Natural Products-based Bioprospecting Program at INDICASAT: Tackling the Panamanian Biodiversity Hotspot for Drug Discovery

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Global Health, Biodiversity, and Therapeutics Seminar

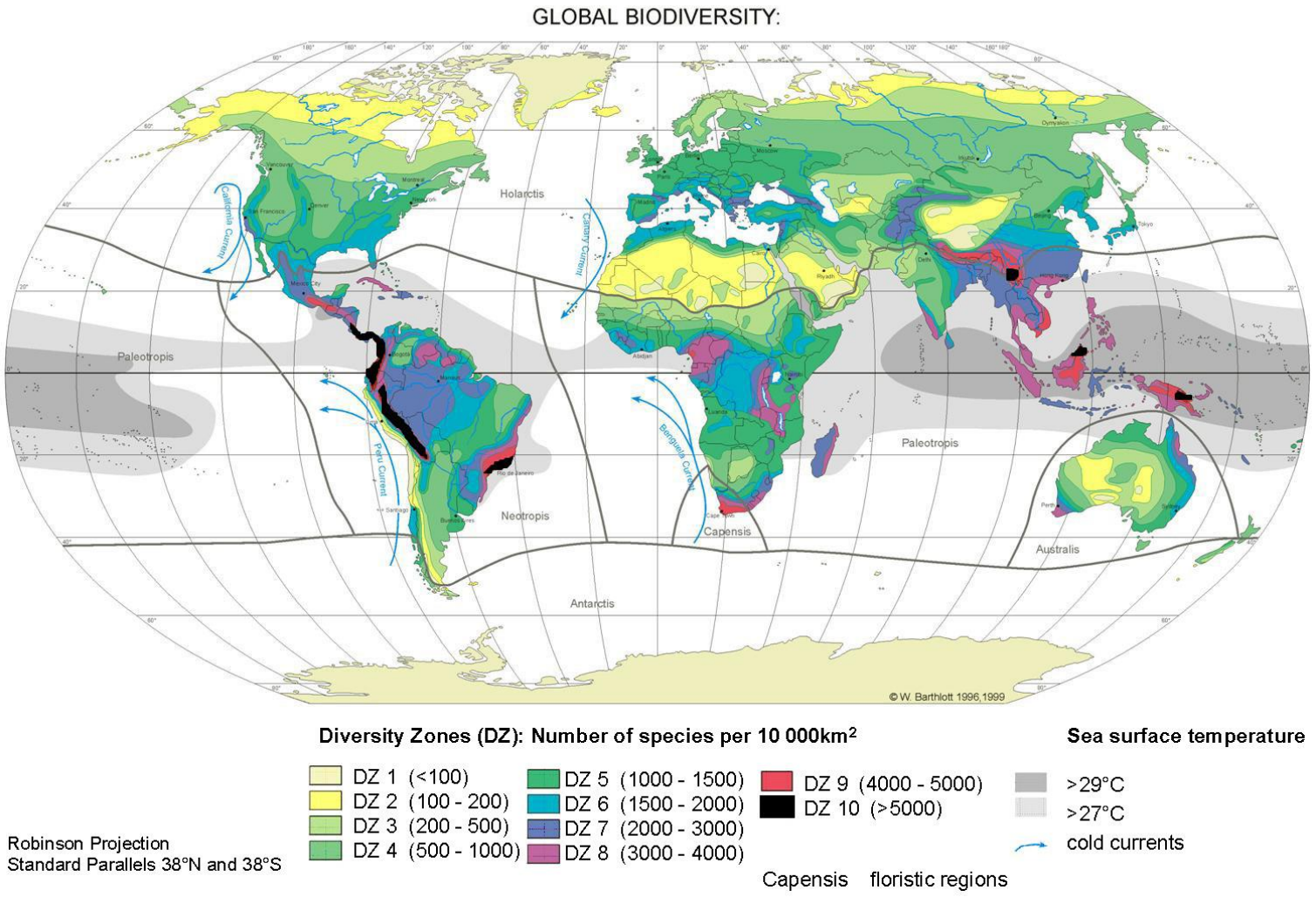
June 9. 2023

DAVID ROCKEFELLER CENTER
FOR LATIN AMERICAN STUDIES
HARVARD UNIVERSITY

Talk Overview

1. Panama as zone of high biological diversity
2. Symbiosis and systems under study at INDICASAT
3. Frogs
4. Coral associated bacteria
5. Corals

Zone of high terrestrial biological diversity



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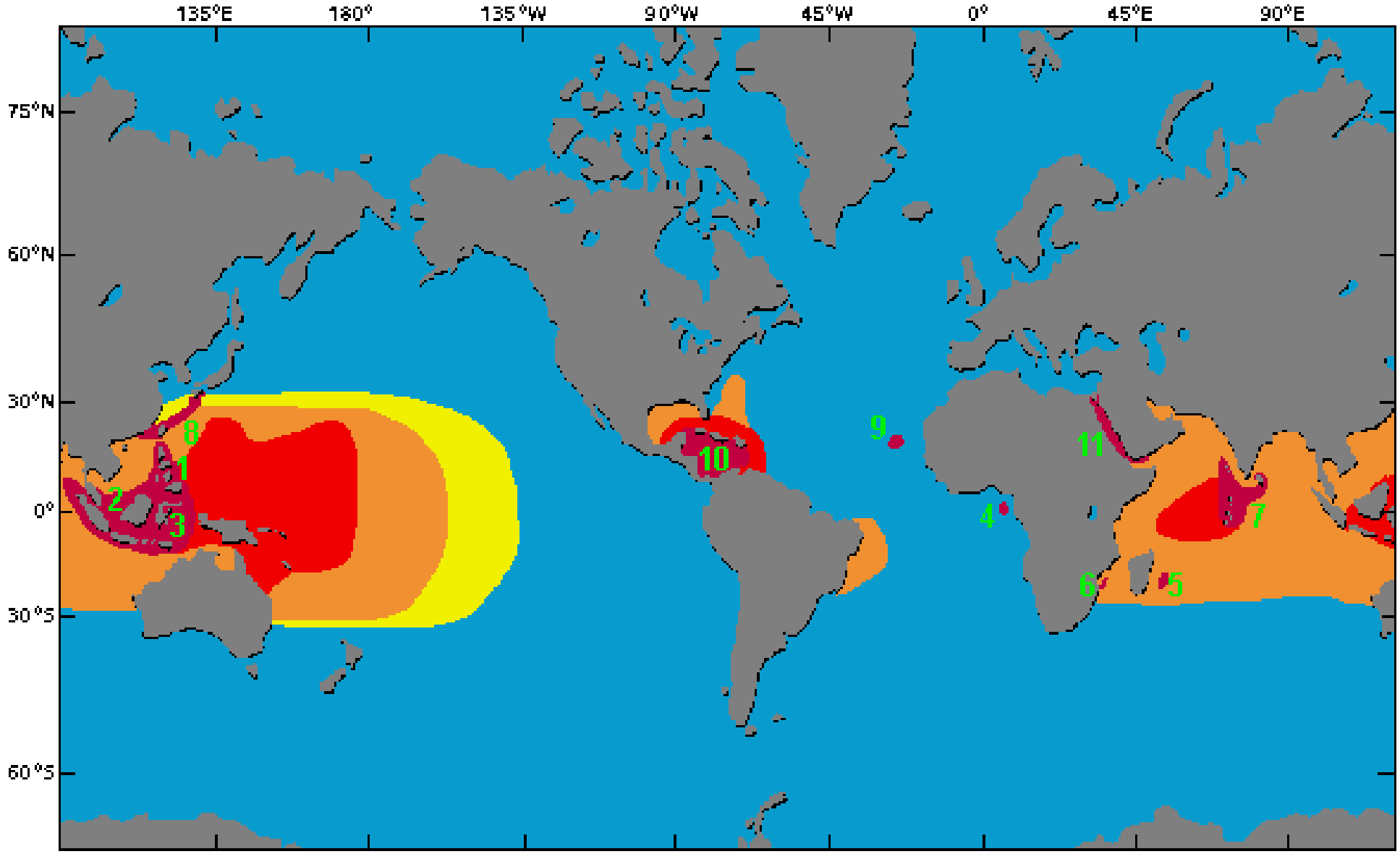
Zones with high marine biodiversity “hot spots”



Yellow = poor species richness/ **orange** = rich/ **red** = very rich/ **dark red** = regions with high number of endemic species(= hotspots)

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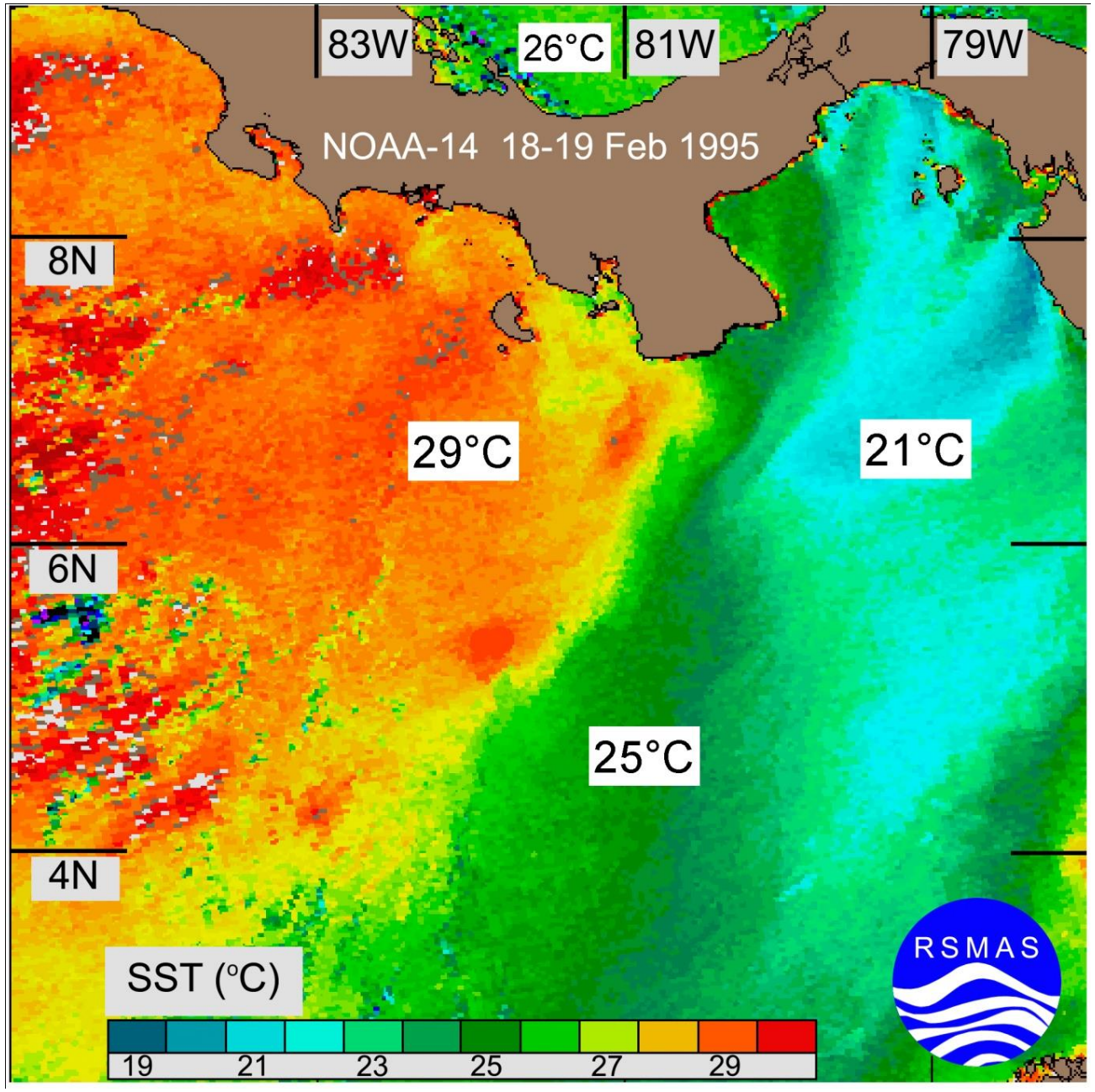

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Coiba National Park
World heritage site

- High level of biological diversity
- High level of endemism

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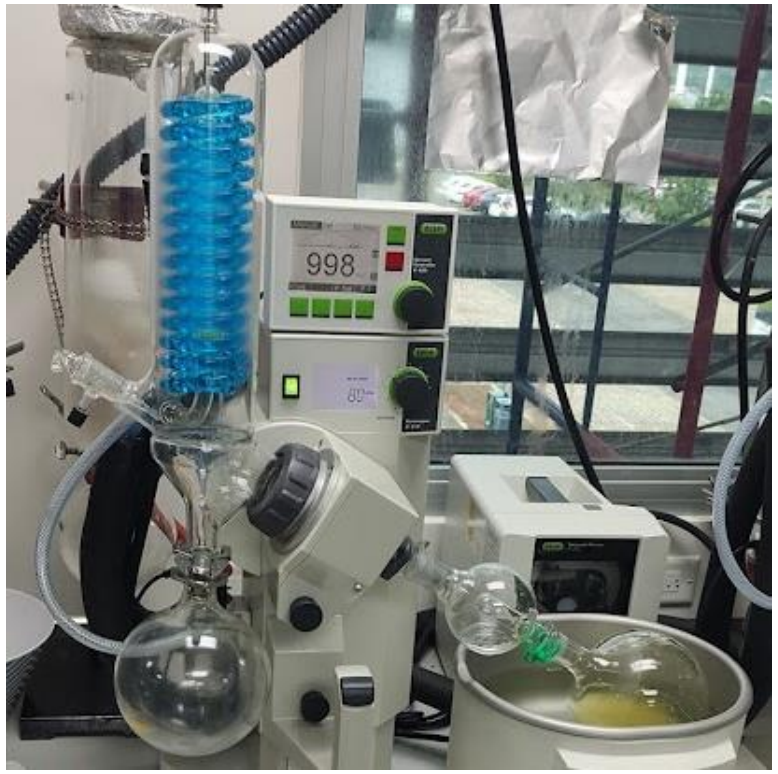
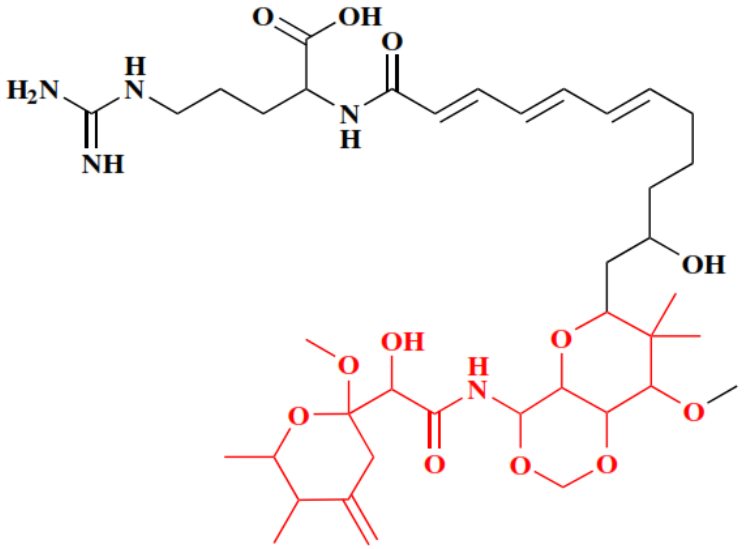
Scientific facilities and instrumentation

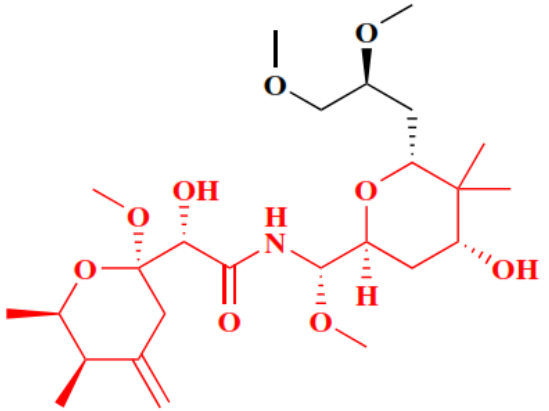


Same chemotype from organisms so distant?



Onnamide A

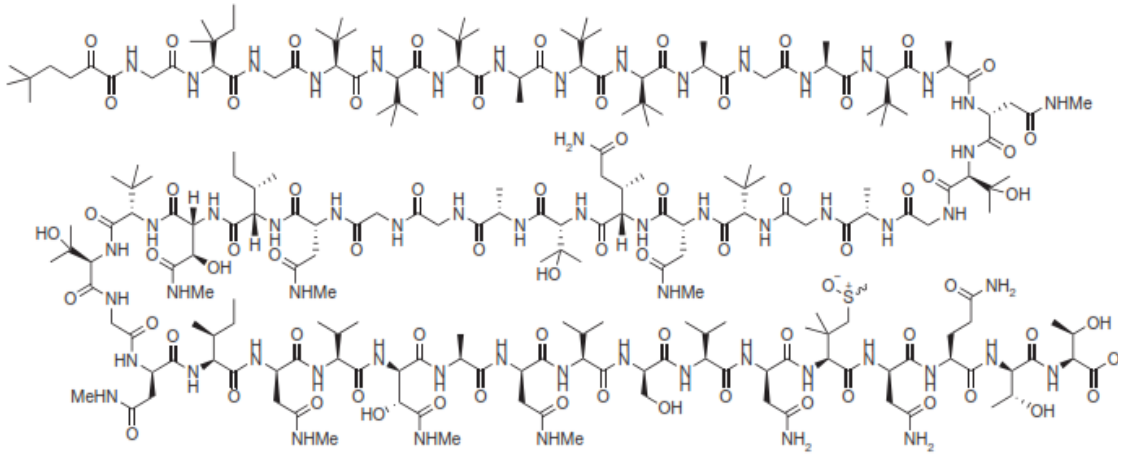
Theonella swinhoei



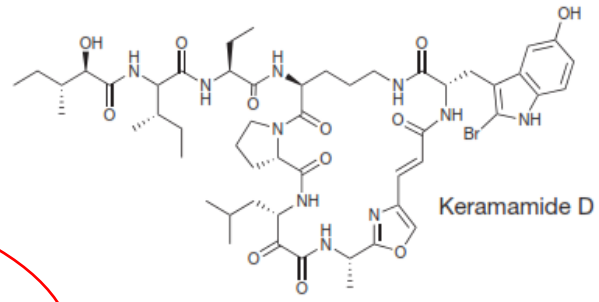
Pederin

Paederus sp.

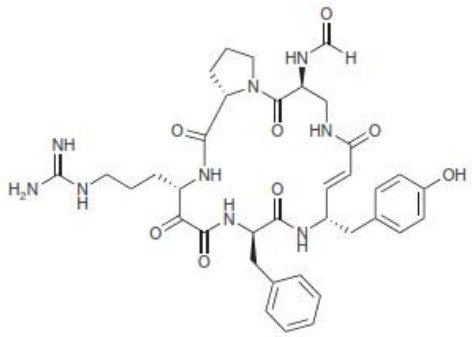
Entotheonella sp. is responsible for the natural product families isolated from the sponge *Theonella swinhoei*



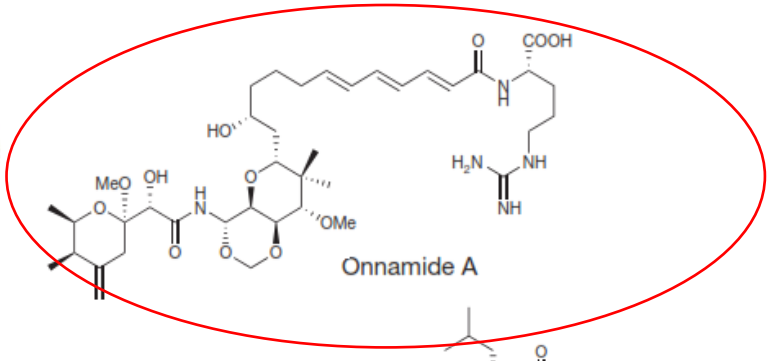
Polytheonamides A and B



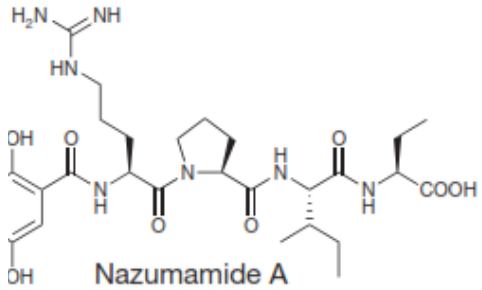
Keramamide D



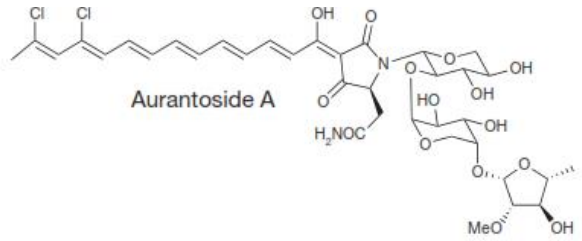
Cyclotheonamide A



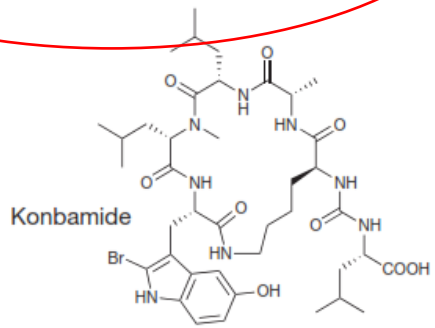
Onnamide A



Nazumamide A



Aurantoside A

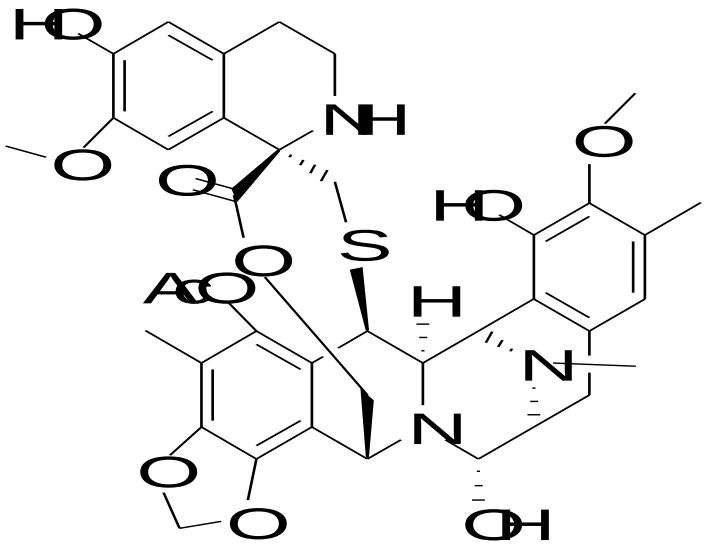


Konbamide

Wilson, M.C., et al., *Nature*, **2014**, doi:10.1038/nature12959

Yondelis®

Eitenascidia turbinata

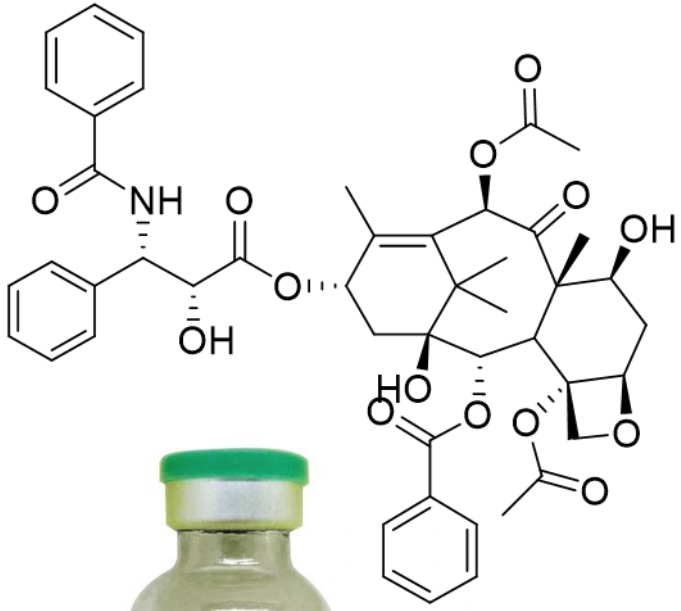


ET-743

Soft tissue sarcoma and ovarian cancer

“Plant-derived” Metabolites

Taxus brevifolia



Newman, D. J. *Trends in Cancer,* 2018, 4, 662-670

Marine Natural products and MNP derivatives that are FDA approved are most likely produced by microorganisms

Compound name	Collected source organisms	Predicted biosynthetic source	Disease area
Cytarabine (Ara-C)	Sponge	Bacterium	Cancer
Eribulin Mesylate	Sponge	Bacterium	Cancer
Trabactedin (Yondelis)	Tunicate	Bacterium	Cancer
Brentuximab vedotin	Mollusk	Cyanobacterium	Cancer
Virabidine (Ara-A)	Sponge	Bacterium	Antiviral
Ziconotide	Cone Snail	Mollusk	Pain
Omega-3-acid ethyl esters	Fish	Microalgae	Hypertrigliceridemia
Iota-Carrageenan	Red seaweed	Algae	Antiviral
Fludaravine (F-Ara-A)	Sponge	Bacterium	Cancer
Lurbinectedin	Tunicate	bacterium	Cancer
Plitidepsin (APLIDIN)	Sea Squirt	Bacterium	Cancer

Gerwick, W. H.; Moore, B.S. *Chemistry & Biology* **2012**, 19, 85-98. Neshatul, H., *et al*. *Marine Drugs* **2022**, 20, 528.

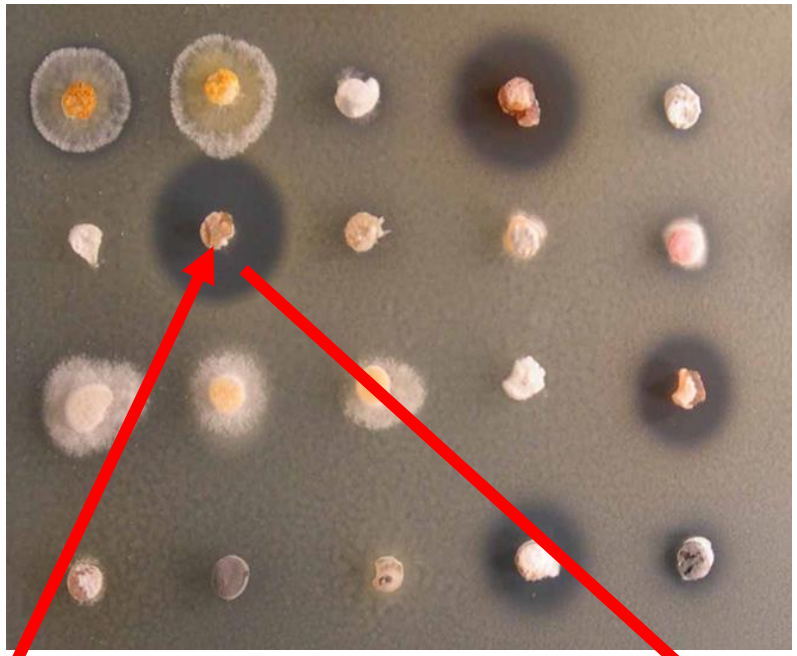
Systems under study for drug discovery at INDICASAT

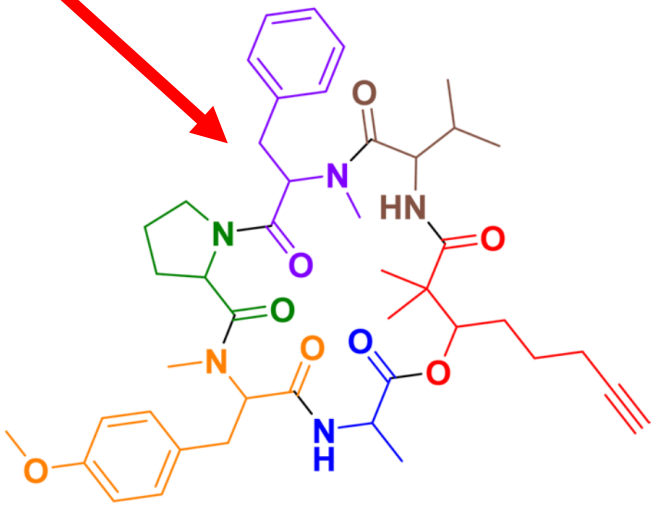
Octocorals

Fungus growing ants

Frogs

Endophytic fungi from coffee as source of bioactive metabolites

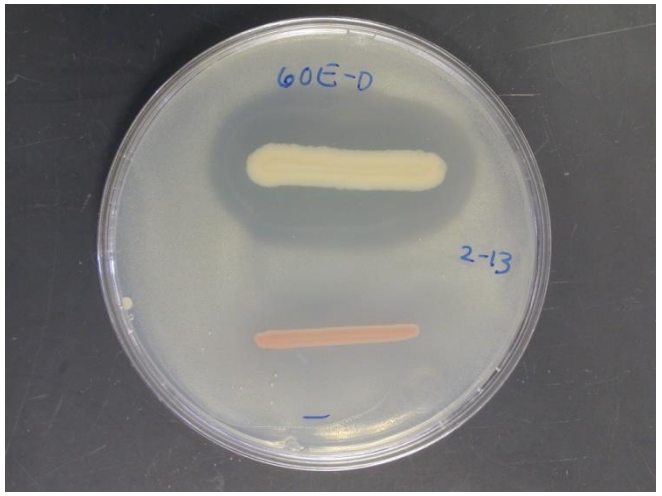




SCIENCE VOL 326 23 OCTOBER 2009

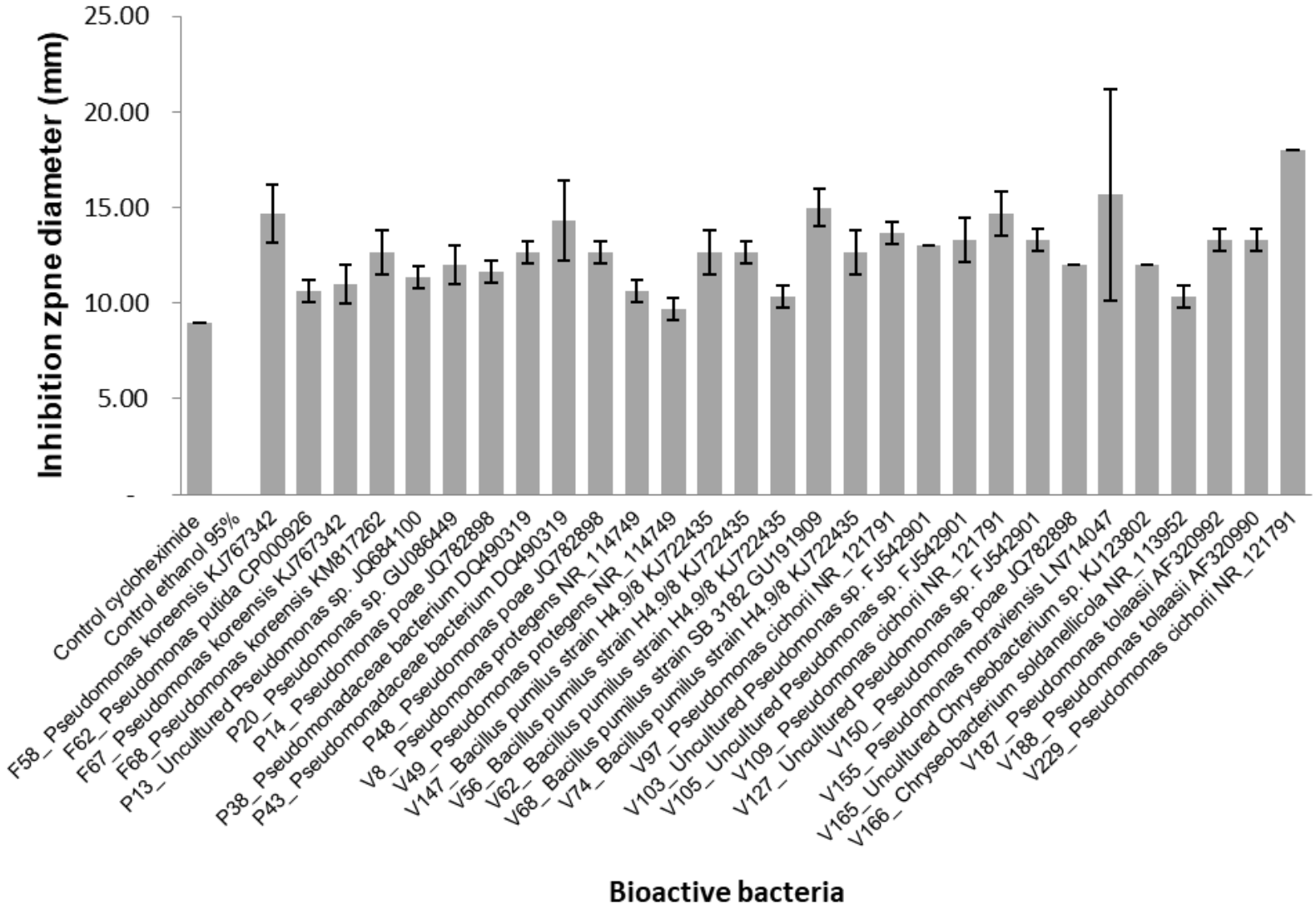
Pathogenesis of Chytridiomycosis, a Cause of Catastrophic Amphibian Declines

Antifungal activity of cutaneous bacteria from frogs



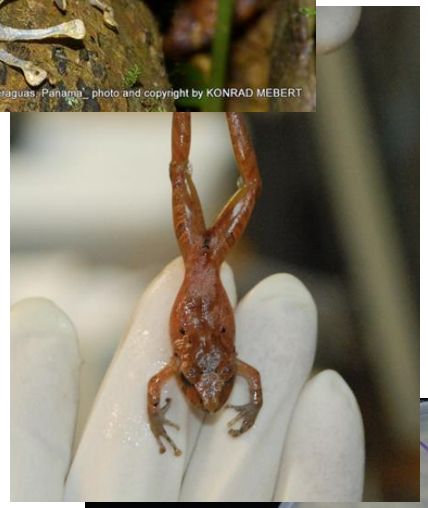
Inhibition of Batrachochytrium Dendrobatidis (Bd)

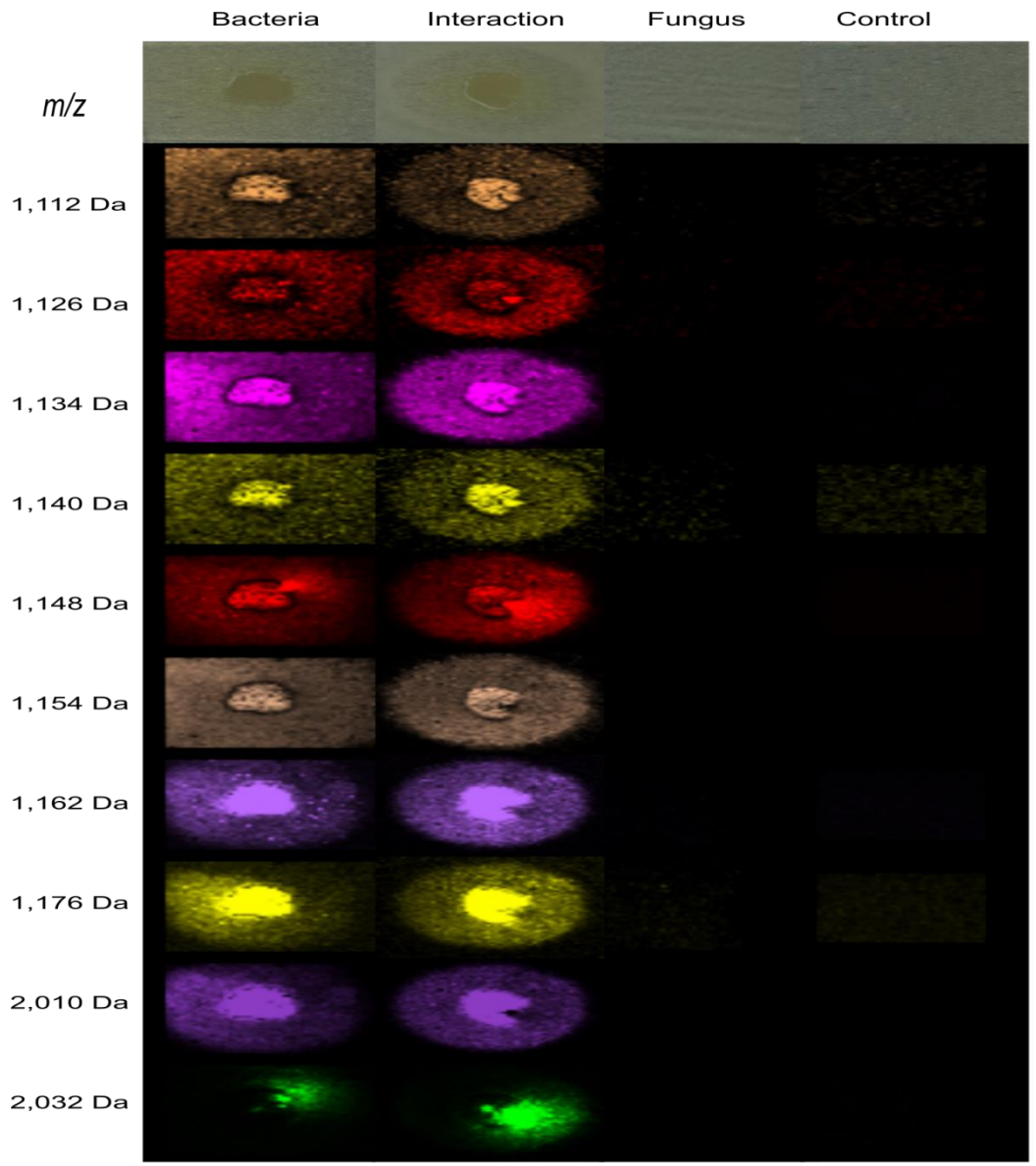
29 of 201 isolates (8 frog species) displayed biological activity against *Aspergillus. fumigatus*.



Martin, C. et. al *Scientific Reports*, **2019**, 9, 3019.

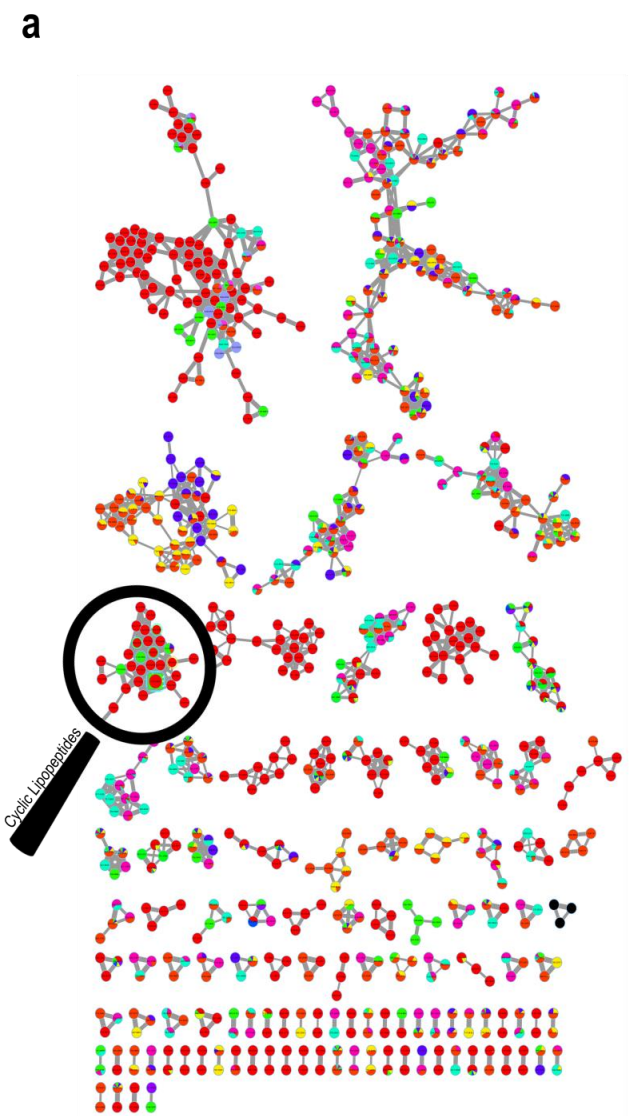
MALDI IMS of *Pseudomonas cichorii and Aspergillus fumigatus.*

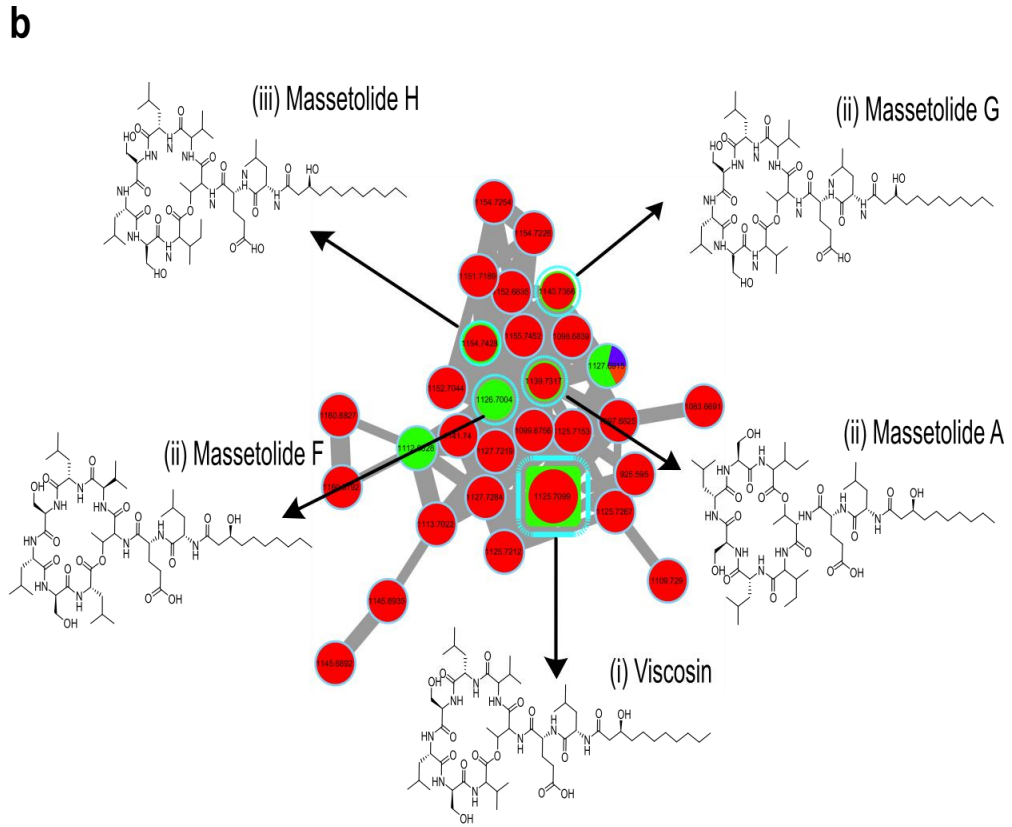




Martin, C. et. al *Scientific Reports*, **2019**, 9, 3019.

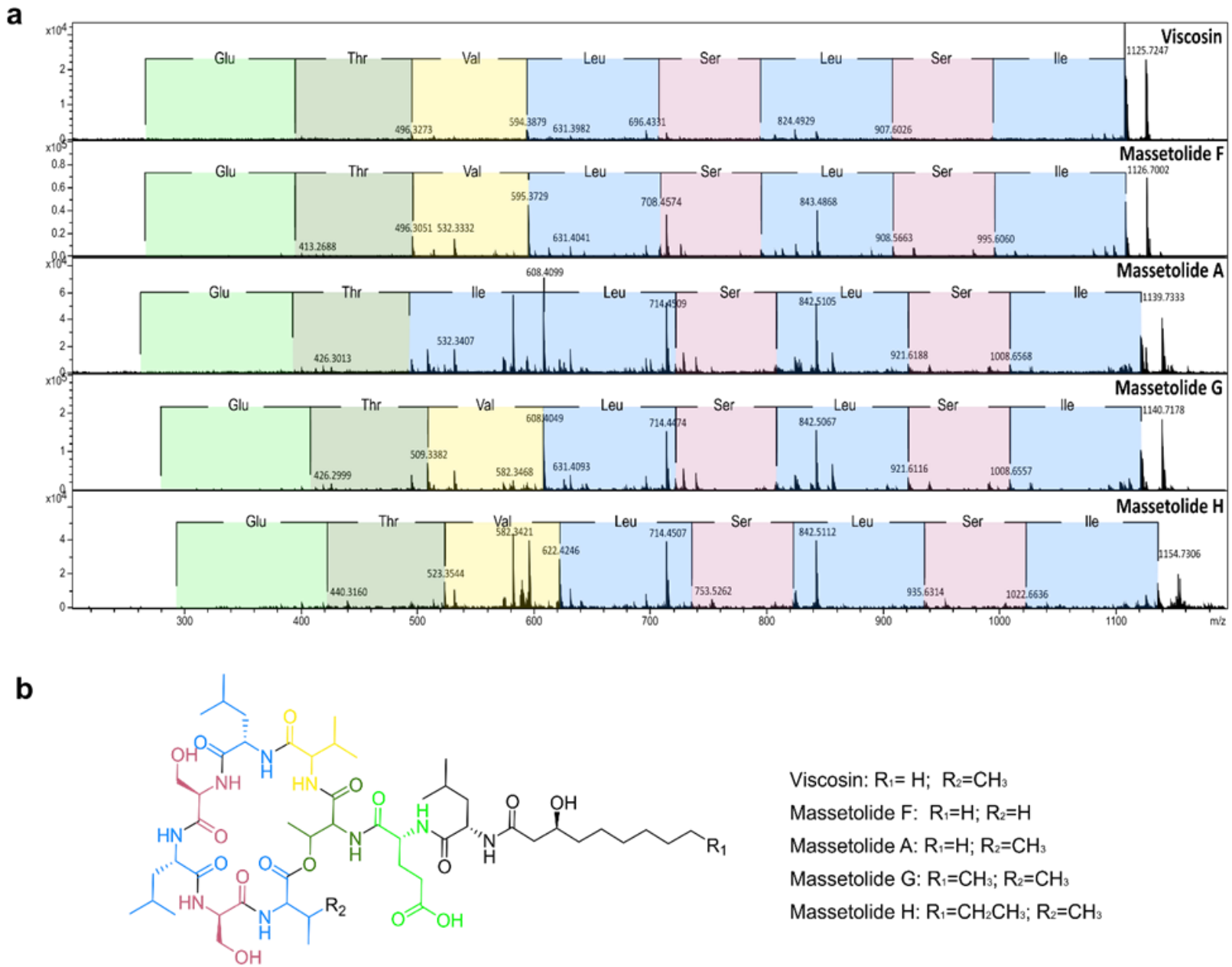
GNPS Molecular Networking of the extracts





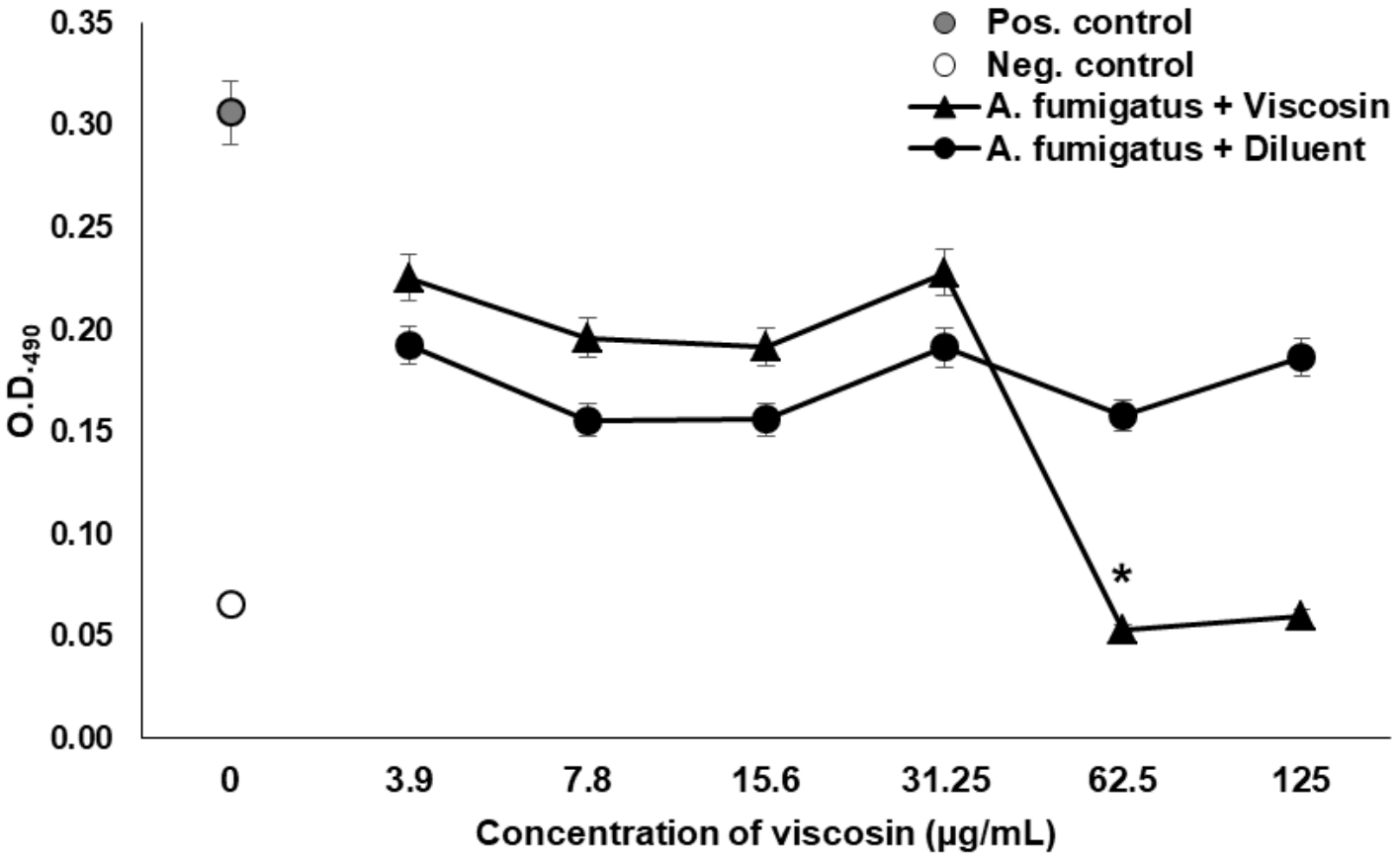
Node information
(i) GNPS library hit clustering with viscosin isolated from *P. cichorii*
(ii) GNPS library hits
(iii) Hit manually annotated

Martin, C. et. al *Scientific Reports*, **2019**, 9, 3019.



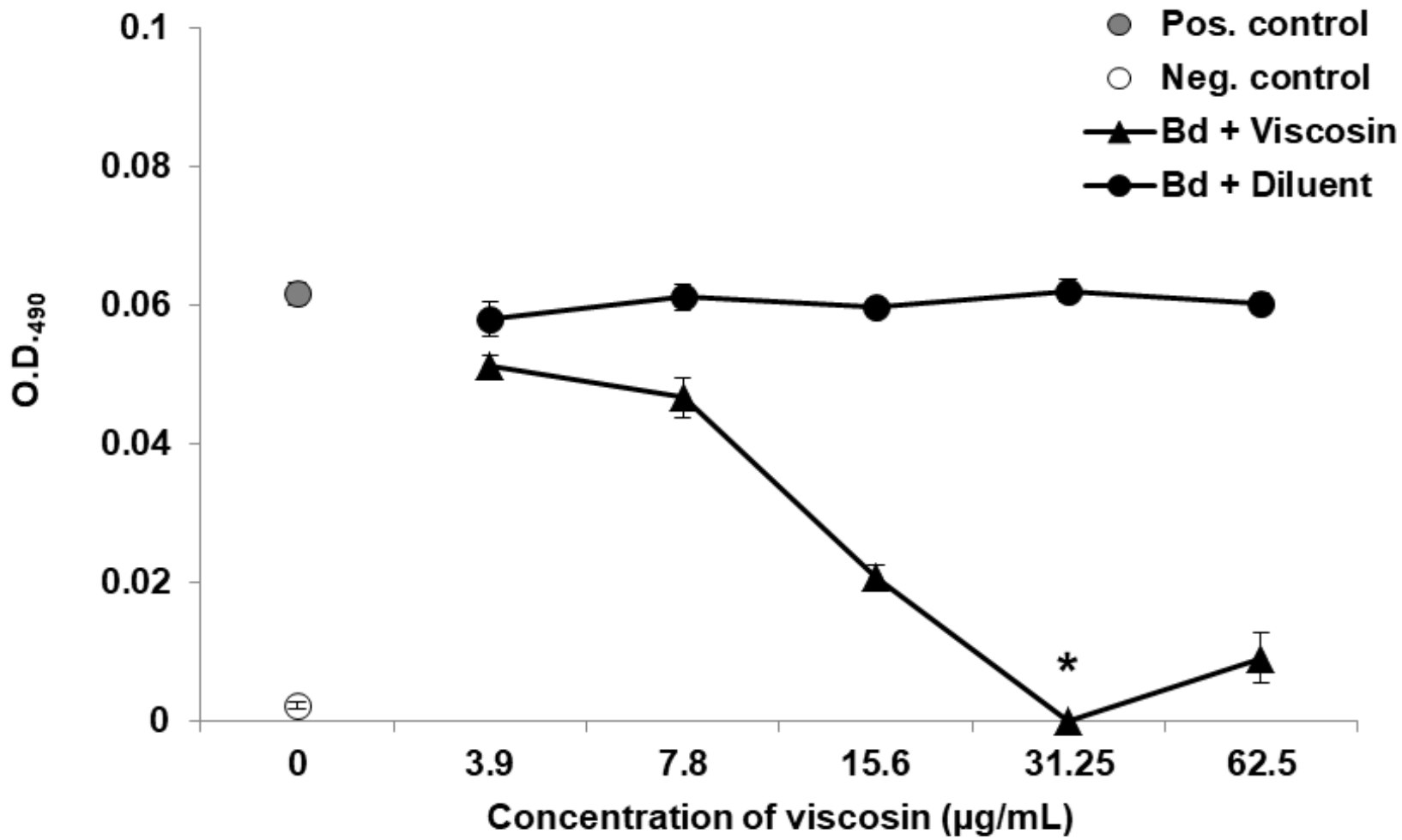
Martin, C. et. al *Scientific Reports*, **2019**, 9, 3019.

In vitro assay of viscosin vs *A. fumigatus*



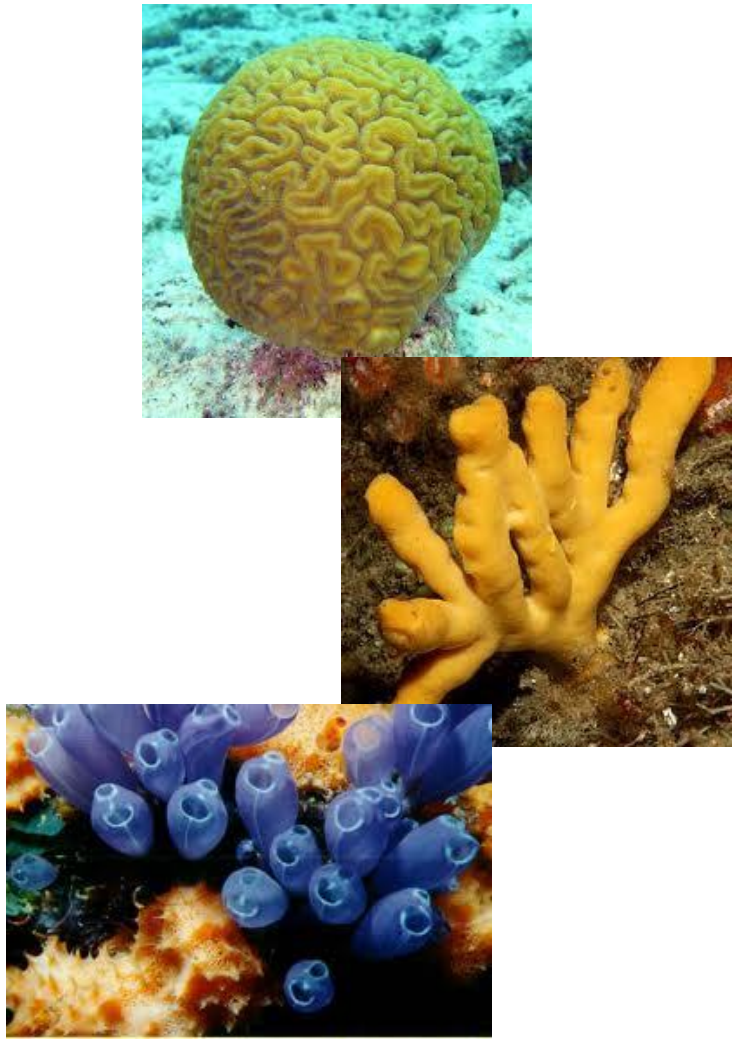
Martin, C. et. al *Scientific Reports*, **2019**, 9, 3019.

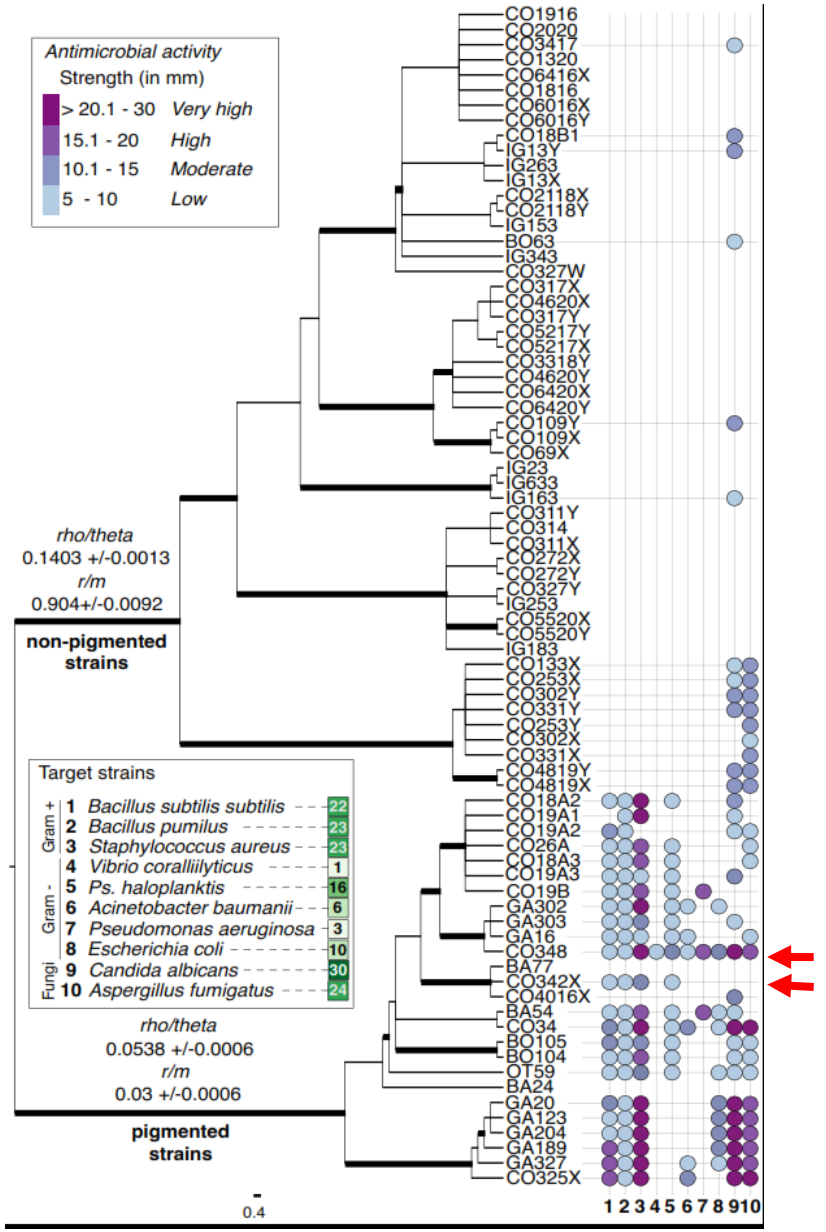
In vitro assay of viscosin vs *B. dendrobatidis*



Martin, C. et. al *Scientific Reports*, **2019**, 9, 3019.

New species of antibiotic producing Pseudoalteromonas





Atencio, L. *et al.*, *Journal of Basic Microbiology, 2018, 1-23*

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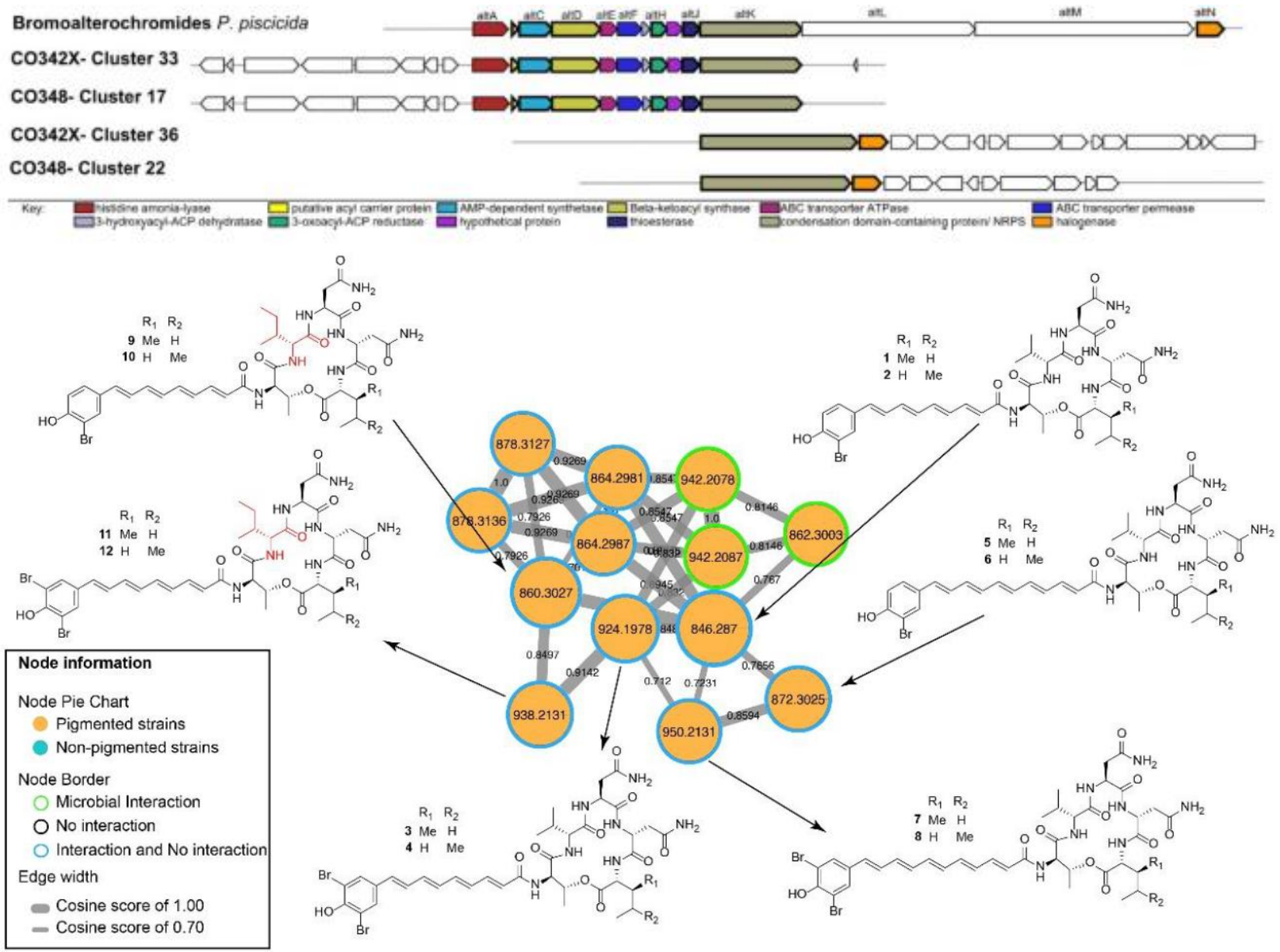
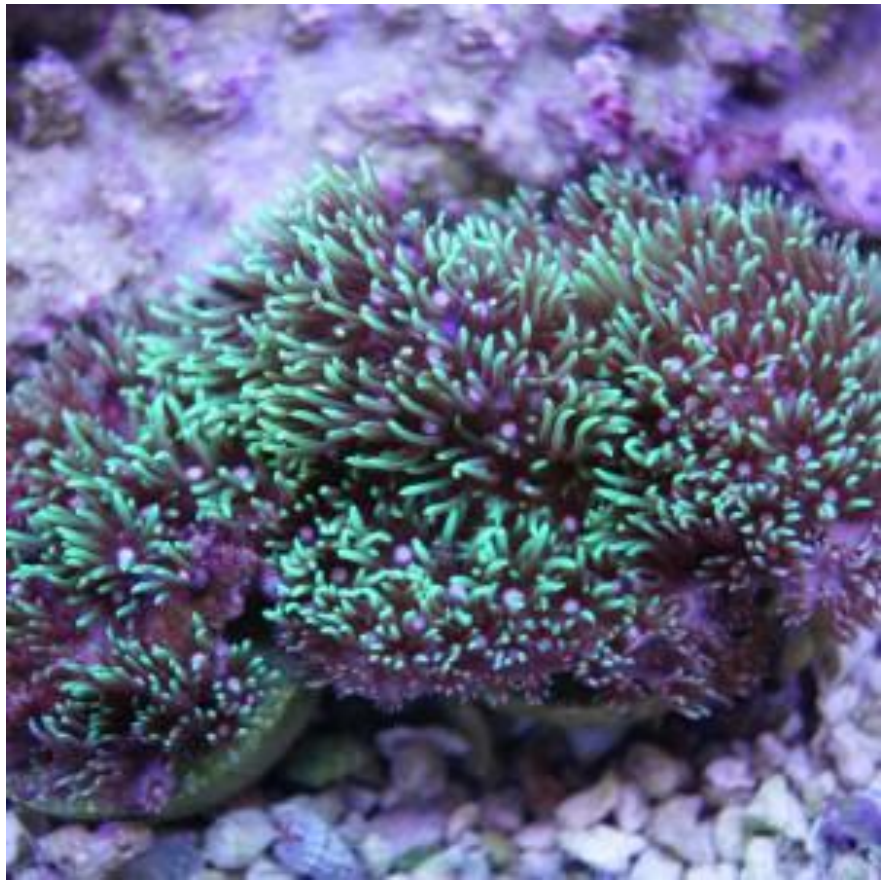
The bromoalterochromides

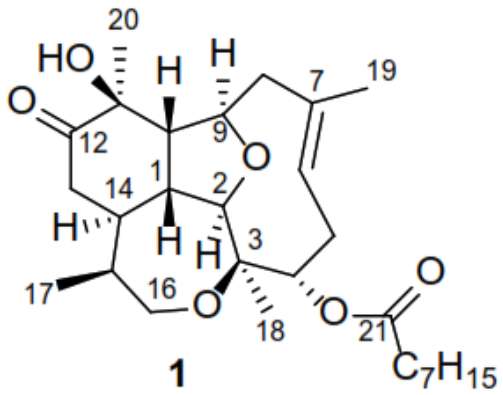


Atencio, L. *et al*., *Marine Drugs, 2020, 18, 456*

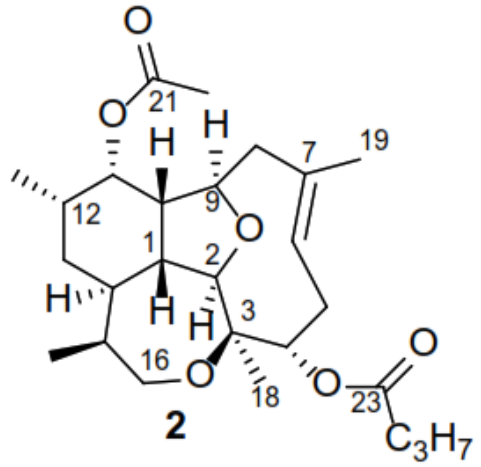
New Eunicelanes with anti-inflammatory activity



Briareum asbestinum



1



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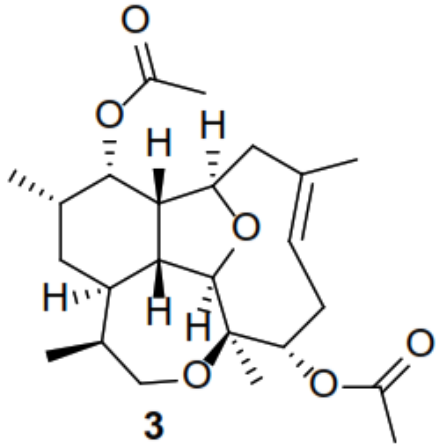

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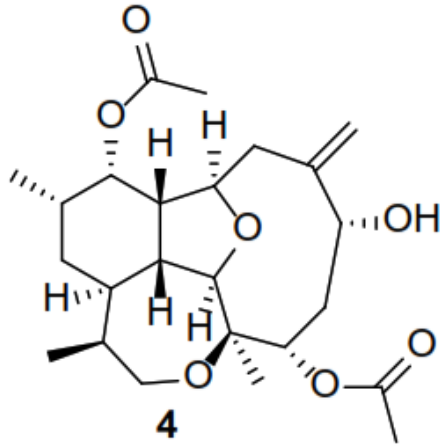
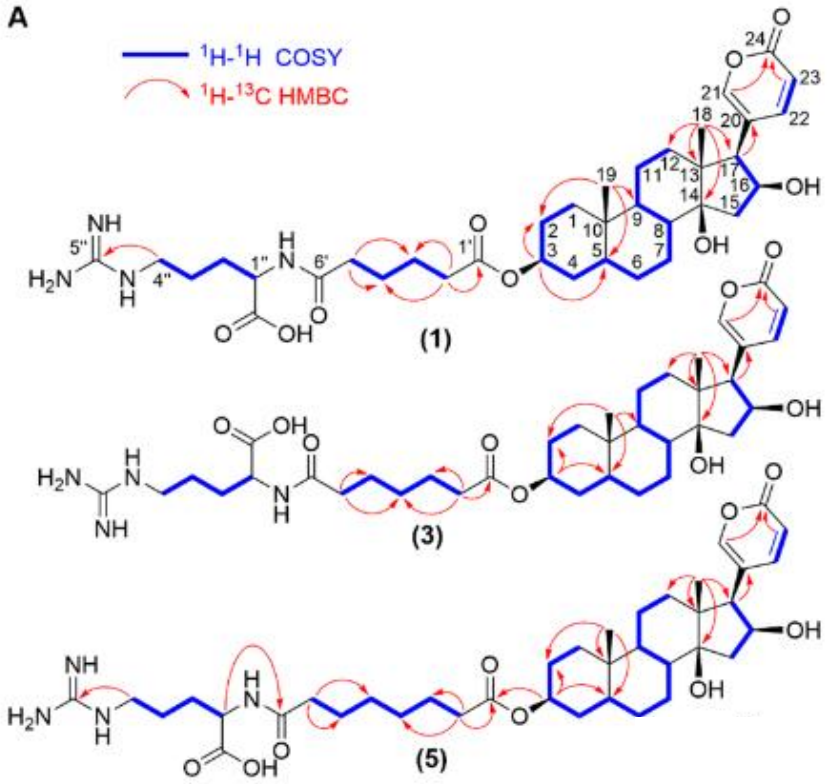
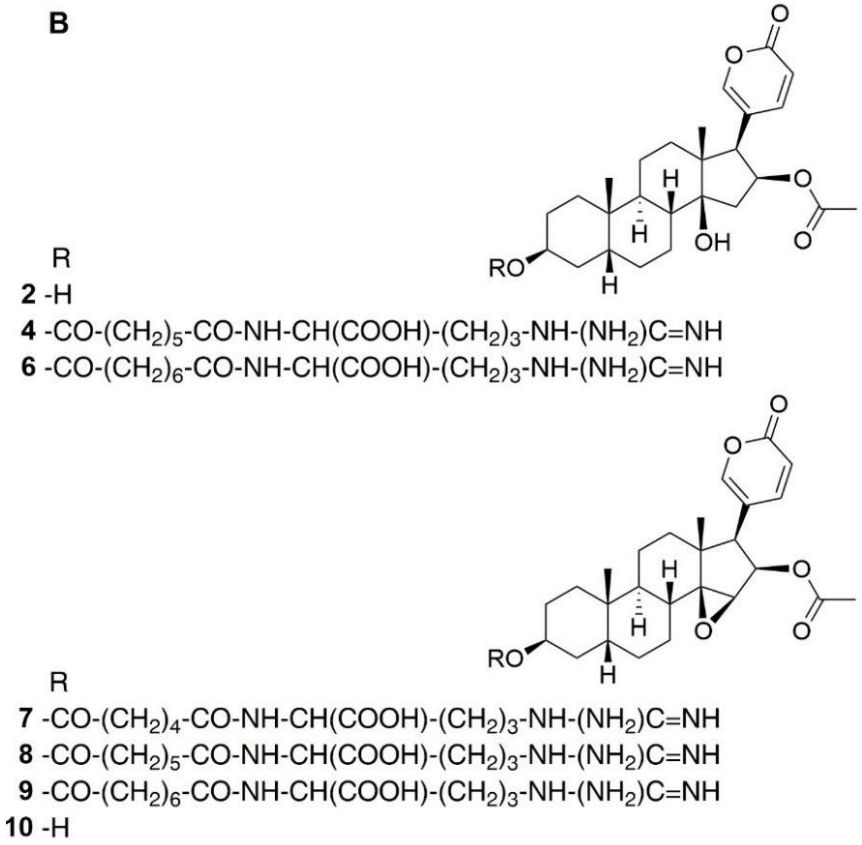


4

Gomez J. F. *et al.*, *J. Mar Drugs.*, Mar. Drugs **2020**, 18, 84

New bufadienolides from the Skin Secretions of the Neotropical Toad *Rhinella alata* with Antiprotozoal Activity against *Trypanosoma cruzi*





C. Rodriguez, et al. *Molecules* **2021**, 26, 4217

Conclusions

- Our results confirm that biological diversity from Panama, beyond of their intrinsic value, have a great capacity to produce molecules with potential in drug discovery.
- The integration of new analytical tools for metabolomic analyses and genomics tools will impact the drug discovery process.

Thanks

Gracias!