

11TH U.S. SYMPOSIUM ON HARMFUL ALGAE

CROSS-SPECIES COMPARISON OF BREVETOXIN (BTX-2) IN VITRO PHASE I BIOTRANSFORMATION IN NORTHERN GULF OF MEXICO FISH AND HUMAN LIVER MICROSOMES

Brevetoxins (BTX) are neurotoxins produced by *Karenia* spp., associated with recurrent blooms of “red tide” along the Gulf of Mexico coast. Numerous studies have shown that BTXs are rapidly metabolized in shellfish and mammals. However, there is limited research on BTX metabolism in fish, despite growing evidence that fish serve as vectors for BTX transfer in marine food webs. In this study, we investigated the *in vitro* biotransformation of BTX-2 (a major constituent of *Karenia* spp. toxin profiles) using hepatic microsomes prepared from several species of northern Gulf of Mexico fish as well as commercially available human microsomes. Metabolism assays focused on Phase I reactions mediated by cytochrome P450 monooxygenase enzymes (CYP), which had been confirmed active in the prepared microsomes using CYP-specific standard substrates prior to the BTX-2 biotransformation experiments. Samples were analyzed by UHPLC-HRMS(/MS) to monitor BTX-2 depletion and to aid in the identification of BTX metabolites. Our results showed that the fish liver microsomes rapidly depleted BTX-2, resulting in 70–98% reduction within 1 hr of incubation. We observed simultaneous production of several functionalized metabolites (22 in total), including previously identified congeners like BTX-3 and BTX-B5, which were verified by comparison with a commercial reference standard, as well as BTX-9. Comparison of metabolite formation across species suggests that variable metabolic pathways may lead to divergent BTX profiles, including significantly higher formation of BTX-3 by the herbivorous Emerald parrotfish (*N. usta*) microsomes, and evidence of human-specific BTX biotransformation pathways. These results confirm that fish are capable of similar BTX biotransformation as reported for shellfish and mammals, and provide evidence to support variation in BTX-2 metabolism across fish species. Collectively, these data have important implications for the determination of the ecotoxicological fate of BTXs in marine food webs.

JESSICA GWINN, PHD CANDIDATE | SCHOOL OF MARINE AND ENVIRONMENTAL SCIENCES, UNIVERSITY OF SOUTH ALABAMA (MOBILE, AL, 36688); DAUPHIN ISLAND SEA LAB (DAUPHIN ISLAND, AL, 36528)

Jessica (Jesse) Gwinn is a PhD Candidate completing a degree in Marine Sciences at the University of South Alabama and Dauphin Island Sea Lab with Dr. Alison Robertson. Jesse is broadly interested in the production, transport, and fate of environmental contaminants and naturally produced bioactive compounds as well as the development of reliable biochemical and chemical methods for their detection. Her dissertation work focuses on understanding the movement of marine microalgal toxins throughout food webs, including their metabolic transformation in marine organisms. Based on this doctoral work, Jesse was recently awarded the Robert L. Shipp Outstanding PhD Student award from the University of South Alabama's School of Marine and Environmental Sciences. Jesse earned B.Sc. degrees in Bioenvironmental Sciences and Wildlife & Fisheries Sciences from Texas A&M University, graduating magna cum laude with Honors and a Senior Merit Award from the Department of Plant Pathology & Microbiology. Gwinn's research is supported by NSF Partnership in International Research and Education (CiguaPIRE), NIH and NSF Greater Caribbean Center for Ciguatera Research, and NOAA NCCOS Ecology and Oceanography of Harmful Algal Blooms. See Jesse's LinkedIn profile (<https://www.linkedin.com/in/jessica-gwinn-64b0b023b/>) for more information.

JGWINN@DISL.ORG

Co-Authors:

Co-author 1: Tyler B. Smith

Affiliation: Center for Marine and Environmental Studies, University of the Virgin Islands (St. Thomas, USVI 00802)

Co-author 2: Alison Robertson

Affiliations: School of Marine and Environmental Sciences, University of South Alabama (Mobile, AL, 36688); Dauphin Island Sea Lab (Dauphin Island, AL, 36528)