Development of New Biosensors to detect Ciguatoxins

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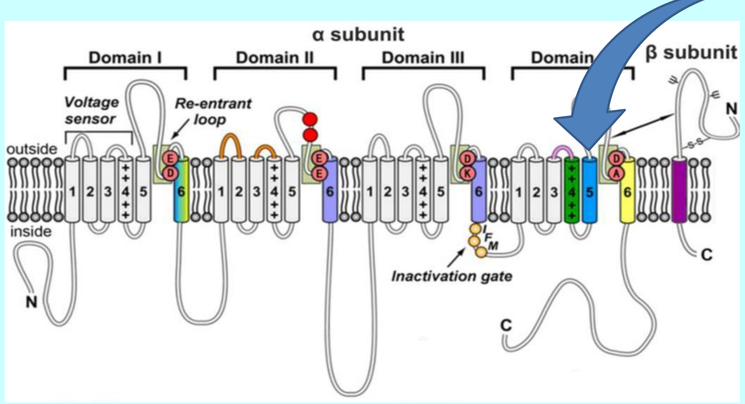
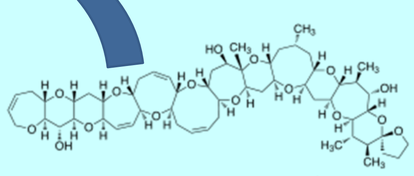
Ciguatera Fish Poisoning: the most prevalent intoxication from seafood worldwide !

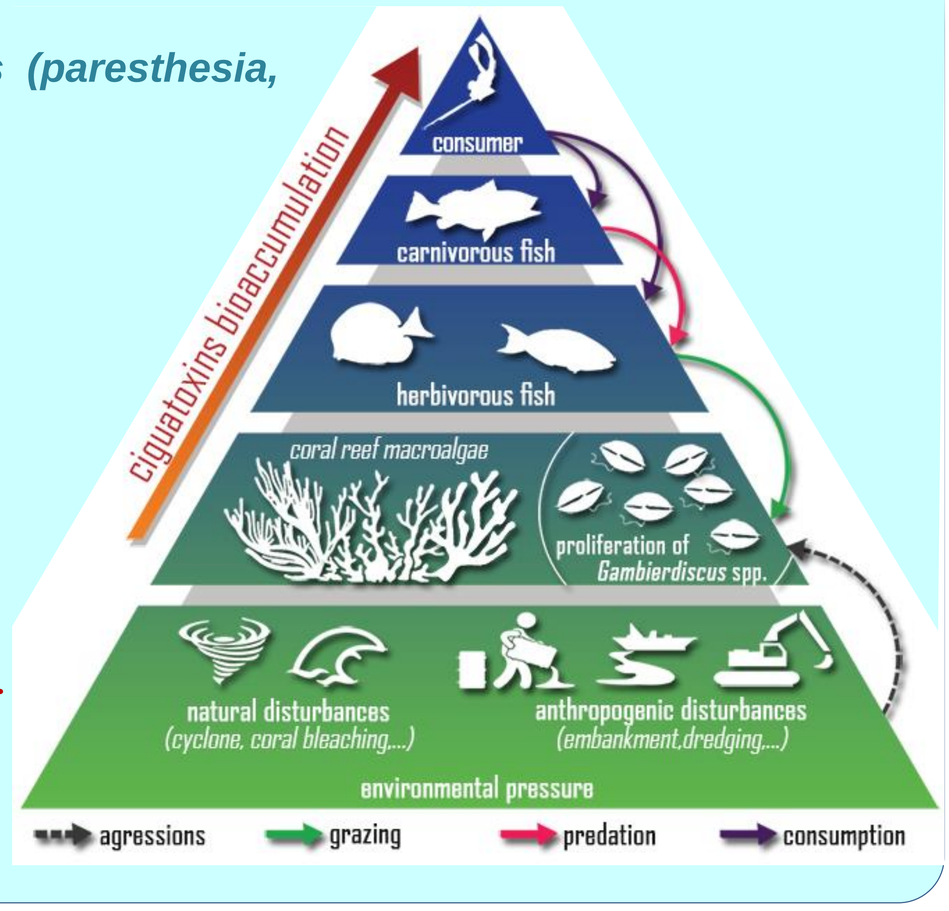
- ***Symptoms:*** *variety of gastrointestinal, cardiovascular, neurological symptoms (paresthesia, ataxia, cold allodynia),* ***with persistent neurological effects***
- ***Cause:*** *Ciguatoxins or CTXs , lipid-soluble polyethers produced by dinoflagellates Gambierdiscus spp.. mostly found in tropical and subtropical zones, and* ***now also present in temperate waters*** [1,2,3,4]
- ***Mechanism:*** *CTXs bind to Voltage Gated Sodium Channels (VGSCs) of human sensory neurons.*



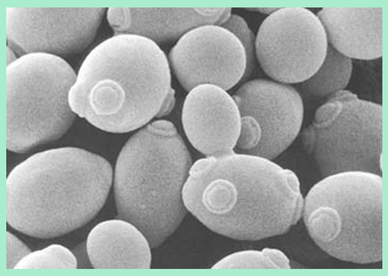


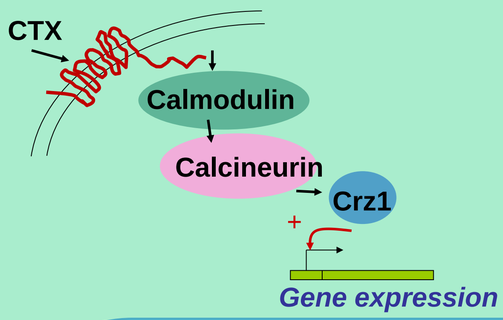
- No effective treatment !

- *Existing functional detection tests for CTXs such as (CBA-N2a, RBA)[5] are heavy, expensive, impossible to transport for an in situ use.*



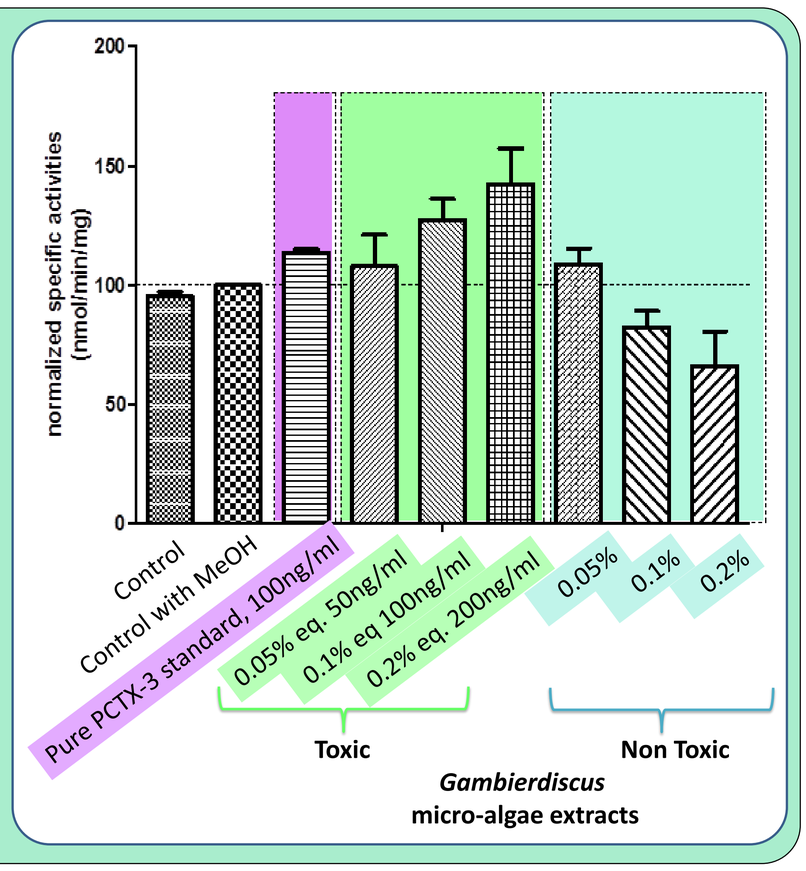
Design of new biosensors based on yeast cells:





- ***Why Yeast cells ?*** *well-known, easy to genetically modify, eukaryotic = good conservation of signaling pathways with higher eukaryotes, fast and easy to grow.*

- ***Methodology:***
The yeast Ca^{2+} channel is very close to Mammalian VGSC. In response to CTXs, it induces a transcriptional signal (here reporter gene lacZ), that we measure in yeast cells.



On-going improvements:

Replace colorimetry by Fluorescence, or other value ***easily measurable in the field***
Use cell wall and signaling mutants to improve CTXs access and ***amplify the signal***
Mutagenesis on the channel protein to ***improve CTXs binding***

Future developments :

Express the Mammalian VGSC in yeast, per se or as chimera with the yeast ion channel, and follow cellular signaling induced.
Measure binding of the different toxins to the receptors by Single Molecule Force Spectroscopy (by AFM or Optical Tweezers).
Develop cell-free sensors systems with the toxins receptor (human VGSC or its yeast homolog) integrated in lipid bilayers.
Create point mutants of the receptors, to identify the residues involved and then design or search for possible cures.

References :
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4 Aligizaki et Nikolaidis, 2008. J. Biol. Res. Thessalon 9, 75.
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