

Preclinical evaluation of marine natural products for neuroscience drug development

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Abstract

As pharmaceutical companies have largely exited neuroscience drug development, longer life spans have resulted in an increased economic and healthcare burden of central nervous system disorders resulting in a substantial need for innovation in neuroscience drug development. Natural products play important roles in ecology, biotechnology and biomedicine, with an estimated 60-70% of active compounds in clinical pharmaceutical formulations derived from or inspired by natural products. The marine environment is an extraordinarily rich source of species diversity, and marine organisms display vast chemical and biological diversity. Adaptation to their unique habitat contributes to marine organisms producing a wide variety of biologically active primary and secondary metabolites. Although major pharmaceutical companies have largely ceased exploring marine natural products following the development of large synthetic compound libraries, marine natural products continue to have a higher success rate than other sources of drug leads. In this study, we screen marine natural products for neuroactivity in murine primary cortical cultures, using a high-throughput FLIPR screening for modulation of calcium channels using Fluo8-AM indicator dye for detection. Additionally, we screen for potassium channel modulation using FMP blue indicator dye. Finally, in neuroactive drugs, we screen for neurite outgrowth and/or neurotoxicity using live-dead assays. Together, these data identify neuroactive compounds which can then be semi-synthetically modified to expand compound libraries for neuroscience drug development. In addition to our laboratory work, we curate an up-to-date Global Marine Pharmaceuticals Pipeline <https://www.marinepharmacology.org/> to track marine drugs through the clinical and preclinical pipeline.

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Biography

Marsha Pierce completed her PhD and Creighton University in the Department of Biomedical Sciences and her postdoctoral research at Creighton University in the Department of

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