

## *Research Prospectus – Genetic Control of Sea Lamprey*

**Purpose**—The purpose of this prospectus is to outline a program of research to develop genetic control for invasive sea lamprey *Petromyzon marinus* eradication in the Laurentian Great Lakes. The objectives herein cover Phase I of the research program (2020-2024).

**Background**—The GLFC faces continuing pressure to reduce reliance on lampricides and barriers to control sea lamprey populations to target levels. The Great Lakes Fishery Commission in 2015 funded a project titled “*Evaluating the risks and potential of genetic technologies for managing the impacts of sea lampreys in the Great Lakes.*” The project attempted to answer several questions including: (1) Will any genetic approach provide a useful tool for eradicating sea lampreys in the Great Lakes? (2) If so, what are the most promising lines of inquiry? (3) What are the logistical/technical constraints on delivering promising options? (4) What are the risks and can they be managed? (5) Will any approach be socially acceptable? Project results suggested genetic control technologies could be effectively applied to eradicate sea lamprey in the Great Lakes, but these technologies have varying levels of risks and social acceptance issues that require mitigation prior to implementation. In an on-line survey, Great Lakes fishery stakeholders strongly supported research and development of genetic control tactics for the sea lamprey, and eventual implementation of options that were demonstrably effective and low risk.

**Authority**—At its 2018 Interim Meeting, the Commission approved a new vision for supplemental controls, which included a directed program of research and development on genetic controls for sea lamprey. As part of this initiative, the Commission is committed to continued dialogue and outreach about genetic control of sea lampreys with parties beyond the Commission family, including First Nations and Tribes.

**Research Program**—The Commission will establish a research program to: (1) identify suitable candidate genes for sea lamprey biocontrol; and (2) identify the most feasible approach to genetic control of sea lamprey.

Objective 1 is a necessary first step toward identifying targets for modification. To achieve objective 1, gene sequences or products (e.g., microRNAs or siRNAs) will be sought that when disrupted, enhanced, or ingested result in species-specific, disruptive, physiological or metabolic changes (e.g., sex determination, morbidity, sterility) in sea lamprey. Possible targets for screening and testing (i.e., effects on phenotype, survival, fertility) include lamprey-specific steroids, egg coat proteins, lymphocyte receptors critical for reproduction, and genes involved in sex determination.

Objective 2 will involve developing and improving tools for genome editing and transformation suitable for implementation in the control program. Several of these tools have been developed, but must be tailored to sea lamprey for control. To achieve objective 2, the following options will be considered and one or two will be pursued during Phase I of the research program: (1) developing and optimizing sea lamprey genome editing and modifying techniques with reversal or stop mechanism to produce genetically modified sea lamprey (GML; e.g., epigenetic enzymes, re-engineered transposases, CRISPR-CAS9, zinc fingers, and TALENs)<sup>1</sup>; (2) assessing and, if needed, developing options for genetically modifying lamprey host species (GMH; e.g., host

vaccination)<sup>1</sup>; and (3) developing cost effective methods for introducing GML into the Great Lakes.

Both objectives will rely on identifying potential genomic targets for editing using the new Genome 10K sea lamprey genome<sup>2</sup>.

**Funding**—GLRI funding will be used to support the first phase of the research program. Individual research projects towards objectives outlined herein will be vetted through the Sea Lamprey Research Board.

<sup>1</sup>Two most supported options by an expert panel (Thresher et al. 2018)

<sup>2</sup>The sequencing and assembly pipeline was developed as part of the mission of the G10K-VGP, which is to generate at least one highly-quality, error-free, near gapless, haplotype phased reference genome of all ~66,000 extant vertebrate species. The minimum metric set is an assembly with contig N50 of 1 million bp (1Mb), scaffold N50 of 10Mb, 90% of the genome assembled into chromosomes, a base-call quality error of QV40 (no more than 1 nucleotide error in 10,000 bp), and haplotype phased.