

**\*\*ABSTRACT NOT FOR CITATION WITHOUT AUTHOR PERMISSION.** The title, authors, and abstract for this completion report are provided below. For a copy of the full completion report, please contact the author via e-mail at [liweim@msu.edu](mailto:liweim@msu.edu) Questions? Contact the GLFC via email at [research@glfc.org](mailto:research@glfc.org) or via telephone at 734-662-3209 ext. 118.

## Determine the Utility of Pheromone Antagonists for Sea Lamprey Control

Project ID – 2018\_LIW\_54075

Anne M. Scott<sup>2</sup>, Nicholas S. Johnson<sup>3</sup>, Richard R. Neubig<sup>4</sup>, Weiming Li<sup>2</sup>

2 Department of Fisheries and Wildlife, 480 Wilson Road, Room 13 Natural Resources Building, Michigan State University, East Lansing, MI 48824 U.S.A.

3 U.S. Geological Survey, Great Lakes Science Center, Hammond Bay Biological Station, 11188 Ray Road, Millersburg, MI 49759 U.S.A.

4 Department of Pharmacology and Toxicology, 1355 Bogue Street, Room B440 Life Sciences

*December 2023*

### **ABSTRACT:**

The sea lamprey (*Petromyzon marinus*) is a jawless fish species that invaded the Laurentian Great Lakes and inflicted catastrophic damage on the native fish community. Existing sea lamprey control efforts including the application of lampricide and implementation of barriers have dramatically reduced sea lamprey population from historic estimates. However, in select systems where lampricides and barriers are less effective, control strategies that exploit sea lamprey behaviors are thought to supplement control efforts. Disrupting the sea lamprey pheromone communication system may offer additional effective and environmentally benign approaches to manage the invasive population. Sea lamprey rely on conspecific odors to locate suitable streams to spawn and synchronize spawning behavior. Spermiated male sea lamprey construct nests and release at least two types of pheromones that collectively attract females: 1) a multi-component sex pheromone mixture from the gills including a main component of 3-ketopetromyzonol sulfate (3kPZS) and other sulfonated bile acids, and 2) a milt pheromone in the seminal plasma including spermine as a component. We found the gill-released pheromone 3kPZS activates two highly related odorant receptors (ORs), OR320a and OR320b. Interestingly, PZS also activates both OR320a and OR320b and acts as a behavioral antagonist, a compound that diminishes attraction to a pheromone, to 3kPZS. When applied in a side-by-side odorant comparison in-stream, fewer ovulated females located and entered an artificial nest activated with synthetic 3kPZS and PZS compared to an adjacent source of 3kPZS alone. We documented petromyzonol tetrasulfate (3sPZS), a synthetic analog of PZS and 3kPZS, also impeded ovulated female search for a 3kPZS activated nest in a stream in a manner similar to that of PZS. However, sex pheromones are often released as mixtures that elicit stronger responses when all components are present at appropriate ratios compared to responses induced by individual components. When we applied a mixture of 3sPZS and PZS upstream of a nest activated with full male sex pheromone, we found the behavioral antagonist mixture synergistically disrupted ovulated female upstream movement, approach, and entry into the pheromone activated nest. Next, we applied 3sPZS and PZS to a high-density spawning ground with a natural spawning population below a sea lamprey barrier over two spawning seasons and recorded reduced spawning activities between released ovulated females and free-ranging (not experimentally released) males and reduced abundance of free-ranging sea lamprey over 3h trials. The antagonist mixture reduced

spawning activities and free-ranging female about when tested over 24 h trials as well. In addition to gill-released sex pheromone 3kPZS and its behavioral antagonists PZS and 3sPZS, we identified the milt pheromone spermine and its behavioral antagonist, cyclen. Spermine activated a trace amine-associated receptor (TAAR)-like receptor (TAAR348) in the olfactory epithelium, evoked concentration-dependent olfactory responses, attracted ovulated females, and promoted mating behaviors. Cyclen is a specific antagonist of TAAR348 that reduced olfactory responses to spermine and nullified ovulated female preference for spermine. Taken together, our results indicate the three pheromone antagonists reduce pheromone-induced olfactory and behavioral responses. These studies provide empirical evidence that supports pheromone behavioral antagonist application as a potential strategy for disrupting sea lamprey reproduction and supplementing sea lamprey control efforts in the Great Lakes.