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New biosensors to detect ciguatoxins and characterization of their binding on mammalian neuronal cell by single molecule force spectroscopy

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Ciguatera is a prominent cause of poisonings by seafood worldwide. It is caused by very potent neurotoxins, ciguatoxins (CTXs) which are lipid-soluble polyether compounds produced by dinoflagellates in the genera *Gambierdiscus* and *Fukuyoa*. CTXs are mostly found in tropical and subtropical areas. However, both CTXs and *Gambierdiscus* spp. have recently been identified in European waters. CTXs bind to voltage gated sodium channels (VGSCs) at the surface of human sensory neurons where they remain, causing Ciguatera Poisoning. This severe disease is characterized by a variety of gastrointestinal, cardiovascular and neurological symptoms (paresthesia, ataxia, cold allodynia), including chronic neurological effects in some cases. Despite the wide range of tests presently available for CTXs detection, there is still no simple and rapid way of detecting these toxins in contaminated samples. In this prospect, we have engineered biosensors based on the yeast model *Saccharomyces cerevisiae*. This unicellular eukaryotic model is well-known and easy to genetically modify, grows fast and presents a very good conservation of signaling pathways with higher eukaryotes. Our approach relies on the detection of a transcriptional signaling activated in yeast cells by exposure to CTXs and their binding to an endogenous receptor homologous to mammalian VGSCs. New results, simplified protocol and attempts to lower down the limit of detection (LOD) will be presented. Moreover, in an attempt to use nanobiotechnology approaches, we are in parallel developing another strategy to characterize and study the binding of Ciguatoxins on mammalian neuronal cells by single molecule force spectroscopy using atomic force microscopy. I will present this project and its potentialities in terms of molecular characterization of the binding between ... and ex-vivo testing of inhibitor compounds.¹

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