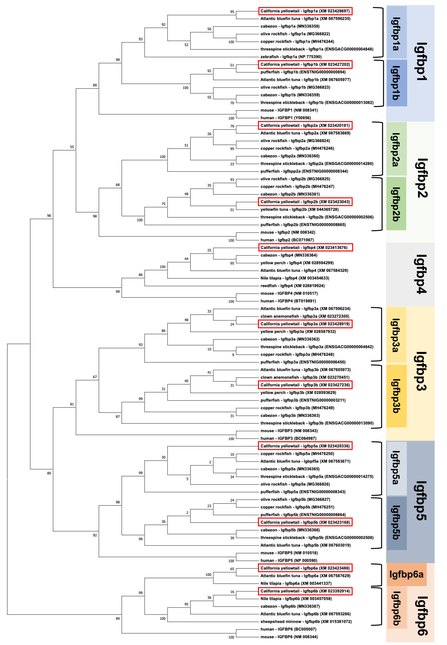
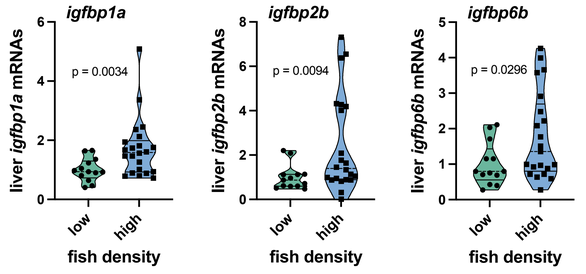


Fig. 10. *Relative mRNA abundances for three of the eleven Igf binding proteins (Igfbps) varied between the* **low density** *and* **high density** *treatments.*



Conclusions

① Individual variation in insulin-like growth factor 1 (*igf1*) mRNA abundance in the liver related positively to an individual fish's mass-specific growth rate (SGR).

② California yellowtail reared under the **low density** and **high density** conditions varied in liver relative mRNA levels for Igfbp genes *igbpb1a, igfbp2b* and *igfbp6b*. While reasons for those Igfbp mRNA expression differences are not clear, type 1, 2 and 6 Igfbp gene expression has been shown to be upregulated by cortisol in another fish,[5] suggesting that fish rearing density conditions may have led to differences in energetic allocations (i.e., glucose regulation, Igf signaling status) that subsequently led to a higher mass-SGR in those fish.

Acknowledgements

This research was made possible by generous support from the Santa Rosa Creek Foundation to Cal Poly San Luis Obispo's Center for Coastal Marine Sciences. The authors thank Samantha Albiani, Luke Ansty, Hailey Benson, Lucy Bensten, Jameson Cagan, Uriel Figuero, Jake Ide, Katherine Jackson, Rentaro Motegi, Ruben Moulton-Huber, Caroline Strickling, Sydney Teves, Lucy Thackray, Annabelle Tweet, and Joshua Valdez for logistical support. The authors thank Sustainable Seafood program of the Hubbs Sea World Research Institute for kindly supplying fish for this study.

References

1. Picha, M.E., Turano, M.J., Beckman, B.R., Borski, R.J., 2008. Endocrine biomarkers of growth and applications to aquaculture: a minireview of growth hormone, insulin-like growth factor (IGF)- I, and IGF-binding proteins as potential growth indicators in fish. *N. Am. J. Aquac.* 70, 196–211.
2. Reindl, K.M., Sheridan, M.A., 2012. Peripheral regulation of the growth hormone - insulin-like growth factor system in fish and other vertebrates. *Comp. Biochem. Physiol. A* 163, 231–245.
3. Duan, C., Ren, H., Gao, S., 2010. Insulin-like growth factors (IGFs), IGF receptors, and IGF-binding proteins: roles in skeletal muscle growth and differentiation. *Gen. Comp. Endocrinol.* 167, 344-351.
4. Hack, N.L., Cordova, K.L., Glaser, F.L., Journey, M.L., Resner, E.J., Hardy, K.M., Beckman, B.R. and Lema, S.C., 2019. Interactions of long-term food ration variation and short-term fasting on insulin-like growth factor-1 (IGF-1) pathways in copper rockfish (*Sebastes caurinus*). *Gen. Comp. Endocrinol.* 280, 168-184.
5. Mapes, H.M., Shew, J.E., Marden, H.M., Journey, M.L., Beckman, B.R. and Lema, S.C., 2025. Cortisol reduces insulin-like growth factor-1 (Igf1) and alters liver Igf binding protein (Igfbp) and muscle myogenic gene expression in blue rockfish (*Sebastes mystinus*). *Gen. Comp. Endocrinol.* 361, 114659.