D. ABSTRACT/PROJECT SUMMARY

Research Category: EPA-G2006-STAR-B1

Title: ECOHAB – Understanding shellfish resistance strategies as a means to predict and manage PSP toxicity

Investigators: T. Scheuer[1], V. Trainer[2], V.M. Bricelj[3], and W. Catterall[1]

[1]University of Washington, Department of Pharmacology, Seattle, WA; [2]Northwest Fisheries Science Center, Seattle WA; [3]Institute for Marine Biosciences (IMB), National Research Council, Halifax, NS.

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The proposed multidisciplinary research collaboration will characterize the complex mechanism underlying bivalve susceptibility to paralytic shellfish toxins (PSTs) and species-specific toxin accumulation. In mammals, PSTs affect nerve function via specific block of the voltage-sensitive Na^+ channel. Bivalves, however, clearly have adaptations that permit them to tolerate toxins in their algal food. Specifically, "insensitive" bivalve species are known to harbor, without apparent harm, high concentrations of PSTs, while more "sensitive" species attain relatively low toxin levels and can suffer sublethal or even lethal effects from harmful algal blooms (HABs) when toxin concentrations are high. This susceptibility to ingested toxins and thus, ability to accumulate toxins, varies markedly both within and among bivalve species. The past research of this collaborative group has characterized up to a 50-fold difference in toxin affinity among populations of softshell clams, *Mya arenaria*, and has shown that a single, conservative mutation in the Na^+ channel confers resistance to PSTs. A key goal of this proposal is to extend this research to more completely characterize the molecular and biochemical basis for the much larger interspecific variation in toxin uptake and sensitivity in bivalves.

The overarching goal of these studies is to understand the factors contributing to shellfish toxicity in the presence of HABs and to reduce their impact by providing tools to predict toxin retention by shellfish.

Specific objectives of this research will be to: 1. characterize the saxitoxin binding region of each of the four functional Na^+ channel domains in several shellfish species selected as representative of extremes of nerve sensitivity/resistance to PSTs, 2. Determine the biochemical basis for PSP insensitivity and toxin sequestration in selected bivalve species characterized by prolonged toxin retention of PSTs, 3. determine the molecular basis for the relative PSP-insensitivity of molluscs compared to vertebrates, 4. develop molecular markers for selection of non-accumulating (nontoxic) bivalve stocks. Interspecific differences in shellfish susceptibility to toxins will be explored using molecular, biochemical and physiological approaches in clams (*Siliqua patula* and/or *Ensis directus*, *Spisula solidissima,* and *Saxidomus giganteus*) and mussels (*Mytlilus edulis*) from historically toxic and non-toxic areas on the Pacific (including Alaska) and Atlantic coasts of N. America. Identification of inter- and intraspecific genetic and biochemical differences will contribute to our fundamental understanding of toxin resistance mechanisms and perhaps open future avenues for detoxification strategies or selective breeding. Regional characterization of bivalve responses to toxic algae will help to predict the impacts of paralytic shellfish poisoning (PSP) over a wide geographical range. Understanding of the relationship of specific toxin vectors to the intensity and frequency of HABs in a given area, will contribute to improved management of commercially important shellfisheries.

Supplemental keywords: Food web, shellfish, resistance, susceptibility, sodium channel, PSP