

**SOMATOSTATIN MODULATES  
THE GROWTH OF SALMONID FISH**

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**EXTENDED ABSTRACT ONLY - DO NOT CITE**

**Introduction**

Somatostatins (SSs) are a diverse family of peptide hormones known to affect various aspects of the growth, development, and metabolism of vertebrates (Sheridan *et al.*, 1997). For example, SSs have been shown to influence organismal growth by inhibition of growth hormone (GH) release (*cf.* Holloway *et al.*, 1997). Extra-pituitary actions of SSs were suggested by previous studies that showed that growth retardation following premature transfer of salmon to seawater was accompanied by elevated plasma levels of SS (Sheridan *et al.* 1998). In addition, growth retardation of rainbow trout resulting from food deprivation was accompanied by altered plasma SS levels and altered expression of pancreatic mRNAs encoding SSs (Ehrman *et al.*, 1997). In this study, we examined further the modulation of the GH-Insulin-like growth factor (IGF-1) axis by SSs in rainbow trout.

### *Effects of SS on the GH-IGF-1 axis*

Short-term (up to 6h) *in vivo* administration of SS to trout reduced plasma levels of GH, Insulin (INS), and IGF-1. Plasma GH levels were reduced from  $4.1 \pm 0.3$  ng/ml in control animals to  $1.9 \pm 0.4$  ng/ml in SS-14-treated animals 6h after injection. SS-14 injection caused plasma INS levels to decline from  $3.1 \pm 0.3$  ng/ml to  $1.9 \pm 0.1$  ng/ml 3h after injection; by 6h, plasma INS levels in SS-14-injected animals rebounded to near control levels. Plasma IGF-1 was reduced from  $185 \pm 19$  ng/ml in control animals to  $104 \pm 19$  ng/ml in SS-14-treated animals 6h after injection. Instantaneous growth, as assessed by  $^{35}\text{S}$ -sulfate incorporation into gill cartilage was reduced from  $35.5 \pm 2.8$  cpm/ $\mu\text{g}$  dry weight in control animals to  $16.4 \pm 1.6$  cpm/ $\mu\text{g}$  dry weight in SS-14-injected animals.

Implantation of SS-14 into trout for 15 days resulted in significant growth retardation. Relative growth (length) was reduced from  $6.31 \pm 0.34\%$  in control animals to  $3.43 \pm 0.57\%$  in SS-14-treated animals. SS-14-induced growth retardation was associated with altered hepatic GH binding and with altered hepatic IGF-1 expression. Hepatic GH binding capacity was reduced from  $1087 \pm 179$  fmol/mg protein in control animals to  $635 \pm 63$  fmol/mg protein in SS-14-injected animals. Hepatic IGF-1 mRNA levels were reduced from  $4.7 \pm 0.3$  molecules of mRNA  $\times 10^{-8}/\mu\text{g}$  total RNA in control animals to  $2.4 \pm 0.5$  molecules of mRNA  $\times 10^{-8}/\mu\text{g}$  total RNA in SS-14-implanted animals. SSs also reduced the number of hepatic GH binding sites in hepatocytes *in vitro*.

### *Growth-reproduction interactions*

SSs also interacted with the reproductive axis of trout. In general, plasma SS-14 levels declined as sexual maturation progressed. For example, in females plasma SS-14 levels declined from  $0.43 \pm 0.03$  ng/ml in females with a Gonad Somatic Index (GSI)  $< 5$  to a low of  $0.23 \pm 0.05$  ng/ml in ovulated females in association with a decline in plasma estradiol (E2) levels. In males, SS-14 levels also declined during sexual maturation, reaching a low of  $0.44 \pm 0.02$  ng/ml in individuals with a GSI  $> 2.5$ ; SS-14 levels increased in spermiated males to  $0.55 \pm 0.03$  ng/ml.

Implantation of trout with E2 elevated plasma GH levels, reduced plasma SS levels, inhibited the expression of mRNAs encoding SS, and inhibited the response of somatotropes to SS challenge. GH levels increased from  $2.9 \pm 0.2$  ng/ml in

control animals to  $4.3 \pm 0.7$  ng/ml in E2-treated fish. Plasma levels of SS-14 fell from  $0.56 \pm 0.02$  ng/ml in control animals to  $0.37 \pm 0.01$  ng/ml in E2-treated animals. Pancreatic expression of mRNAs encoding the precursor of SS-14 was reduced from  $4.1 \pm 0.1$  molecules of mRNA  $\times 10^{-8}$ /μg total RNA in control animals to  $2.6 \pm 0.3$  molecules of mRNA  $\times 10^{-8}$ /μg total RNA in SS-14-injected animals. GH release from isolated trout pituitary fragments was reduced by nearly 40% in the presence of SS-14 for 20 min. However, SS-14 did not affect GH release from pituitary fragments obtained from fish treated with E2 for 2 weeks.

### **Conclusions**

These findings indicate that SSs modulate the GH-IGF-1 axis, perhaps underlying nutritional regulation of growth, and suggest that SSs may coordinate reproductive events with growth.

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