Researchers identify key reproductive hormone in oldest vertebrate

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University of New Hampshire professor of biochemistry Stacia Sower and colleagues have identified the first reproductive hormone of the hagfish, the world's oldest living vertebrate. Credit: Courtesy of Stacia Sower.

Looking at a hagfish – an eyeless, snot-covered, worm-like scavenger of the deep – the last thing that comes to mind is sex. Yet the reproductive functioning of these ancient vertebrates is such an enduring enigma that a gold medal was once offered to anyone who could elucidate it.

Although the prize expired, unclaimed, long ago, University of New Hampshire professor of biochemistry Stacia Sower and colleagues at two Japanese universities have identified the first reproductive hormone of the hagfish – a gonadatropin -- representing a significant step toward unraveling the mystery of hagfish reproduction. Their findings, "Evolutionary origin of a functional gonadotropin in the pituitary of the

most primitive vertebrate, hagfish," were published in the journal *Proceedings of the National Academies of Science* (*PNAS*) in September.

"This is a significant breakthrough with hagfish," says Sower, who was second senior author on this paper, co-authored by principal investigator Katsuhisa Uchida and Sower's long-time collaborator Masumi Nozaki, both of Niigata University in Japan. Gonadatropins (GTHs) are a protein secreted from the pituitary, stimulating the gonads (ovaries and testes) to produce and release the sex steroid hormones which prompt their growth and maturation. GTHs are produced in response to hypothalamic gonadotropin-releasing hormone (GnRH), what Sower calls the "master molecule" for reproduction in vertebrates; its discovery remains the holy grail of understanding hagfish reproduction.

At 500 million years old, hagfish are the oldest living vertebrate, predating the dinosaurs. "They're one of evolution's great success stories," says Sower, who has devoted the majority of her 30-year career researching hagfish and the similarly un-charismatic lamprey eels. "Here's this animal with a backbone that we don't know anything about." They're notoriously difficult to study, in part because their habitat is the ocean floor at 100 meters or more.

Yet their important evolutionary position makes hagfish worthy of scientific inquiry. "We look at the evolution of the hormones and receptors and say, 'have they retrained characteristics of their ancestral forms, or are they more similar to higher vertebrates?'" says Sower. "They're a key to understanding the evolution of later evolved vertebrates."

Compounding the urgency of better understanding hagfish reproduction is their growing importance as a fishery in the Gulf of Maine. Despite their vicious nature and least appealing characteristic – the stress-induced secretion of mucous from up to 200 slime glands along their

bodies – hagfish are prized, particularly in Asian markets. Their tough, soft skin is marketed as "eel" skin for wallets, belts and other items ("Because they're not going to sell something that says 'hagfish,'" says Sower, pulling out her own flawless 20-year-old eel skin wallet).

Fished in the Gulf of Maine since 1992, hagfish have been fished out of the waters off Korea and Japan and overfished on the U.S. West coast. They also play a significant role in nutrient cycling and ocean-floor clean-up, feeding primarily on dead and dying fish. Lacking knowledge on their reproductive functions – how, when and where they spawn – the hagfish could be fished to extinction, says Sower.

Sower, who directs the Center for Molecular and Comparative Endocrinology at UNH, has worked with Nozaki on hagfish reproduction since both scientists were postdoctoral researchers at the University of Washington in 1980. The two, along with Hiroshi Kawauchi of Kitasato University in Japan, have shared students and researchers through a formal collaboration that's produced more than 30 papers. It's also, notes Sower, produced many failures as they've labored to identify the hagfish GTH.

"Now we're filling in the gaps of what we know," she says.

More information: www.pnas.org/content/107/36/15832.long

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