

**« Discovery and mode of action of Ingrilimine, a novel cyclic imine toxin active on nicotinic acetylcholine receptors »**

Romulo Araoz<sup>\*1,2</sup> & Muriel Delepierre<sup>3</sup>

<sup>1</sup>CNRS, ERL9004. CEA-Saclay, bât. 152, 91191 Gif sur Yvette, France

<sup>2</sup>CEA, DRF, JOLIOT, DMTS, SIMoS. CEA-Saclay

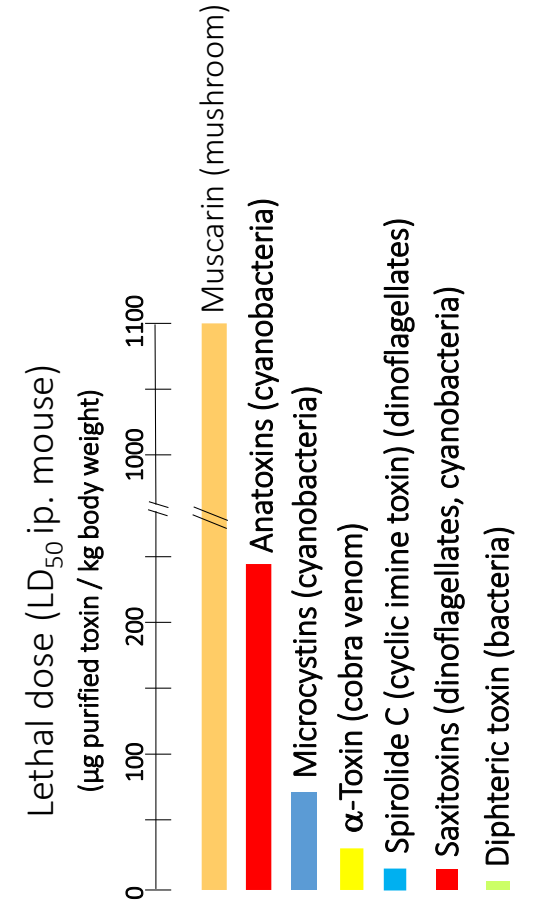
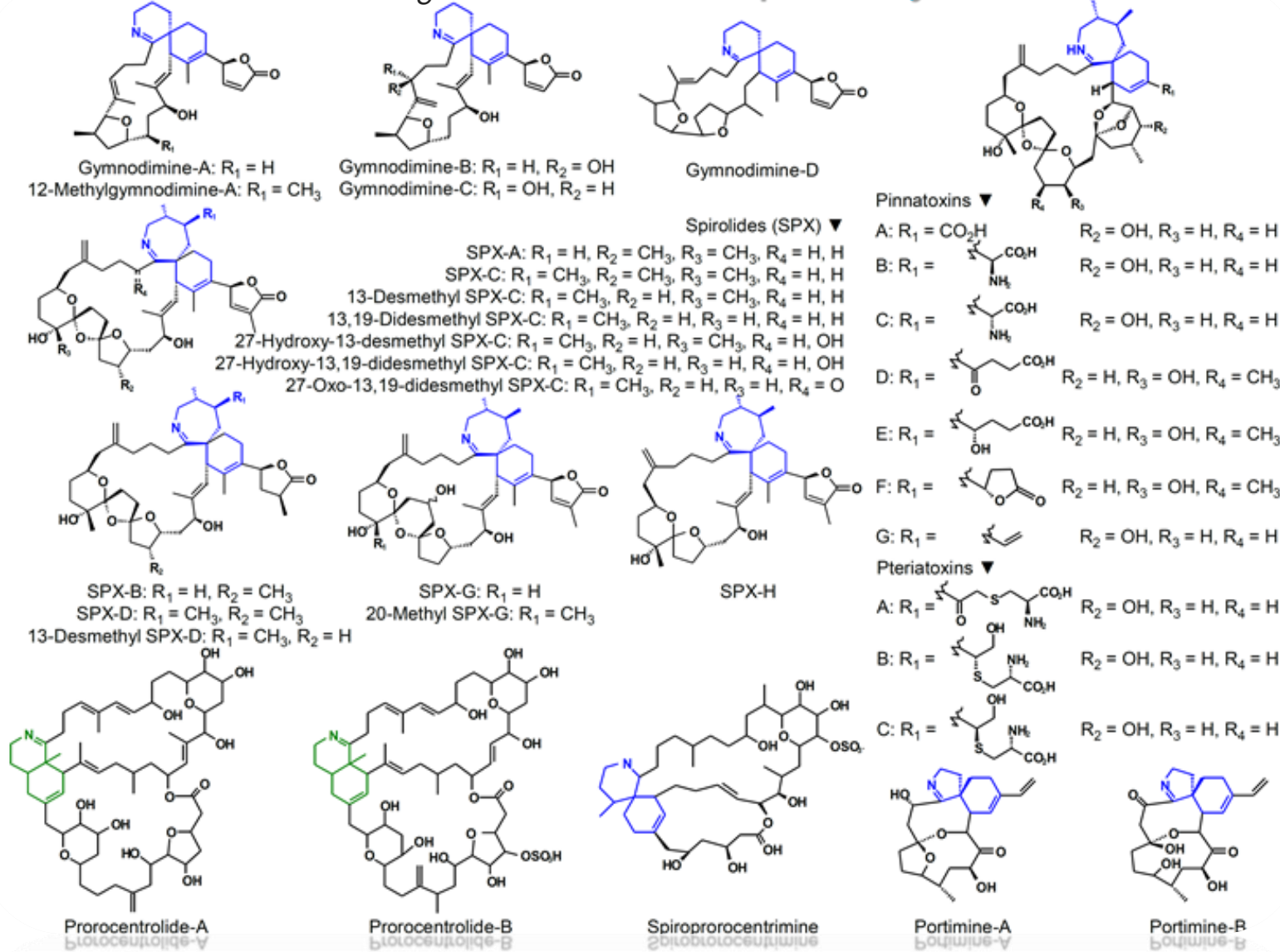
<sup>3</sup>Institut Pasteur, Dept Struct Biol & Chem, CNRS, UMR3528, Paris, France



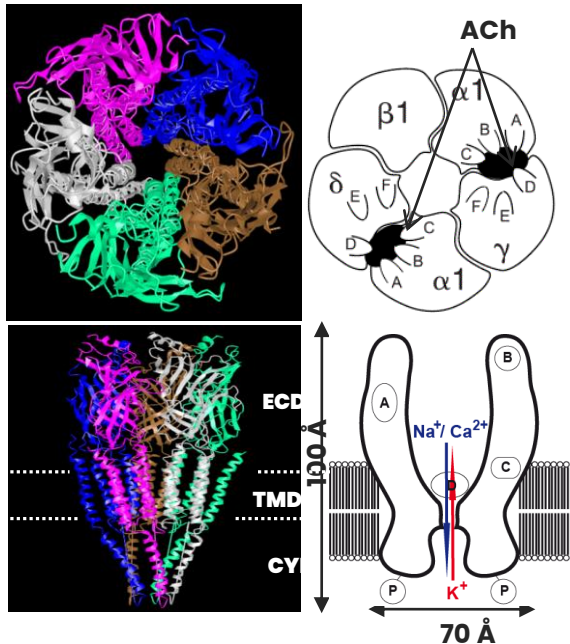
**anr** © ANR-21-CE34-0024  
ICH-NEURO-MET

# CiTXs are fast-acting toxins neurotoxins of dinoflagellate origin that kill mice by respiratory arrest.

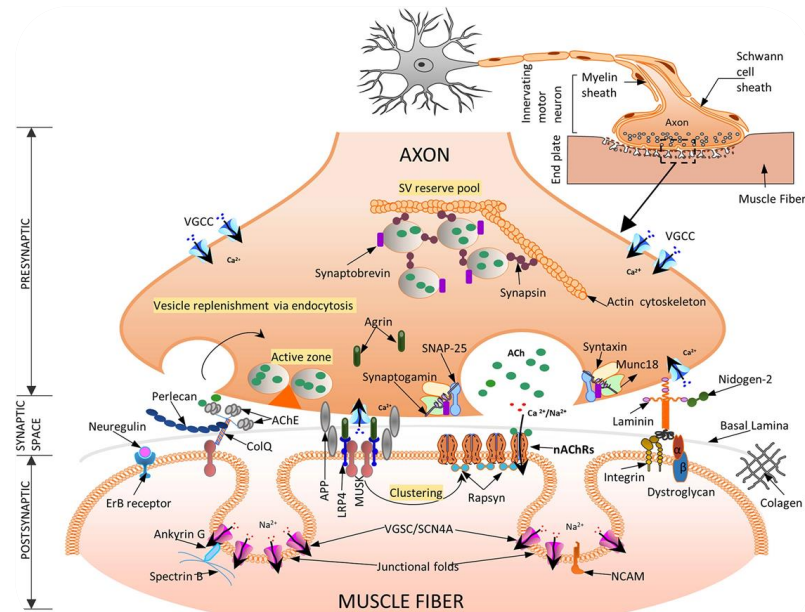
Aráoz R et al. 18th ICHA Proceedings: hal-024131151



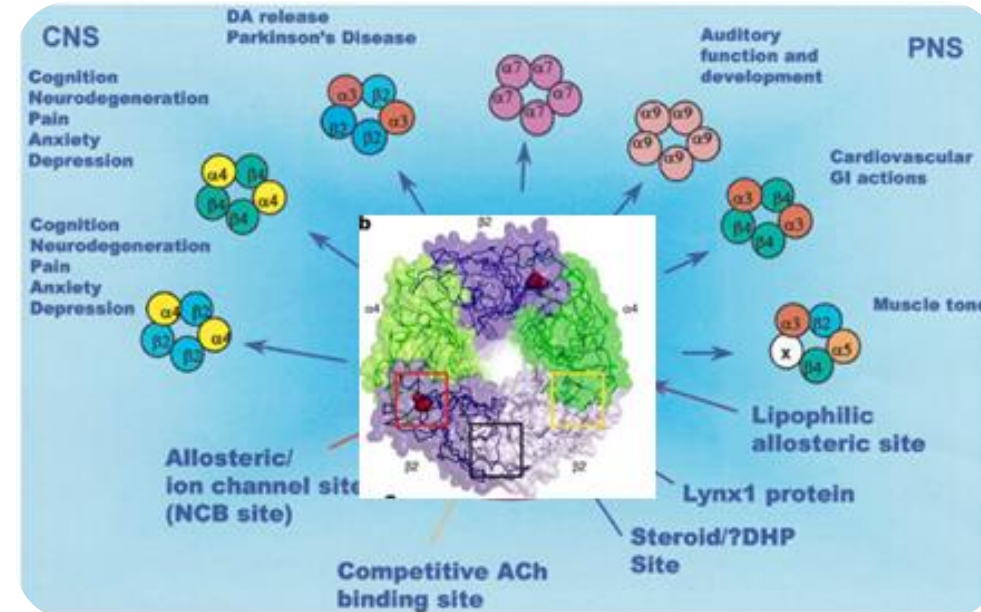
# Nicotinic acetylcholine receptors (nAChRs) are essential for muscle contraction at the PNS and modulate the release of neurotransmitters at the CNS



Corringier P-J et al. (2000). Annual Review of Pharmacology and Toxicology, 40, 431-458



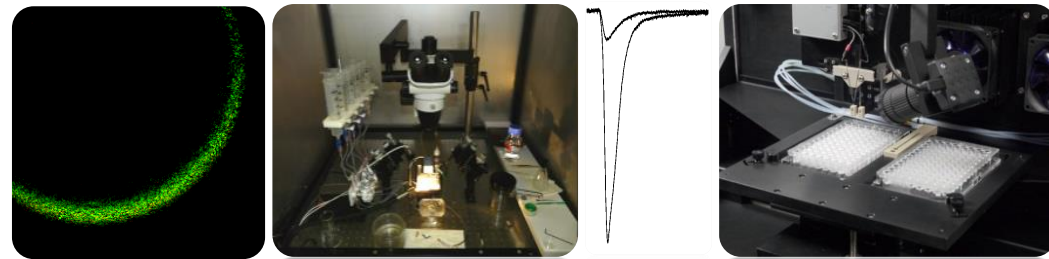
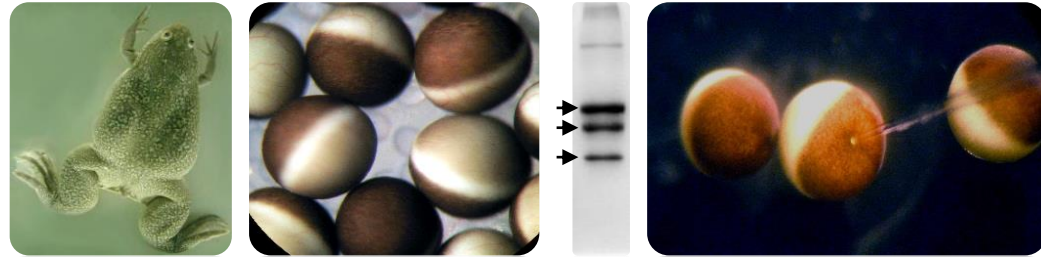
Mukund K. and Subramaniam S (2020). Wiley Interdisciplinary Reviews-Systems Biology and Medicine, 12(1), Article e1462



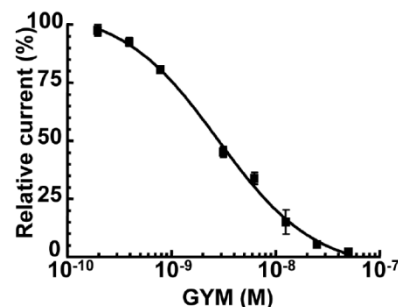
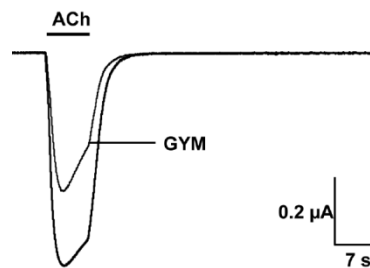
Lloyd, G. K. and M. Williams (2000). J Pharmacol Exp Ther 292(2): 461-467



# MOA: Cyclic Imine Toxins are potent antagonists of muscle and neuronal nAChRs



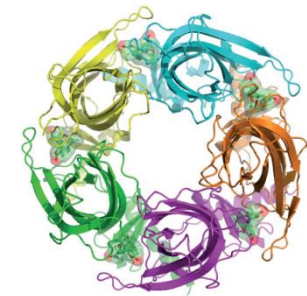
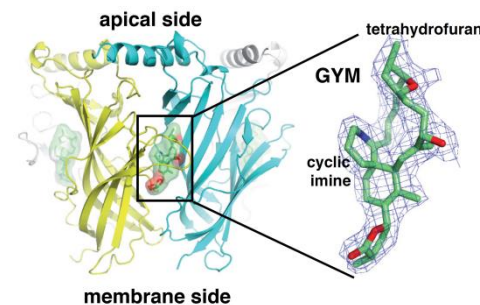
Araoz R et al. (2024) BNT242387EP00



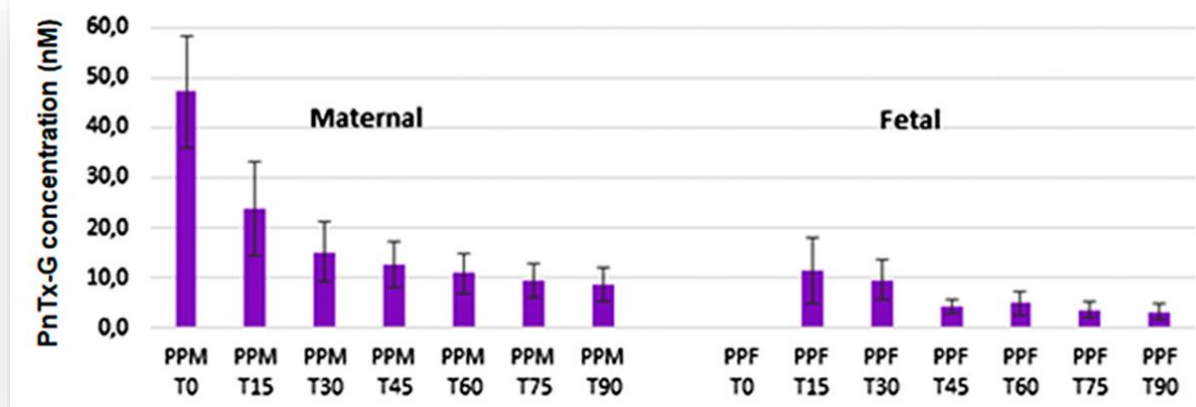
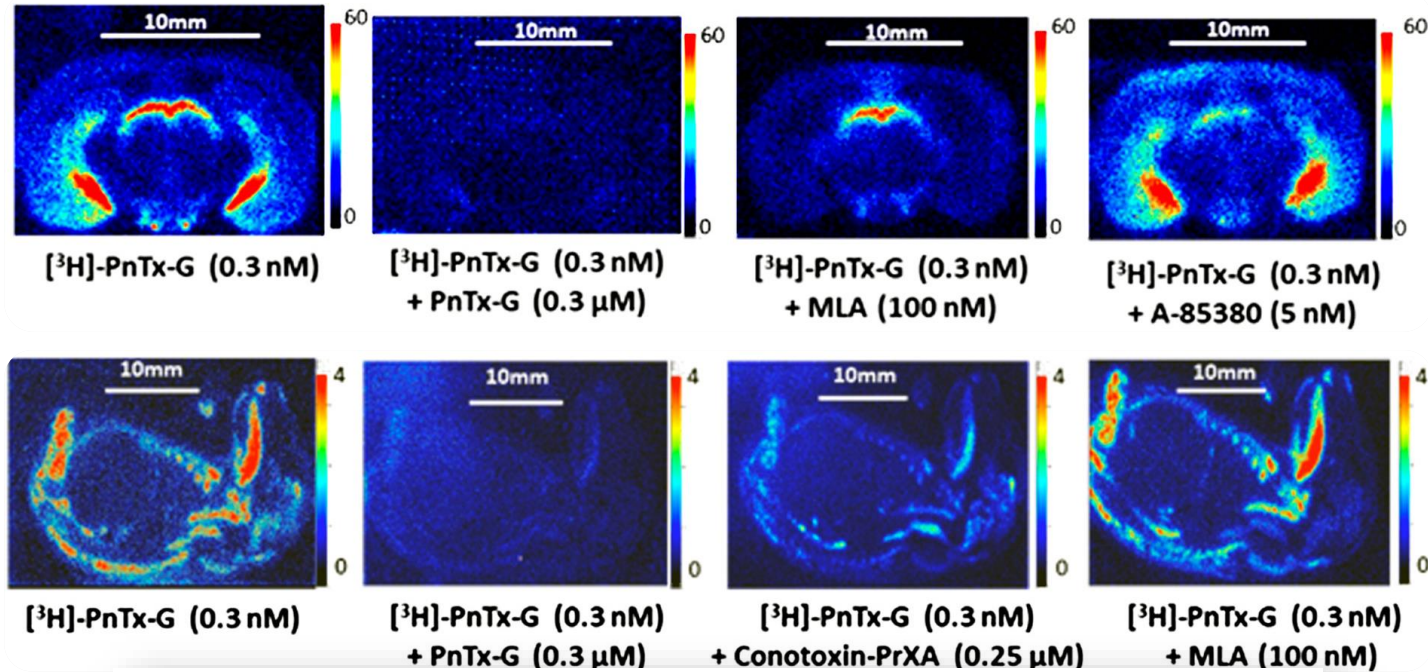
Bourne Y. et al. (2010). Proc Natl Acad Sci USA 107: 6076-6081

Cyclic imine toxin	$\alpha_1\beta_1\gamma\delta$ (Torpedo)	$\alpha_7$ (human)	$\alpha_4\beta_2$ (human)
20-meSPX-G	0.36 (0.29-0.45)	0.48 (0.15-1.4)	2.1 (1.4-3.1)
13,19-ddSPX-C	0.20 (0.16-0.26)	0.25 (0.24-0.27)	6.26 (4.7-8.3)
13-SPX-C	0.51 (0.4-0.6)	0.18 (0.16-0.21)	3.9 (2.9-5.1)
GYM-A	2.8 (1.9-4.1)	n.d.	0.9 (0.6-1.2)
PnTX-A	5.53 (4.5-6.8)	0.107 (0.086-0.132)	30.4 (19.4-47.5)
PnTX-G	3.82 (2.99-4.88)	5.06 (3.84-6.67)	4.90 (3.97-6.06)

Araoz R et al. (2024) BNT242387EP00



# Pinnatoxin-G can cross the Brain Blood and the Placental Barriers interacting with nAChRs with high specificity



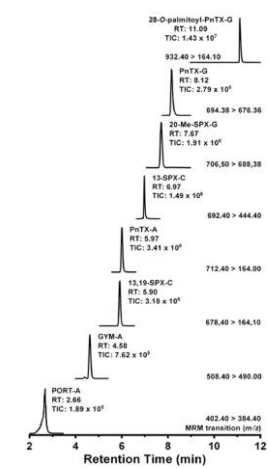
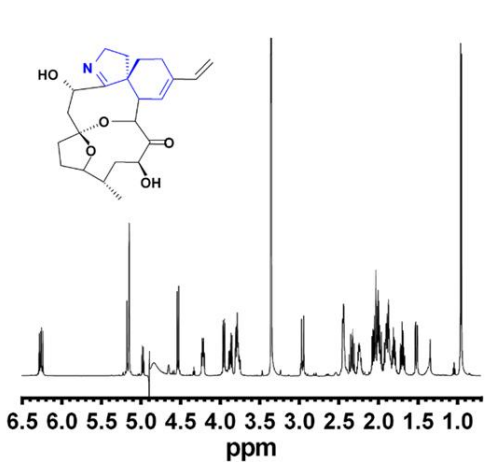
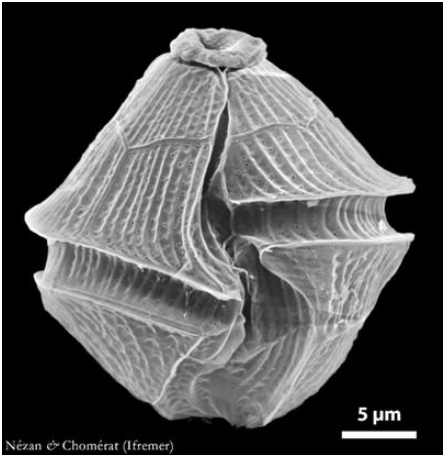
Servent D et al. (2021). *Science of the Total Environment*, 790, Article 148125

Romulo ARAOZ\_Symposium on Aquatic Toxins, Berlin 10.-11.06.2024

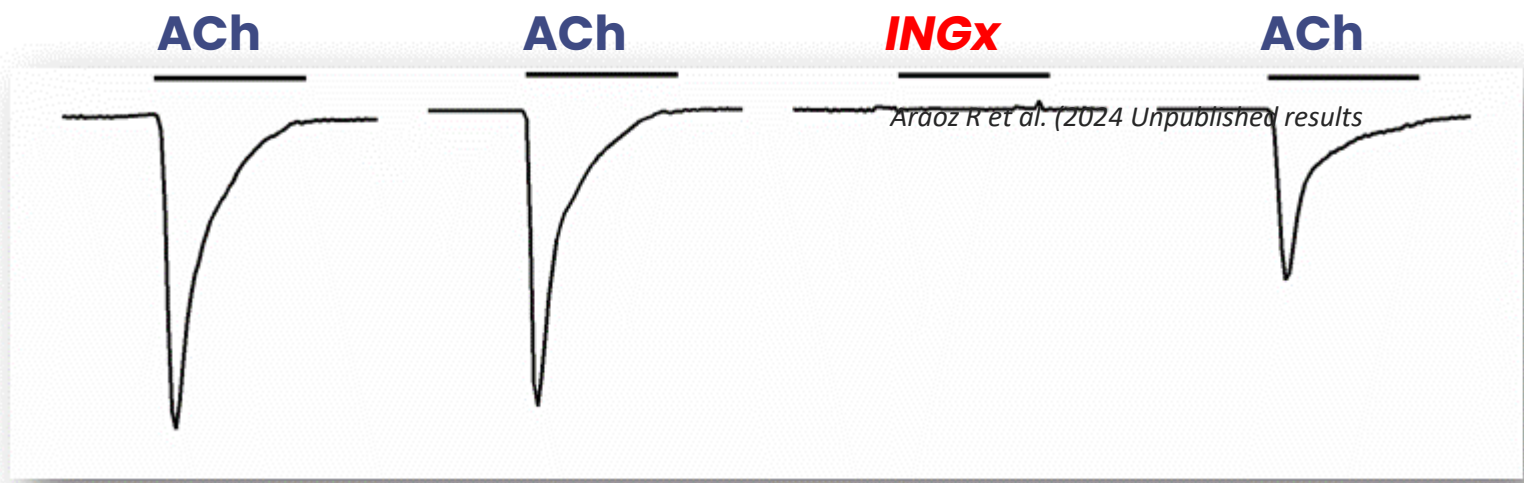




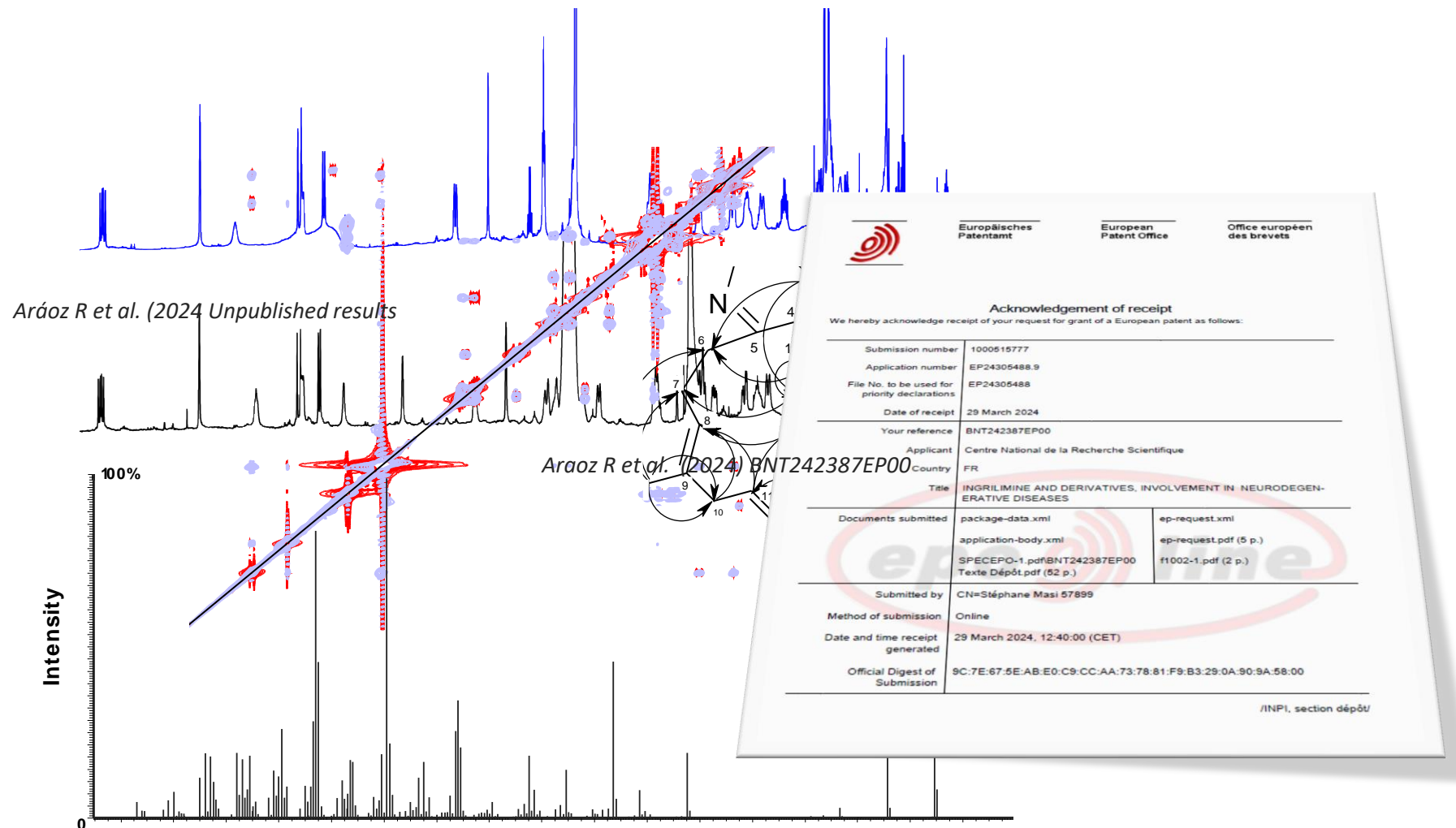
# Demonstration of portimine bioaccumulation led us to discover a novel Cyclic Imine Toxin (*Ingrilimine*) produced by *Vulcanodinium rugosum* IFR-VRU-01



Araoz R et al. (2020) Harmful Algae, 98, Article 101887



# Ingrilimine is a novel Cyclic Imine Toxin

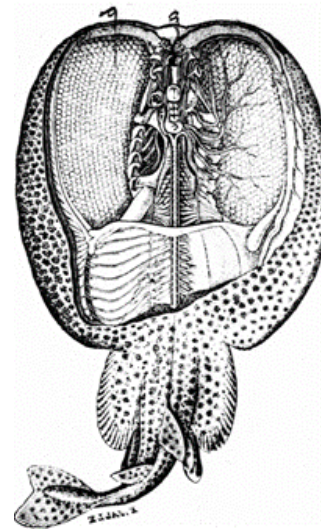
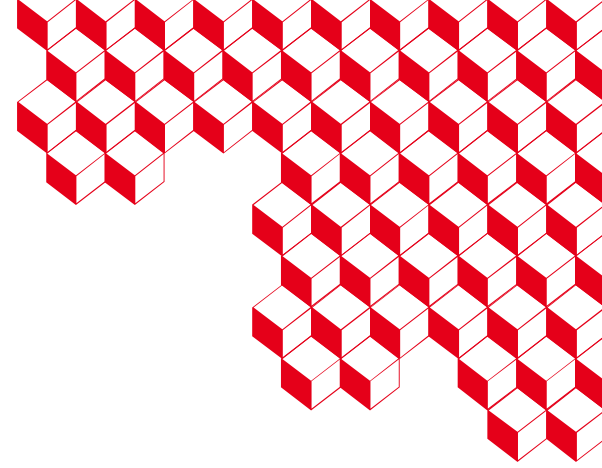




« The novel compound belongs to the cyclic imine family of neurotoxins showing cytotoxic and apoptotic properties and a strong affinity for the human neuronal  $\alpha 7$  nicotinic acetylcholine receptor »

*Araoz R et al. (2024) BNT242387EP00*





DANKE  
für  
ihre  
Aufmerksamkeit

**anr** © ANR-21-CE34-0024  
ICH-NEURO-MET



EMBRC  
EUROPEAN  
MARINE  
BIOLOGICAL  
RESOURCE  
CENTRE



**ALERTOXNET**

RED ATLÁNTICA DE SISTEMAS INNOVADORES DE ALERTA DE  
TOXICIDAD EN PRODUCTOS MARINOS MÁS SEGUROS



**Phycotox**  
Groupement de Recherche

Romulo ARAOZ\_Symposium on Aquatic Toxins, Berlin 10.-11.06.2024

Aquatic Toxins  
Symposium

