



New strategies in the fight against Ciguatera

Hélène Martin-Yken, Camille Gironde, Hélène Taiana Darius, Christophe Furger, Mireille Chinain, Etienne Dague

► To cite this version:

Hélène Martin-Yken, Camille Gironde, Hélène Taiana Darius, Christophe Furger, Mireille Chinain, et al.. New strategies in the fight against Ciguatera. Nano In Bio 2018 Nanosciences for Life and Materials, May 2018, Le Gosier, France. hal-02950613

HAL Id: hal-02950613

<https://hal.inrae.fr/hal-02950613>

Submitted on 28 Sep 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



New strategies in the fight against Ciguatera

Hélène Martin-Yken

LISBP Toulouse.



CIGUATERA

Poissons dangereux à la consommation

* Pêches et ventes interdites en tous lieux et en tous temps.
** Pêches et ventes interdites au nord du 16,5° parallèle (cf. carte).
*** Pêches et ventes interdites, quel que soit le lieu de pêche, si le poids dépasse 1 kg.

Poissons interdits à la pêche et à la vente
(Arrêté préfectoral n°2002-1249)



POISSONS VÉNÉNEUX

La pêche et la vente de ces poissons sont interdites en tout temps et tous lieux.

TÉTRODONS
ET DIODONS
Puffer, Spotfin
Burrfish, Spotfin
Porcupinefish,
Chilomycterus et *Diodon*



BARRACUDA
BÉCUNE
Great Barracuda
Sphyraena barracuda



CARANGUE JAUNE
Yellow Jack
Caranx bartholomaei



GRANDE SÉRIOLE
Greater Amberjack
Seriola dumerili



SÉRIOLE LIMON - BABIANE
Almaco Jack
Seriola rivoliana

La même interdiction s'applique aux poissons pêchés au nord du parallèle 16° 50' de latitude Nord, appartenant aux espèces suivantes :



CARANGUE NOIRE
Black Jack
Caranx lugubris



CARANGUE FRANCHE
CARANGUE BLEUE
Bar Jack
Caranx ruber



CARANGUE GROS-YEUX
MAYOL
Horse Eye Jack
Caranx latus



MURÈNE CONGRE VERT
Green Moray
Gymnothorax funebris



VIEILLE À CARREAUX
Yellow Fish Grouper
Mycteroperca venenosa



VIEILLE MORUE
Tiger Grouper
Mycteroperca tigris



VIEILLE VARECH
Mutton Hamlet
Alphistes afer



VIEILLE BLANCHE
Red Grouper
Epinephelus morio



PAGRE DENTS DE CHIEN
Dog Snapper
Lutjanus jocu
Concerné par les deux interdictions



VIVANEAU OREILLES NOIRES
Blacklin Snapper
Lutjanus buccanella



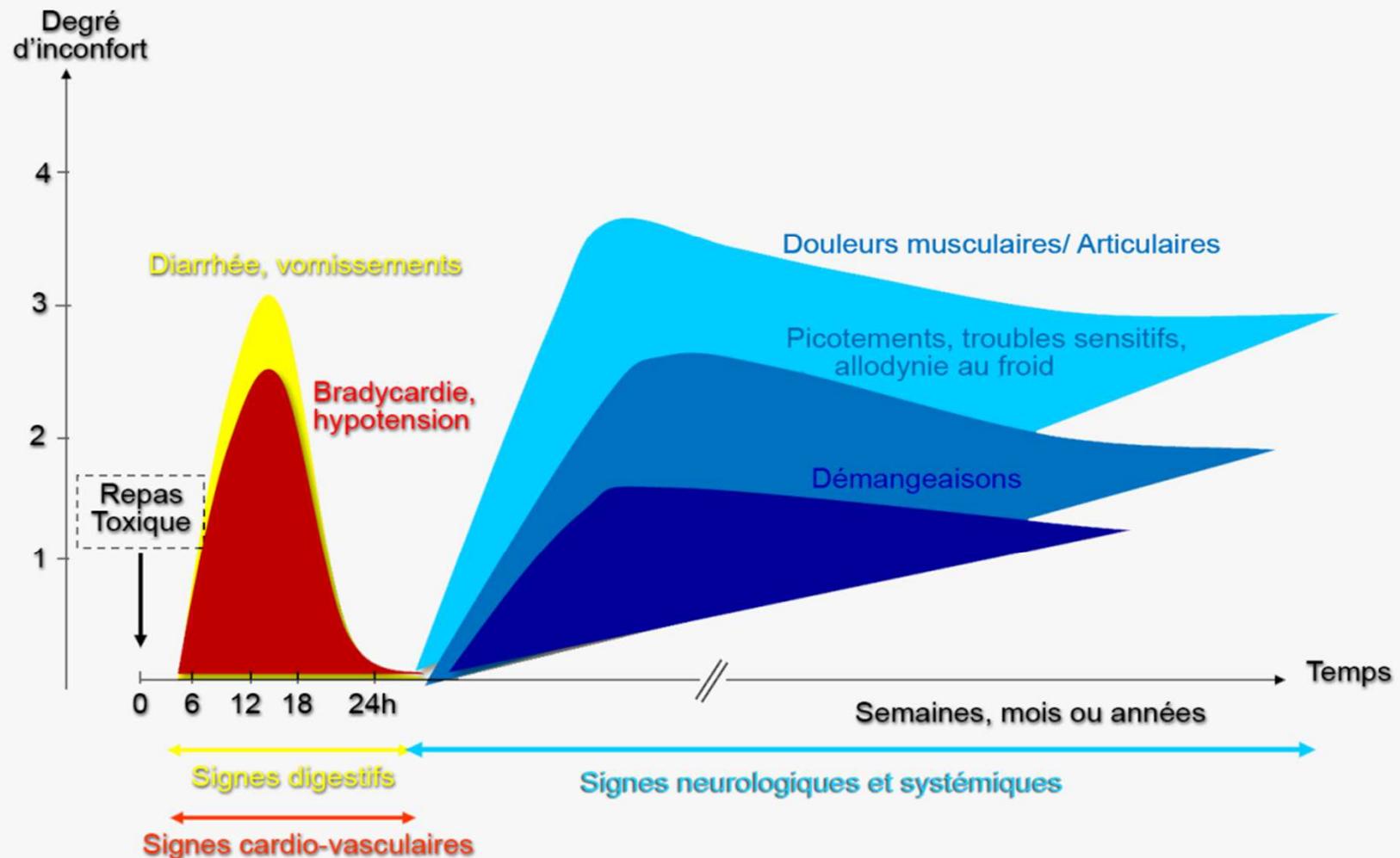
PAGRE JAUNE
Shoolmaster Snapper
Lutjanus apodus

Ciguatera Food Poisoning

- Considered as the **most frequent food poisoning of marine origine worldwide** ($\sim 200\,000$ cases /year).
- **Symptoms** : digestive, **neurological** (hypotension, bradycardia, paresthesia, cold allodynia, myalgia, arthralgia) and **cardiac**, potentially lethal.
- **Long term** prevalence and **body sensitization** effect = increase of symptoms severity upon next exposure, cross effects (ex : alcohol).

Ciguatera Food Poisoning

SYMPTOMES

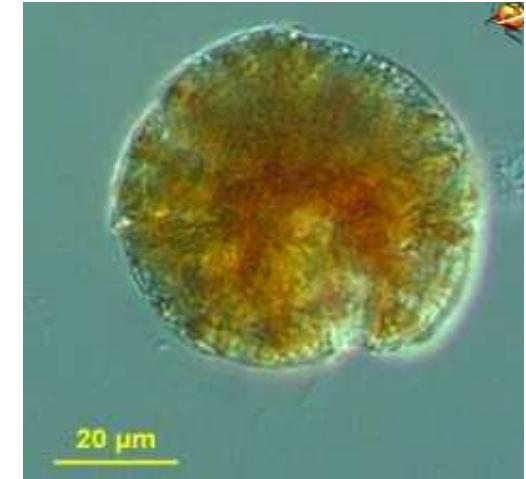


History :

- First mention : Chen Tsang Chi, chinese doctor of the T'ang dynasty (~650).
- From the XVth century, Colomb, Magellan, Cortes, Vasco de Gama describe the disease in the Caribbeans ; Fernandes de Quiros, Cook, Bligh,... in Pacific.
- First precise description of a ciguatoxin intoxication : James Cook, Sept. 7th 1774 Nouvelles-Hébride.
- The term ciguatera : attributed to cuban Felipe Poey, 1866 for a neuro-digestive intoxication due to a marine gasteropode (*Livona pica*) whose cuban name is « *cigua* ».

THE CAUSAL AGENT : CIGUATOXINES (CTXS)

- ***Among the most powerful marine biotoxines***
(1 microgramme can kill a man)
- Produced by the dinoflagellate micro-algae
Gambierdiscus toxicus, upon coral reefs damage
- Polycyclic polyethers, liposoluble, MW~1100 Da
- 3 families : Pacific = P-CTXs, Caribbean = C-CTXs,
Indian Ocean = I-CTXs.



Gambierdiscus toxicus,
(B Anderson, MBL.)

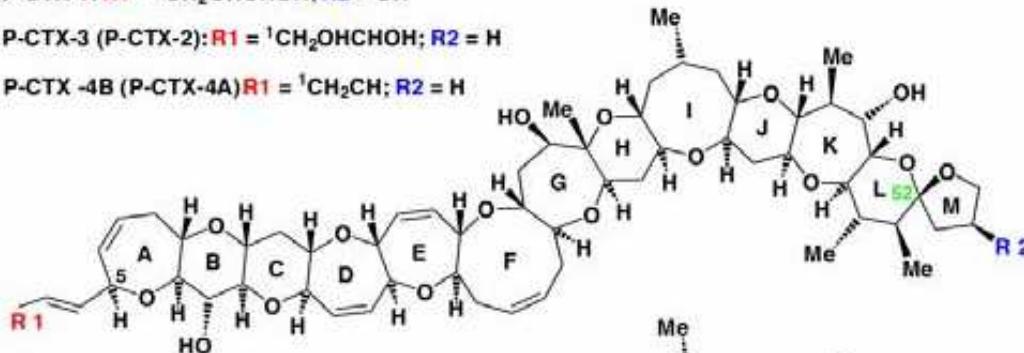
No simple detection test available !!!

Ciguatoxines Molecular Structures

P-CTX-1: R1 = $^1\text{CH}_2\text{OHCHOH}$; R2 = OH

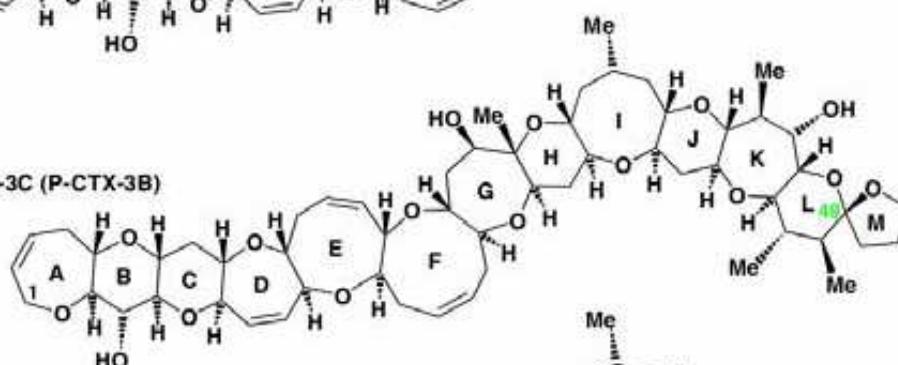
P-CTX-3 (P-CTX-2): R1 = $^1\text{CH}_2\text{OHCHOH}$; R2 = H

P-CTX-4B (P-CTX-4A) R1 = $^1\text{CH}_2\text{CH}$; R2 = H

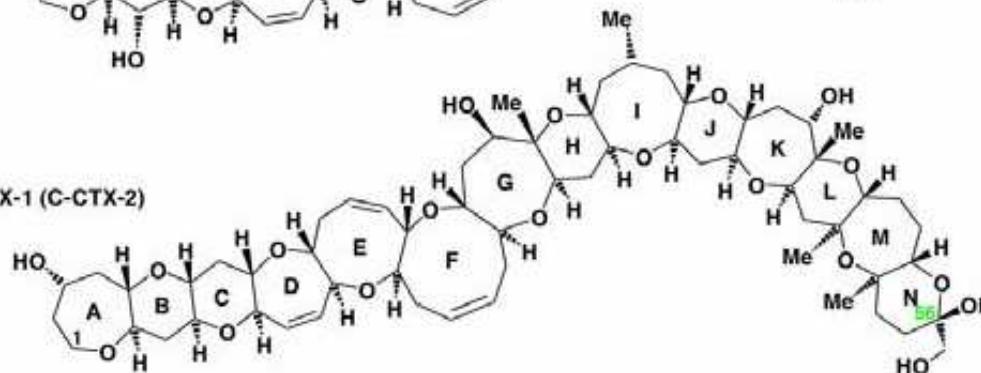


Pacific Ciguatoxines

P-CTX-3C (P-CTX-3B)

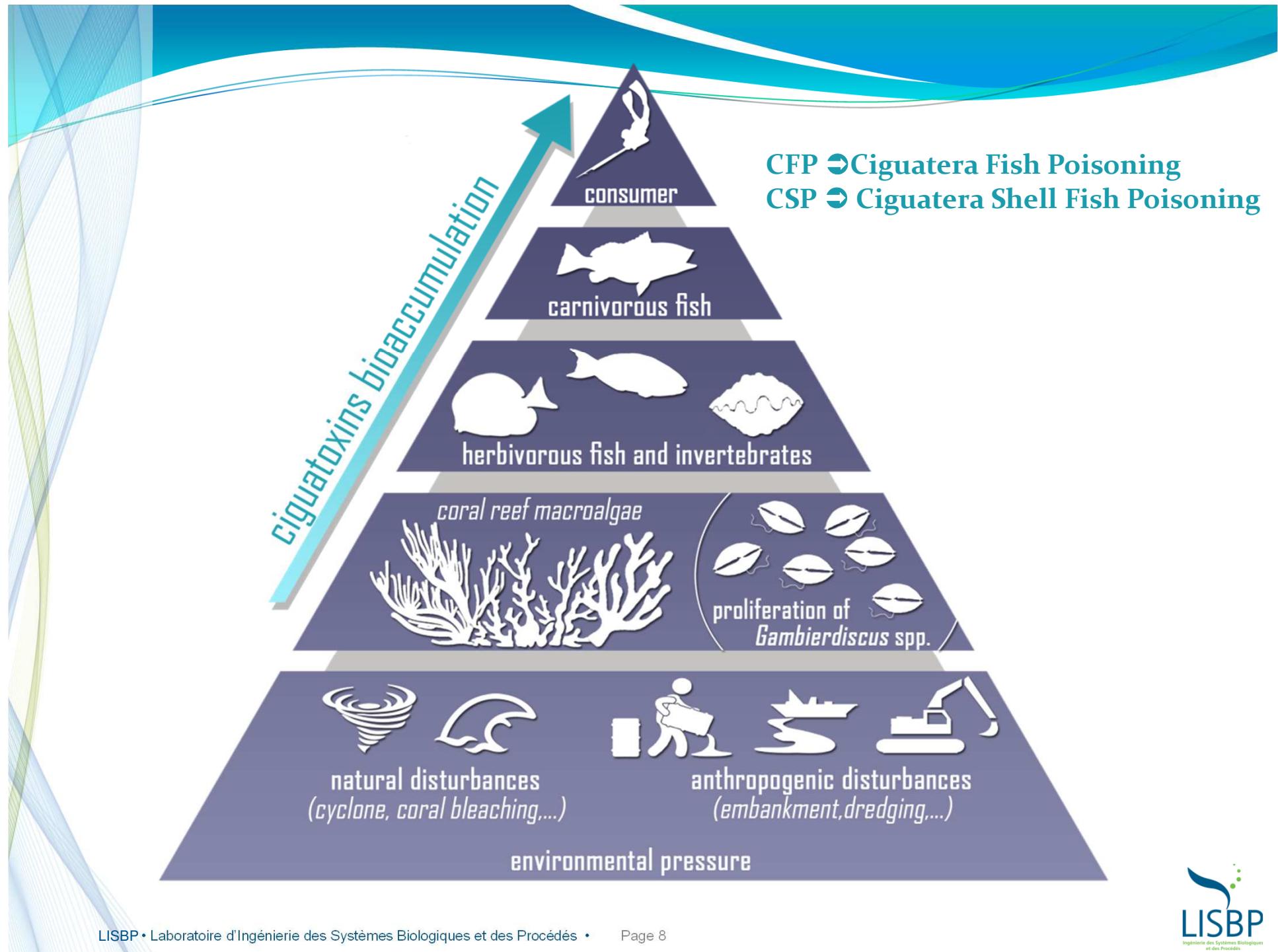


C-CTX-1 (C-CTX-2)

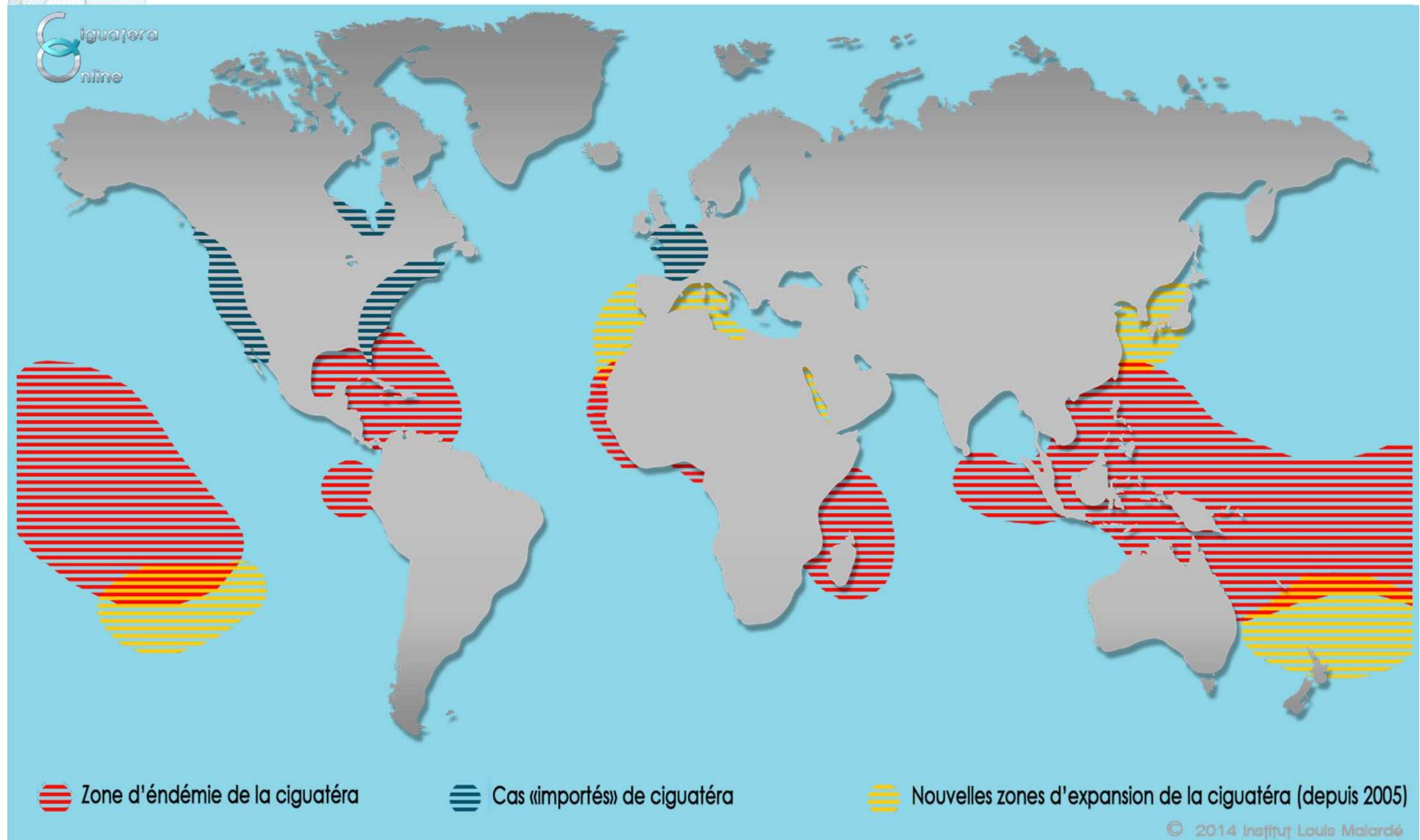


Caribbean
Ciguatoxines

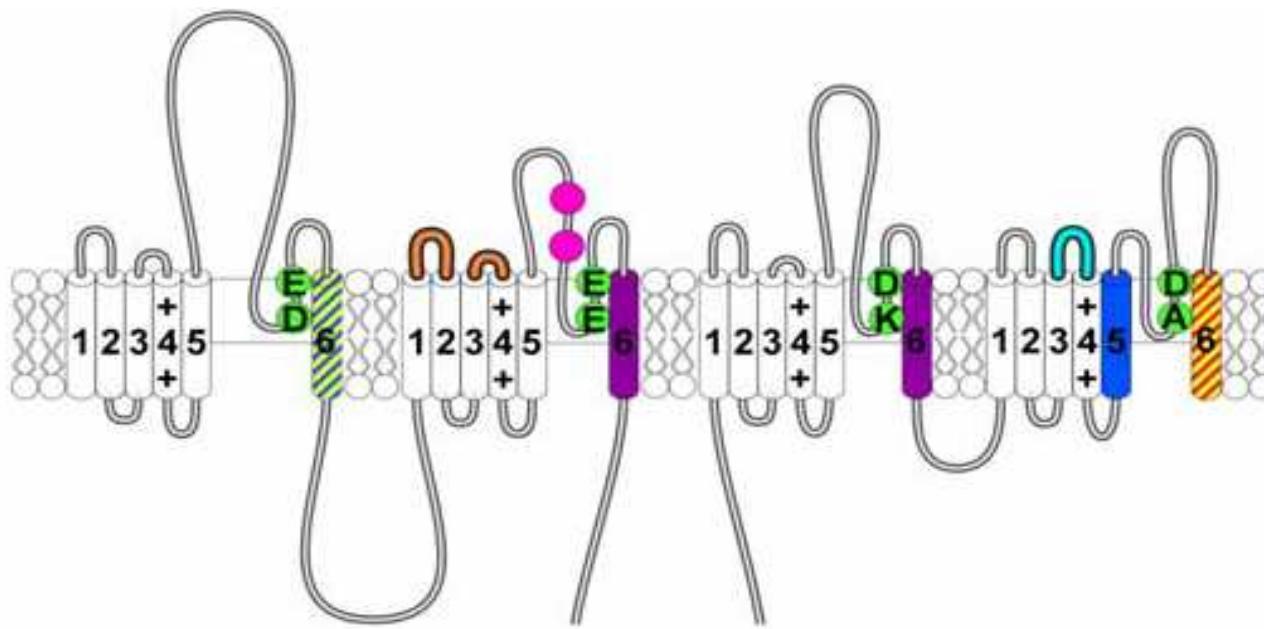
(Nicholson and Lewis, *Marin Drugs*, 2006).



World Repartition of Ciguatera



CTXs Targets : Voltage Gated Sodium Channels



Site 1 Tetrodotoxin
Saxitoxin

Site 1 μ-Conotoxins

Site 2 Batrachotoxin
Veratridine

Site 3 Scorpion α-toxins,
Sea anemone toxins,
Spider δ-toxins

Site 4 Scorpion β-toxins
Magi 5

Site 5 Ciguatoxin
Brevetoxin

Site 7 Pyrethroids

Drugs Local anaesthetics
Anticonvulsants

CTXs Targets : Voltage Gated Sodium Channels

- VGSC play key roles **in electric signal propagation** in excitable tissues (nerves, heart, muscles).
- Mechanism : local activation of VGSCs provokes a transient depolarization, responsible of the ascendant phase of the action potential.
- **CTXs stay fixed and prevent repolarization of VGSCs.**

CTXs Detection : problematic

- Current assays : heavy, difficult, long, expensive, and/or unethical (*Mouse bioassay, RBA, CBA, HPLC...*)

→ ***URGENT NEED FOR A SIMPLE DETECTION TOOL !!!***

- Can we design a biosensor for Ciguatoxins ?

- Yeast based bio sensors : interesting for several reasons

Developping yeast-based Biosensors

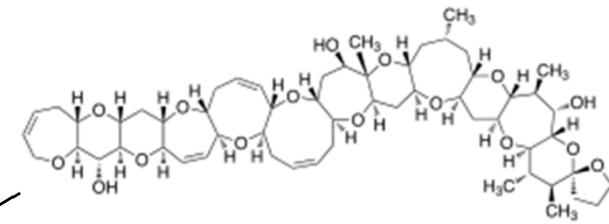
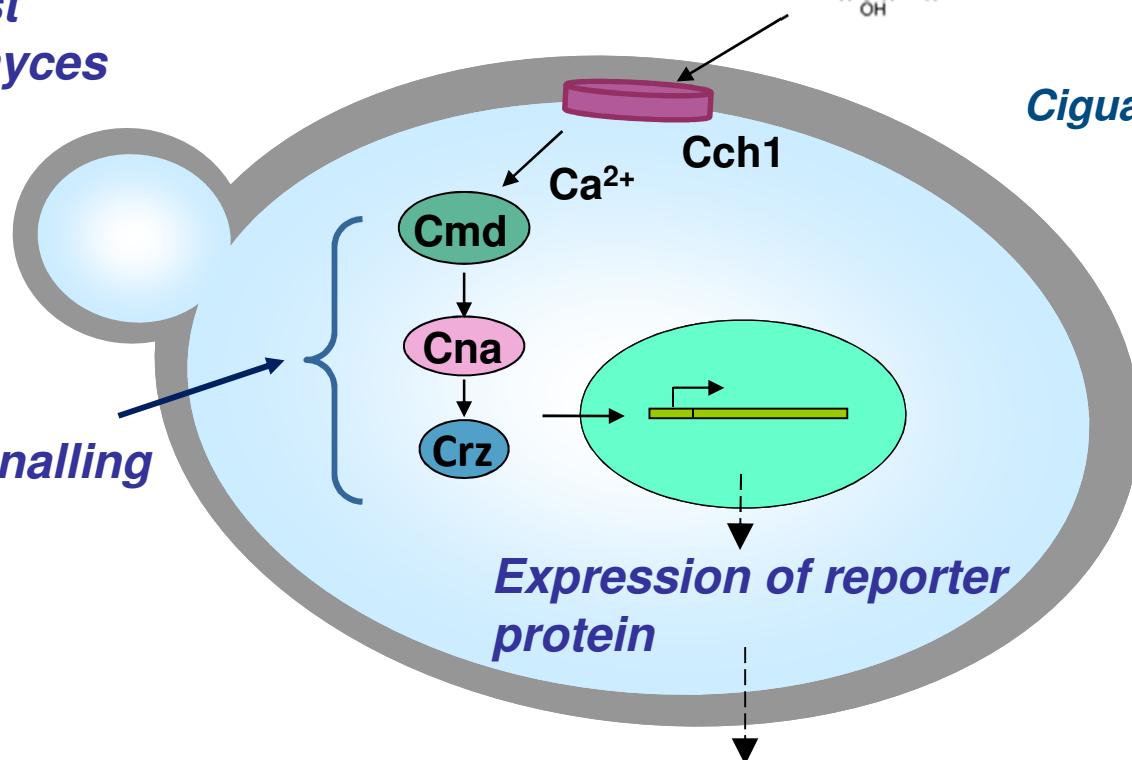
Scientific Questions :

- Cell wall permeability/reactivity towards toxins?
Investigation tools : cell wall mutants, tagged toxins.
- Membrane target (receptor)? Binding?
Investigation tools : Cloning,
SMFS with Atomic Force Microscopy.
- Cellular signalisation pathways?
Investigation tools : reporters, Fluorescent proteins,
western blotting, RT-PCR.

Biosensor strains design

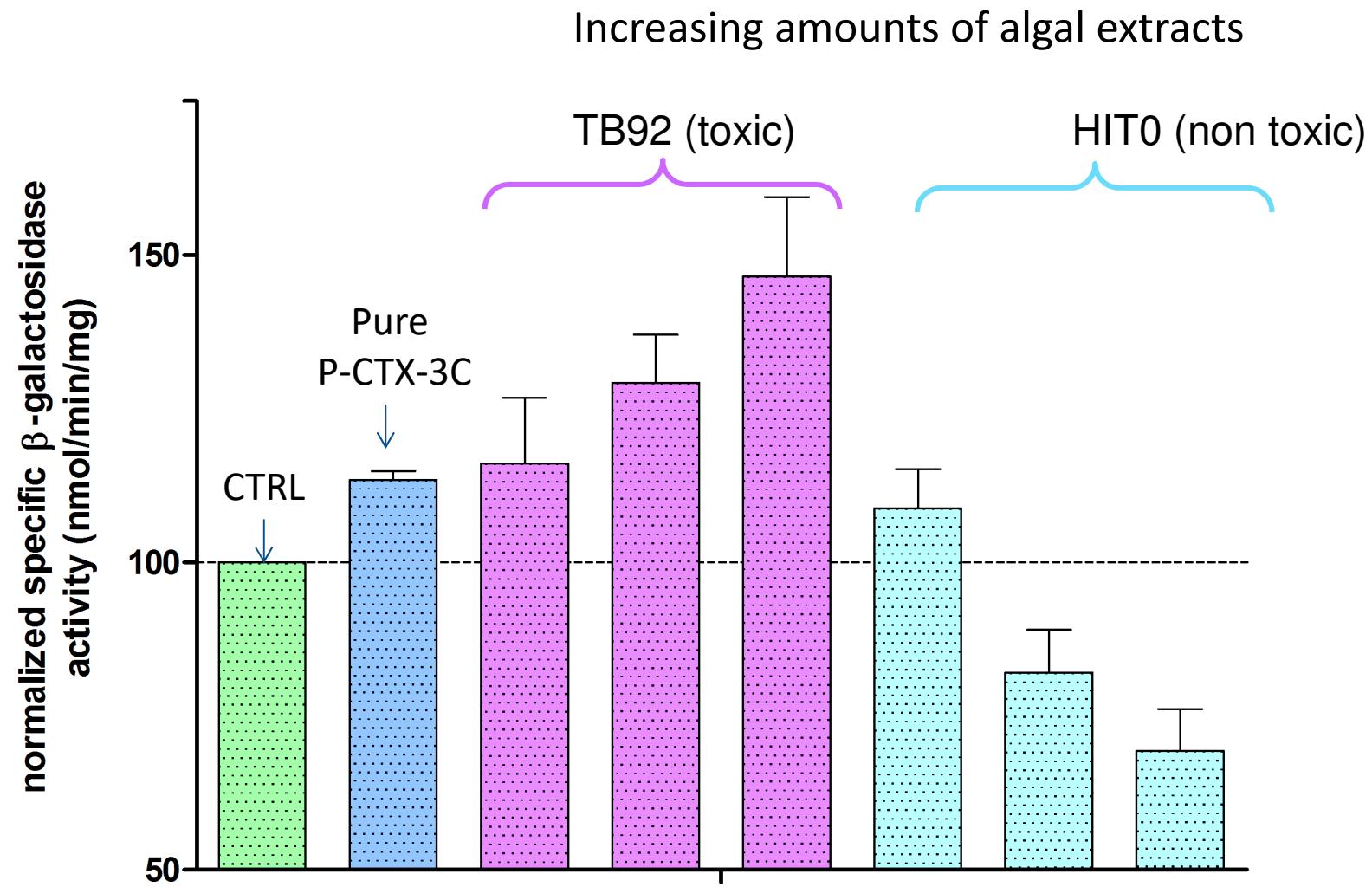
Model Yeast
Saccharomyces cerevisiae

Cellular signalling pathway



Ciguatoxins

Response to Algal extracts



Perspectives :

Understanding yeast cellular response to CTXs

- Cell wall transfert
- Competition CTXs - Rosmarinic acid and tetrodotoxin.
- Inhibitory Effect of HIT0 extracts ????
- Activators / repressors / blockers of VGSC and Cch1
- Hyper-active point mutants of Cch1 and Crz1, Chimera Cch1-VGSC

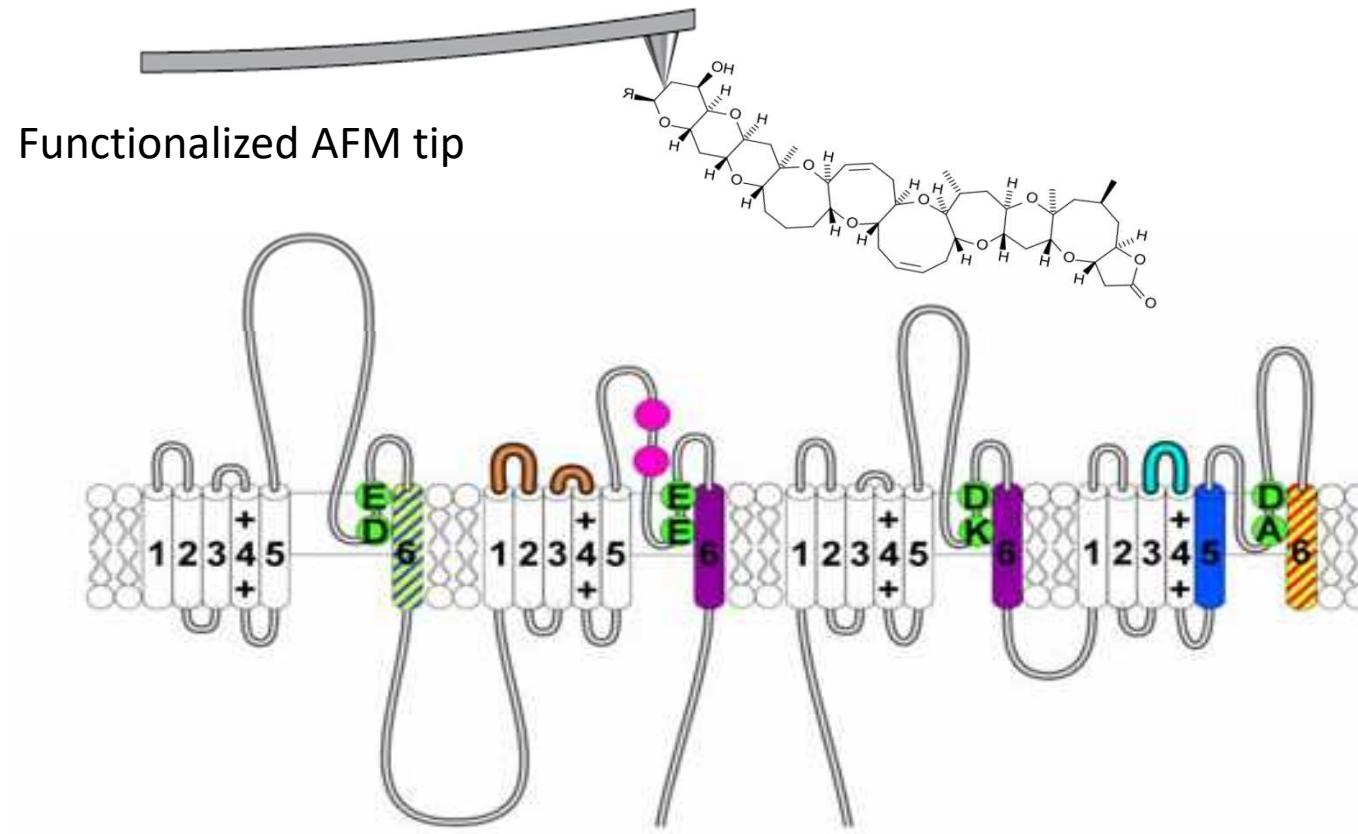
Response Optimisation

Develop a generic approach, apply to other toxins and drugs binding VGSCs.

Future applications : build a bio-sensor : huge interest for Pharmacology and Environmental domains

NeuroSens Project : LISBP-LAAS

Using Atomic Force Microscopy to study Neurotoxines Binding on VGSCs



NeuroSens :

A totally Innovating Approach, very powerfull and precise.

- Informations on nature and intensity of molecular interactions between **key receptors of our neuronal and cardiac cells** and ligands of pharma. and env. interest.
- *Ex vivo* testing of the inhibition of toxin fixation by **potential therapeutic molecules**
- Apply to other toxines (brevetoxines, ciguatoxines, rosmarinic acid, tetrodotoxin...)

Collaborations :

- Institut Louis Malardé, Papeete (French Polynesia) :
Dr Mireille Chinain, Dr Hélène Taiana Darius.
- IRD Polynésie française : Dr Dominique Laurent.
- LAAS CNRS Toulouse :
Dr Etienne Dague, Dr Emmanuelle Trévisiol,
Dr Christophe Furger, Camille Gironde.

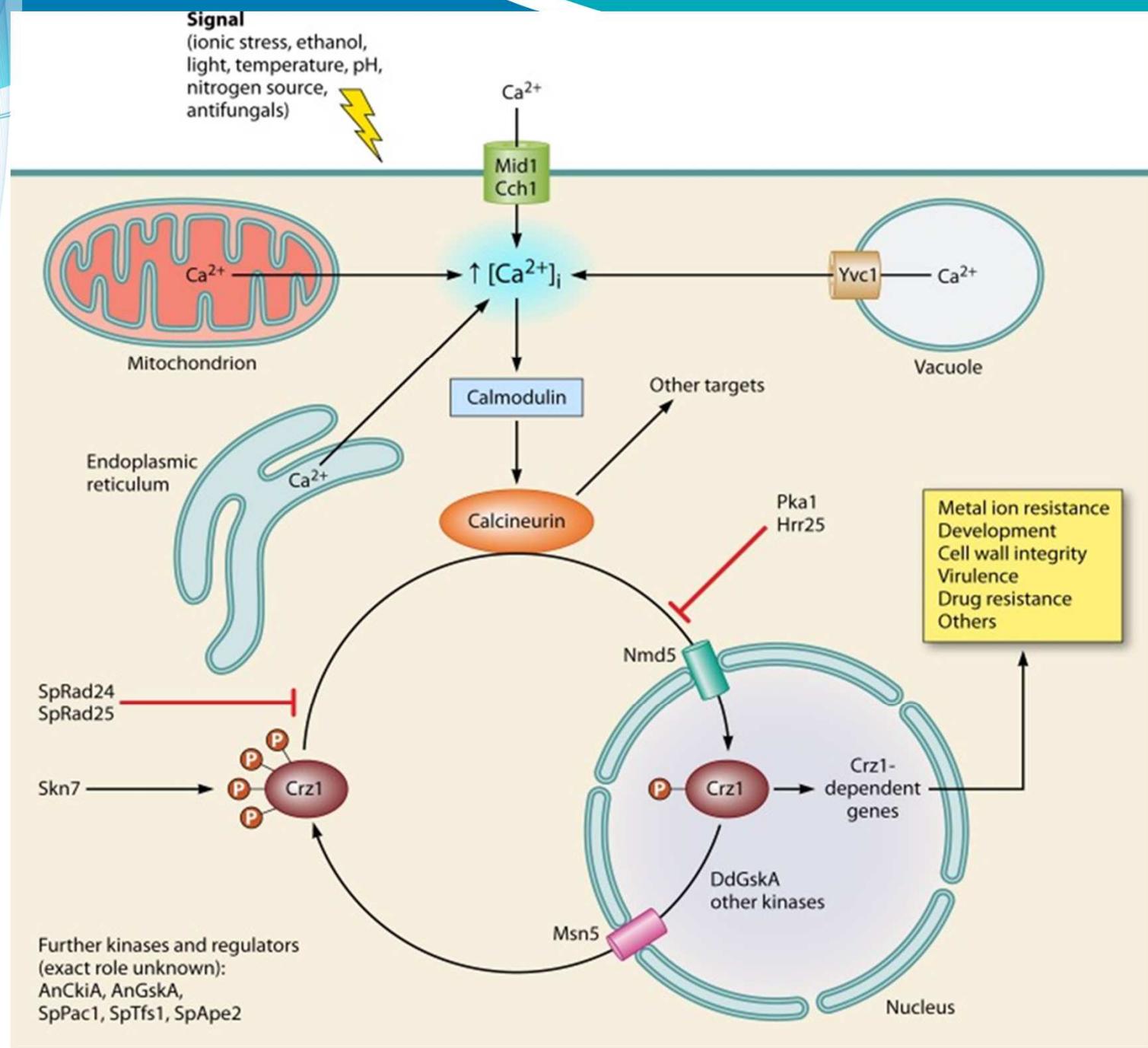


Thanks for your attention !

Interested in Microbial Adhesion ?

*Come to **BioPhysAdh** meeting, 10-11 septembre, Toulouse.*

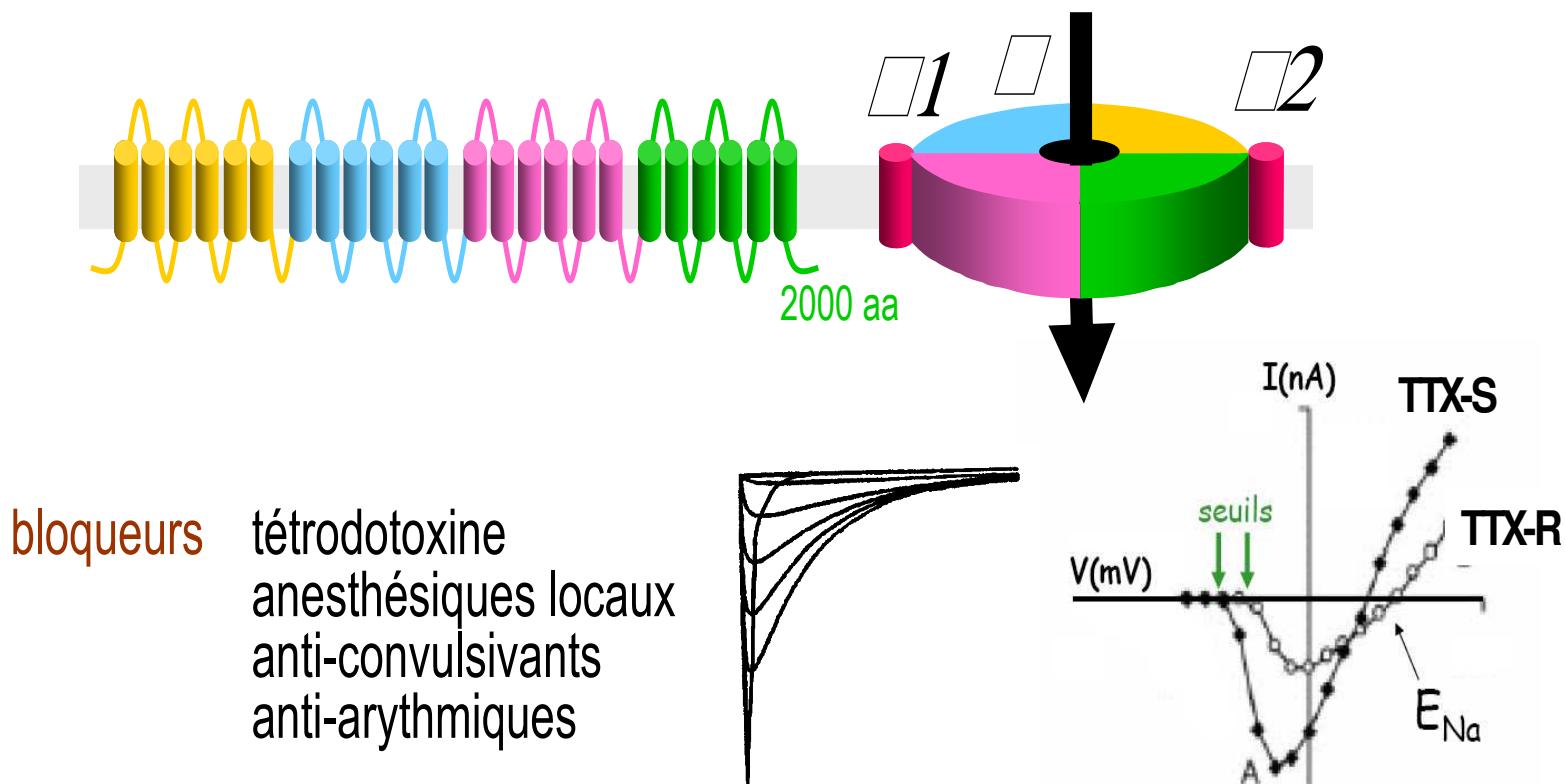
website : <https://biophysadh.sciencesconf.org>



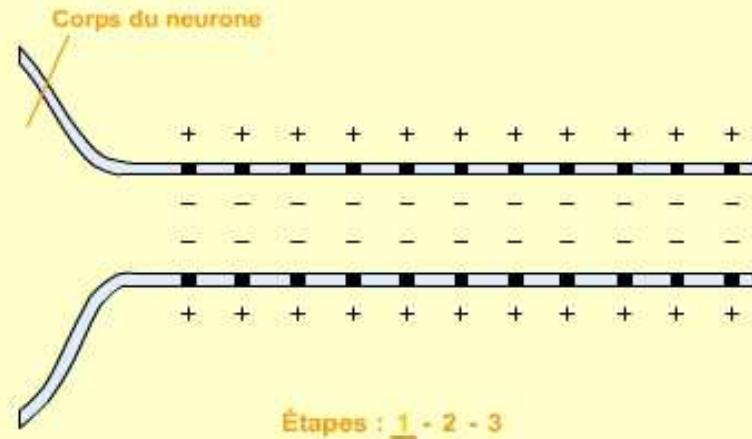
(Thewes, 2014)

CTXs Targets : Voltage Gated Sodium Channels

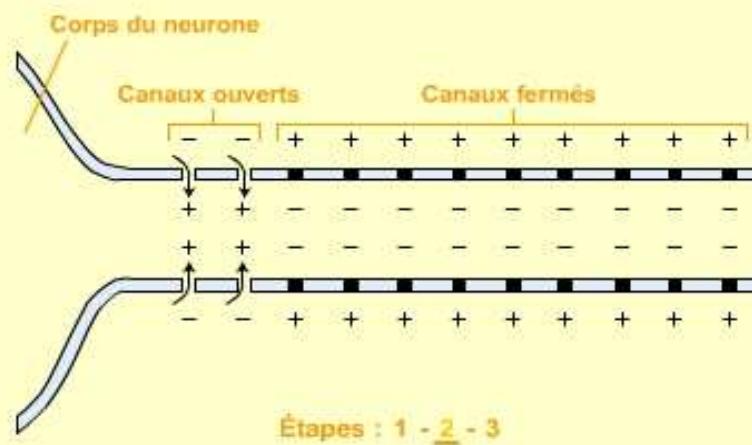
rôles dépolarisation de la membrane du neurone et propagation du PA



1. À l'état de repos, les canaux de la membrane du neurone créent une répartition inégale des charges : davantage de charges négatives à l'intérieur et plus de charges positives à l'extérieur.



2. L'influx nerveux, en ouvrant et fermant certains canaux, va inverser le potentiel électrique de part et d'autre de la membrane : durant un bref instant, l'intérieur devient plus positif que l'extérieur.



3. Le potentiel de repos est rapidement rétabli par le travail d'autres canaux. Mais déjà, dans la région voisine, le phénomène se répète, propageant ainsi l'influx nerveux le long de l'axone du neurone.

