From the Yeast cell wall to new strategies in the fight against Ciguatera

Hélène Martin-Yken, Etienne Dague, Christophe Furger, H. T. Darius, M. Chinain

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H. Martin-Yken[1,2,3,4],

E. Dague[2,] C. Furger[5], H. T. Darius[4], M. Chinain[4]

(1) LISBP INSA Université de Toulouse, UMR CNRS 5504, UMR INRA 792, Toulouse, France.
(2) LAAS-CNRS, 7 avenue du colonel Roche, Toulouse, France.
(3) IRD Polynésie française, Papeete, Polynésie française.
(4) Laboratoire des Micro-Algues Toxiques, UMR EIO, Institut Louis Malardé, Papeete, Polynésie française.
(5) Antioxydant Power and LAAS-CNRS, 7 avenue du colonel Roche, Toulouse, France.

I will attempt to explain my scientific journey, from studying the cell wall and stress response mechanisms of yeasts, up to the development of innovative approaches to fight Ciguatera, a major cause of food poisonings by seafood worldwide.

Yeasts are eukaryotic microorganisms traditionally used by man to make bread, beer and wine and thus very well studied. Their cells are surrounded by a thick cell wall composed of glycans and proteins organized in a complex multilayered architecture. Essential for the survival of yeasts and fungi, this highly dynamic organelle gets constantly remodeled during the cell cycle to allow morphogenetic events as well as upon environmental changes. It is a key player in cellular adhesion and resistance to antifungal compounds. While studying the mechanisms of cell wall adaptations to various stresses, I came across the different cellular signaling pathways involved notably MAP kinase cascades and the Calcineurin pathway which are conserved with higher eukaryotes.

Ciguatoxins (CTXs) are lipid-soluble, highly neurotoxic, polyether compounds produced by dinoflagellates from the genus *Gambierdiscus spp..* mostly found in tropical and subtropical zones. CTXs bind to Voltage Gated Sodium Channels at the surface of human sensory neurons where they remain, causing Ciguatera Fish Poisoning or CFP. This severe disease is characterized by with a variety of gastrointestinal, cardiovascular and neurological symptoms (paresthesia, ataxia, cold allodynia), including persistent neurological effects. Despite the importance and prevalence of CFP, there is so far no simple and quick way of detecting these toxins in contaminated samples. Currently, only heavy and expensive laboratory methods are available to detect them: LC-MS/MS, receptor-binding assays by competition with labeled compounds, and neuroblastoma cell-based assays performed on mammalian neurons. We have started to engineer biosensors based on the detection of a transcriptional signal in the model yeast *Saccharomyces cerevisiae*, using the very good conservation of its signaling pathways with higher eukaryotes.

Finally, I will also present a smaller project (NeuroSens) based on a different strategy, to study and characterize the binding of Ciguatoxins on mammalian neuronal cells by Single Molecule Force Spectroscopy using Atomic Force Microscopy.