

From Mollusks to Medicine: Discovery and Characterization of Peptides from Venomous Marine Snails

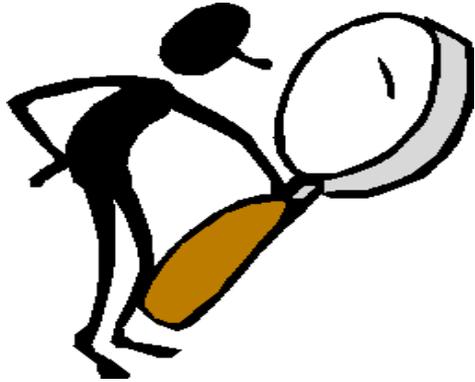


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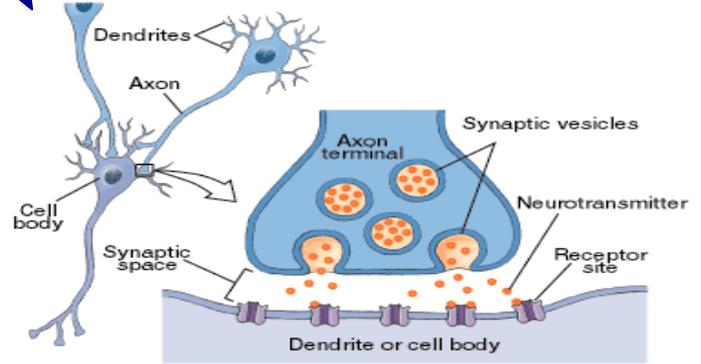
@scimaven

Holford Group Research Goals



Discovery

**novel peptides
that modulate
cell signaling**



Characterization

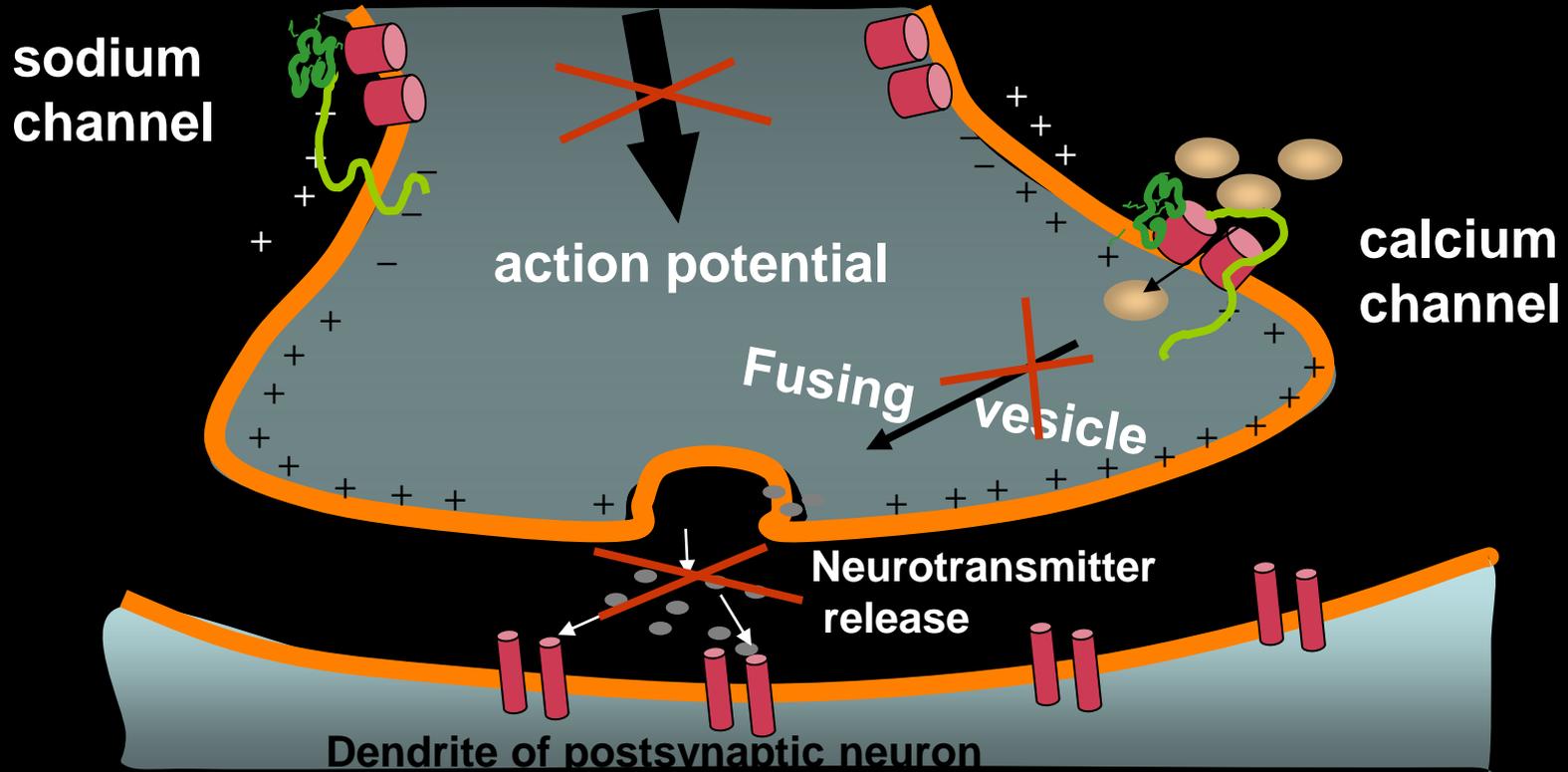


Delivery

VENOM

}

Characterization of snail peptides in the neuronal circuit



Inhibit specific signals in cellular communication

*venom
peptides*

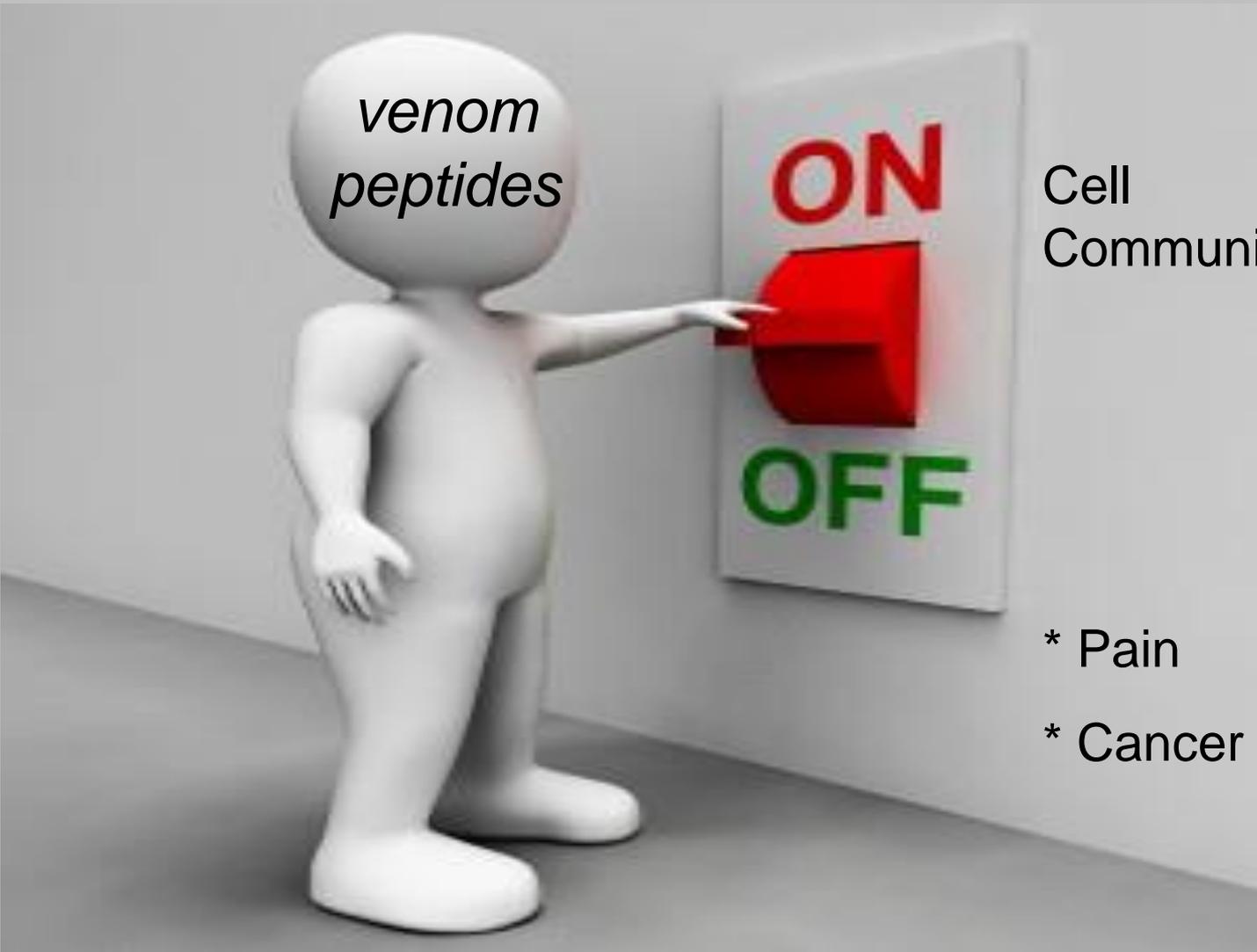
ON

OFF

Cell
Communication

* Pain

* Cancer



Venomous marine snails: Conoidean Superfamily



Cones



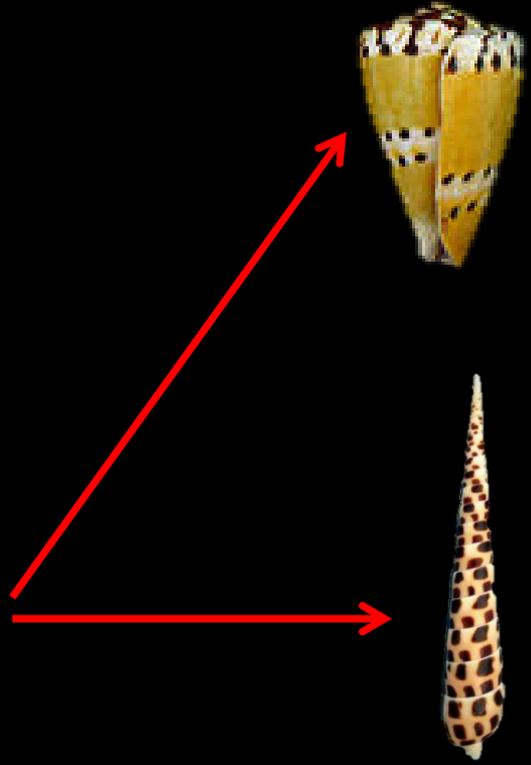
Terebrids



Turrids

Terebridae Venom Evolution

Eon	Era	Period		Epoch	Start Date (mya)
Phanerozoic	Cenozoic	Quaternary		Holocene	0.01
				Pleistocene	1.64
		Tertiary	Neogene	Pliocene	5.2
				Miocene	23.3
			Paleogene	Oligocene	35.4
		Eocene		56.5	
		Paleocene		65	



Tropical Deep Sea Collections



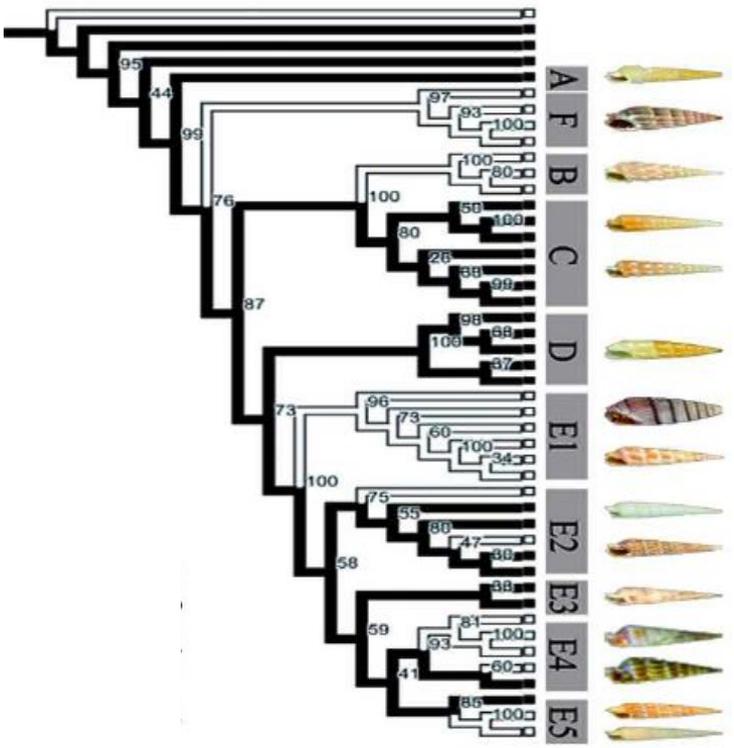
Traditional



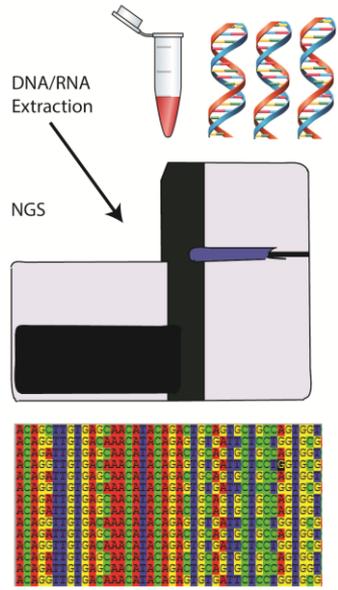
Size + Quantity

Venomic Snail Peptide Discovery

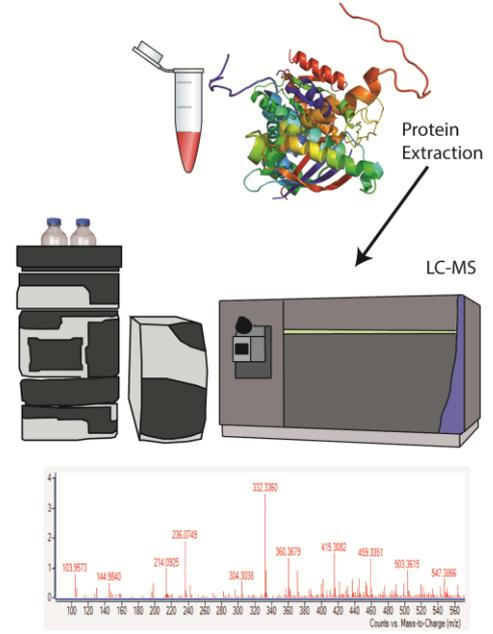
Phylogenetic



Transcriptomic



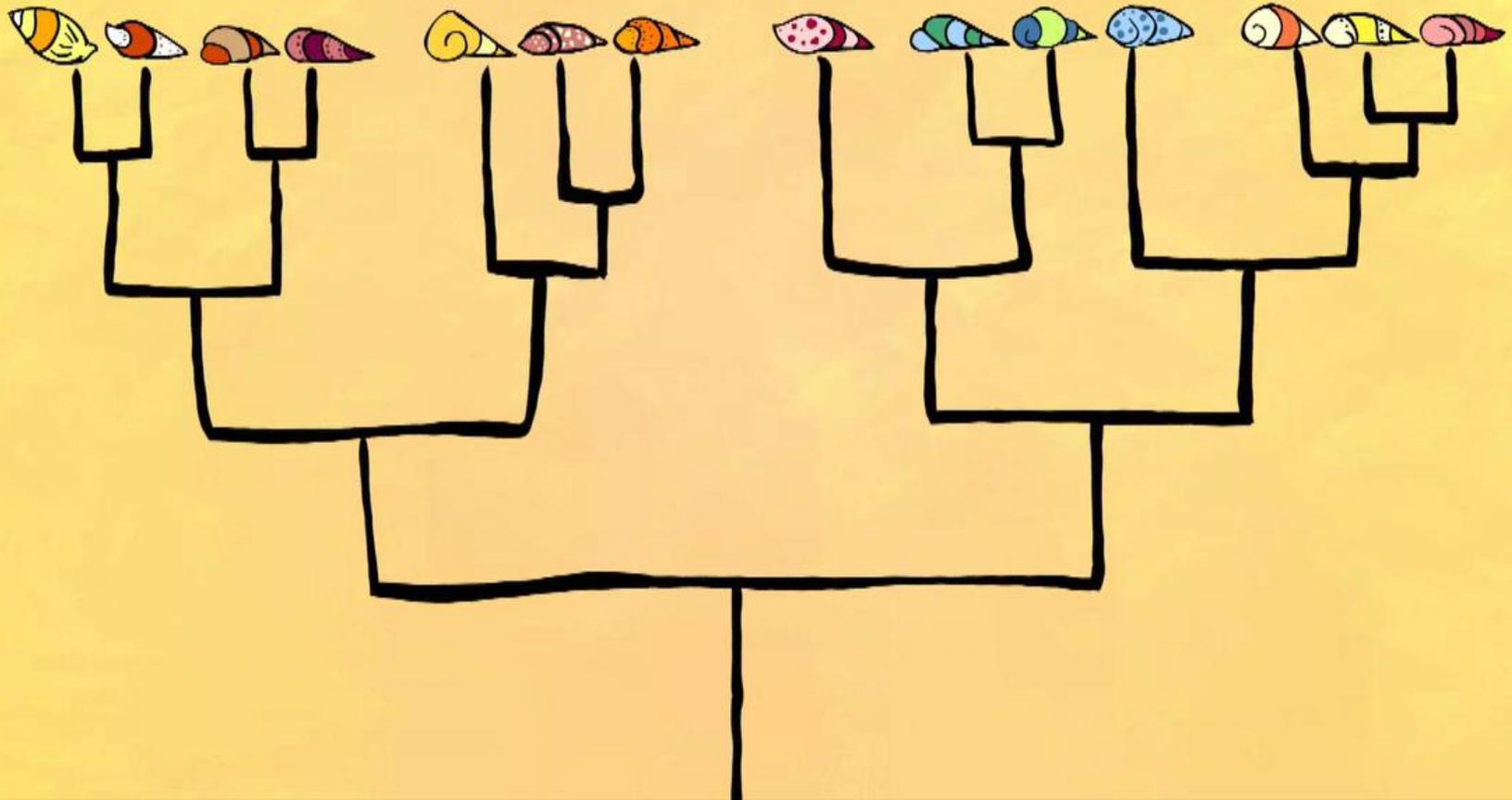
Proteomic



```

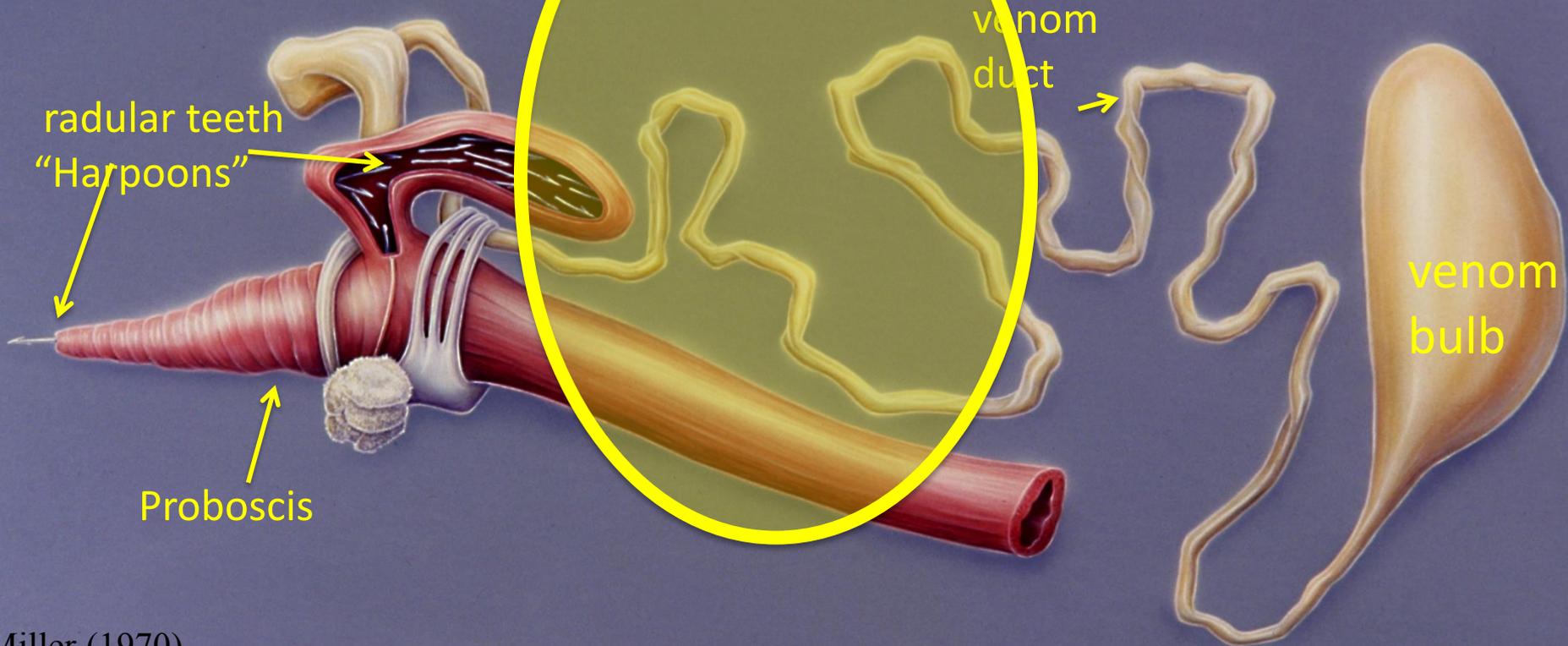
TSGCCAVLSLNNCCGOTEHICC
SLCQFPLCHMNTKCTENGRAS
QRENYAKKQDSCCTPLLCTENC
RFEFIEGRASCRCCTPPLCHGLCQFPL
QAKVCCHFCDRDGQCDGNODTFYCTCT
DEEDSKPGVYRFCCIPTGRAIKCLACSC
CCRIOCDIMYDTGSCRSRKMDGAKCV TCT
    
```

Validated Databases



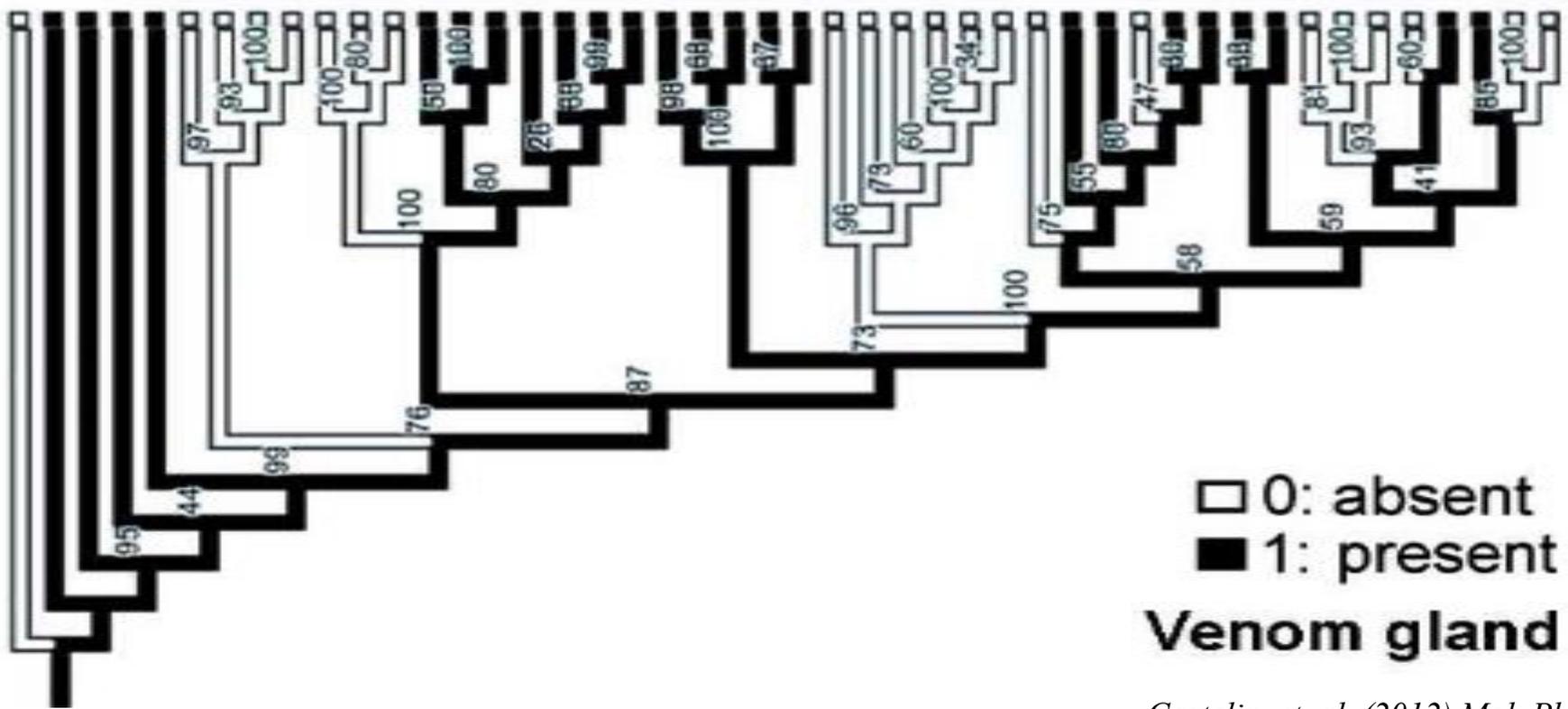
Cone Snail Venom Apparatus

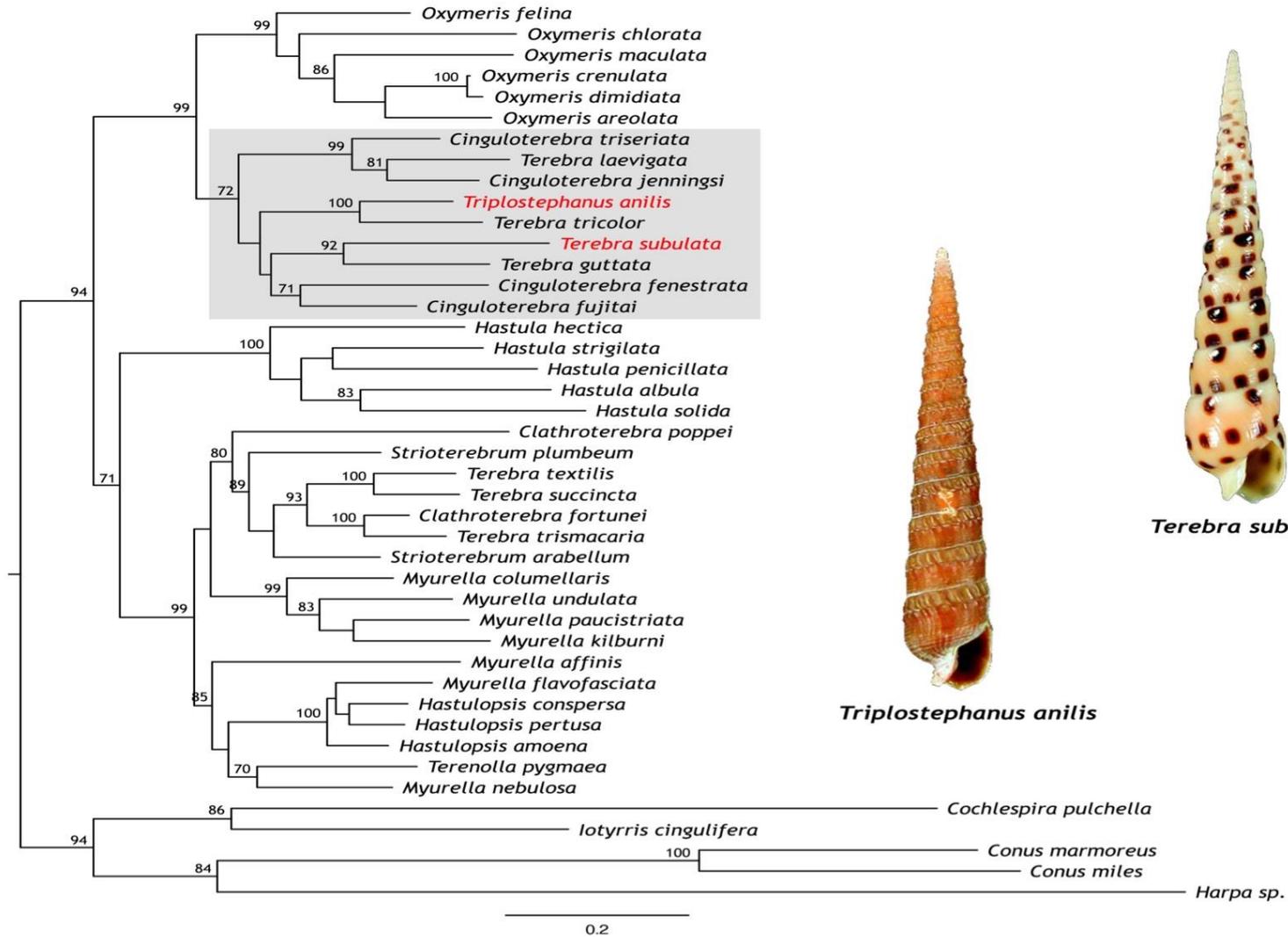
CONUS SNAIL VENOM APPARATUS



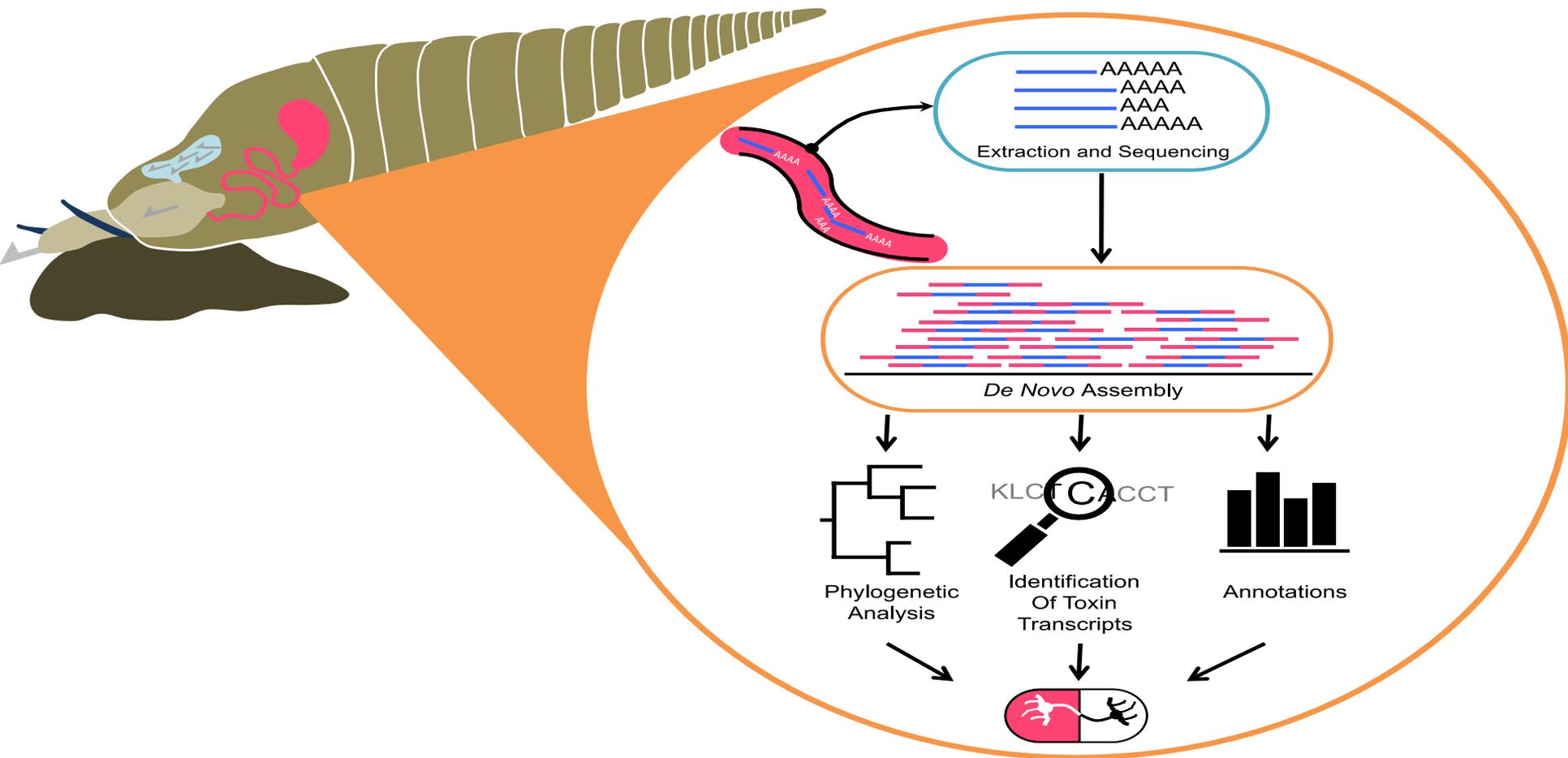


A F B C D E1 E2 E3 E4 E5





Transcriptomic sequencing and *de novo* assembly of *Terebrid* Venom



Venom peptides expressed as single genes

Conserved



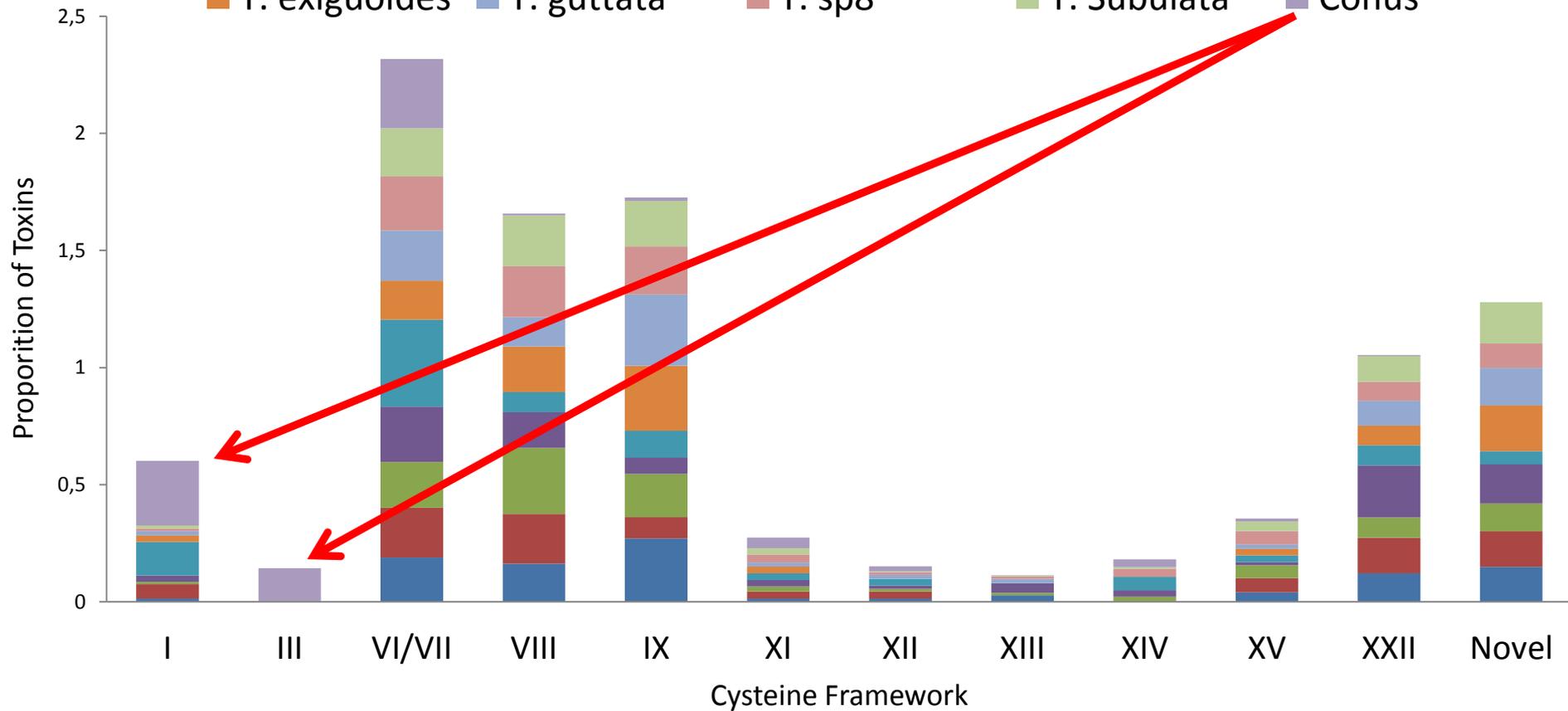
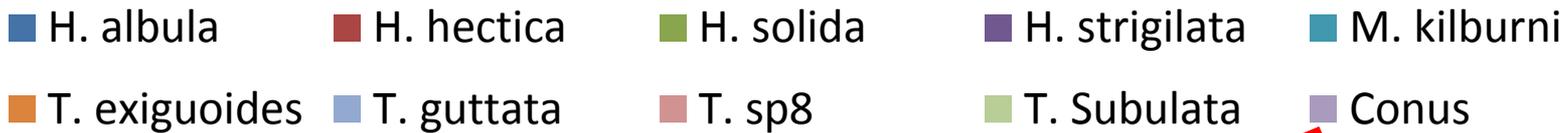
The diagram illustrates the structure of a venom peptide gene. It consists of three colored segments: a red segment for the 'Signal sequence', an orange segment for the 'Pro region', and a green segment for the 'Cys-rich Mature toxin'. A white bracket above the red and orange segments is labeled 'Conserved', indicating that these two regions are conserved across different species.

Signal sequence

Pro region

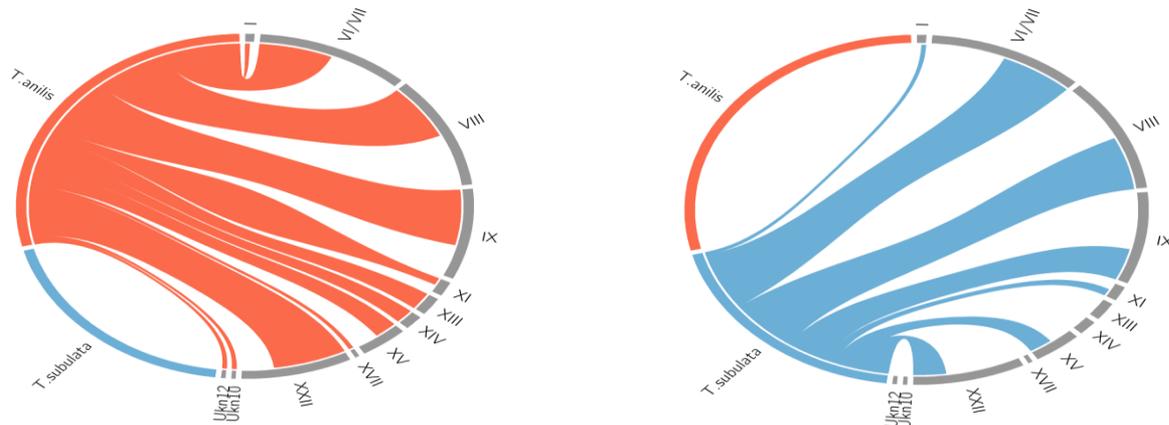
Cys-rich Mature toxin

Teretoxins Distinct from Conotoxins

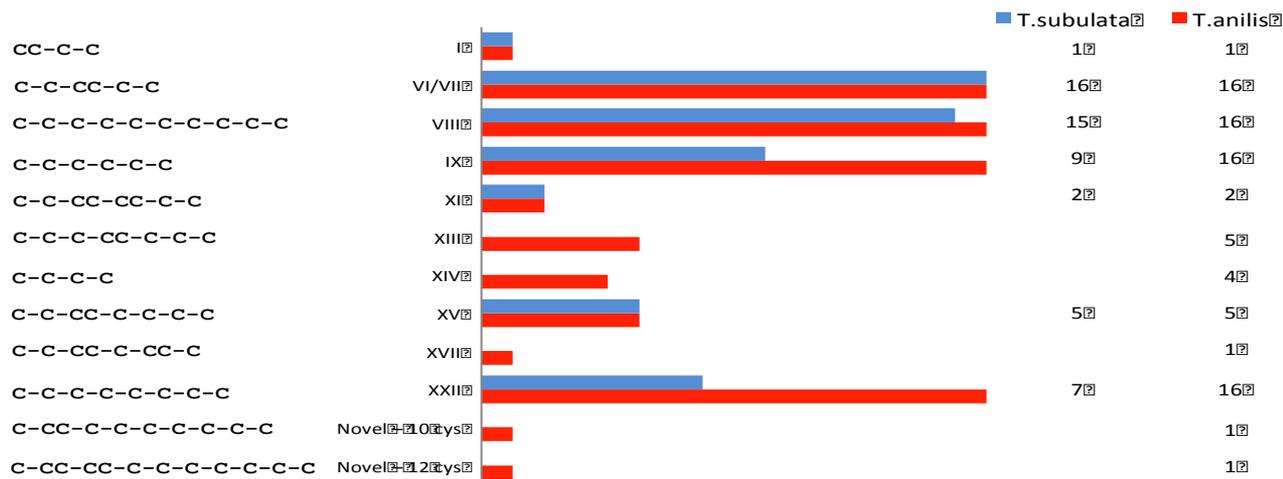


Teretoxin Venom Diversity

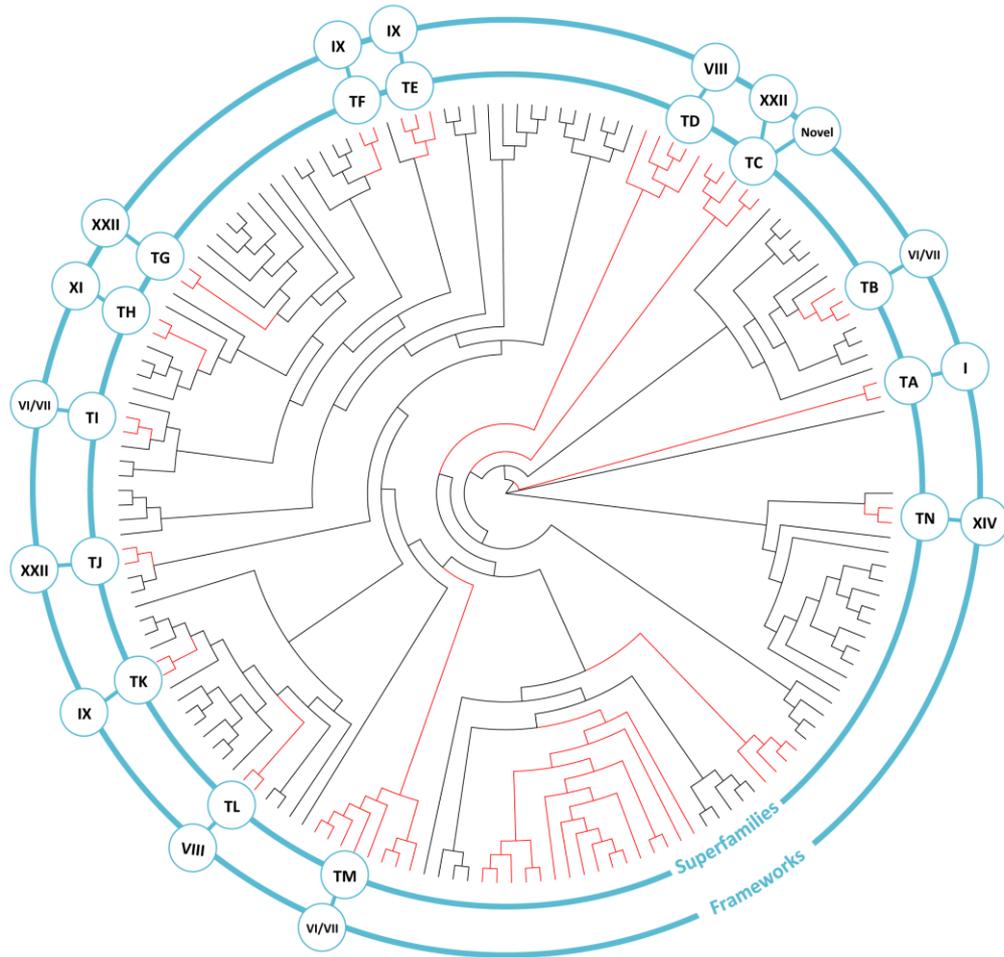
a)



b)



Total: **55** **84**

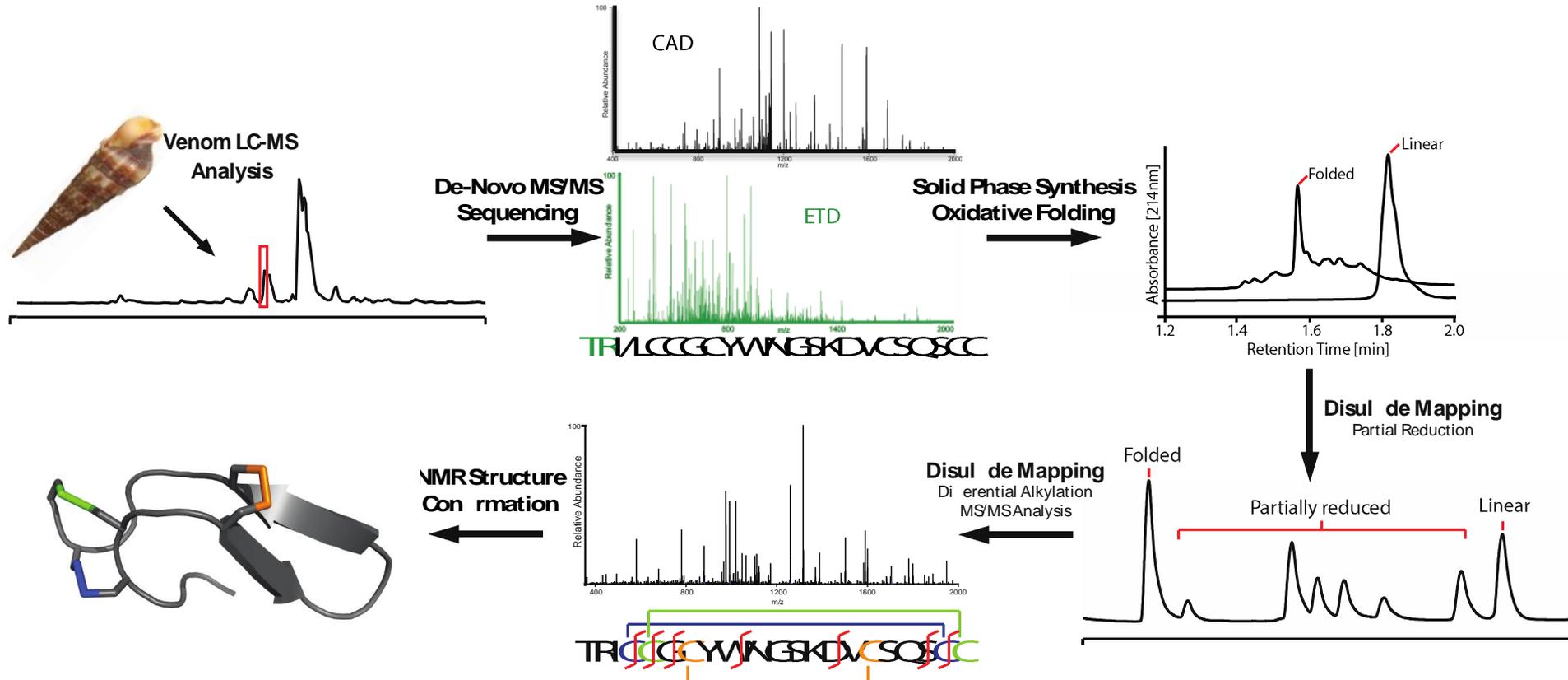


(i) independent lineage (≥ 70 bootstrap & ≥ 90 posterior probability)

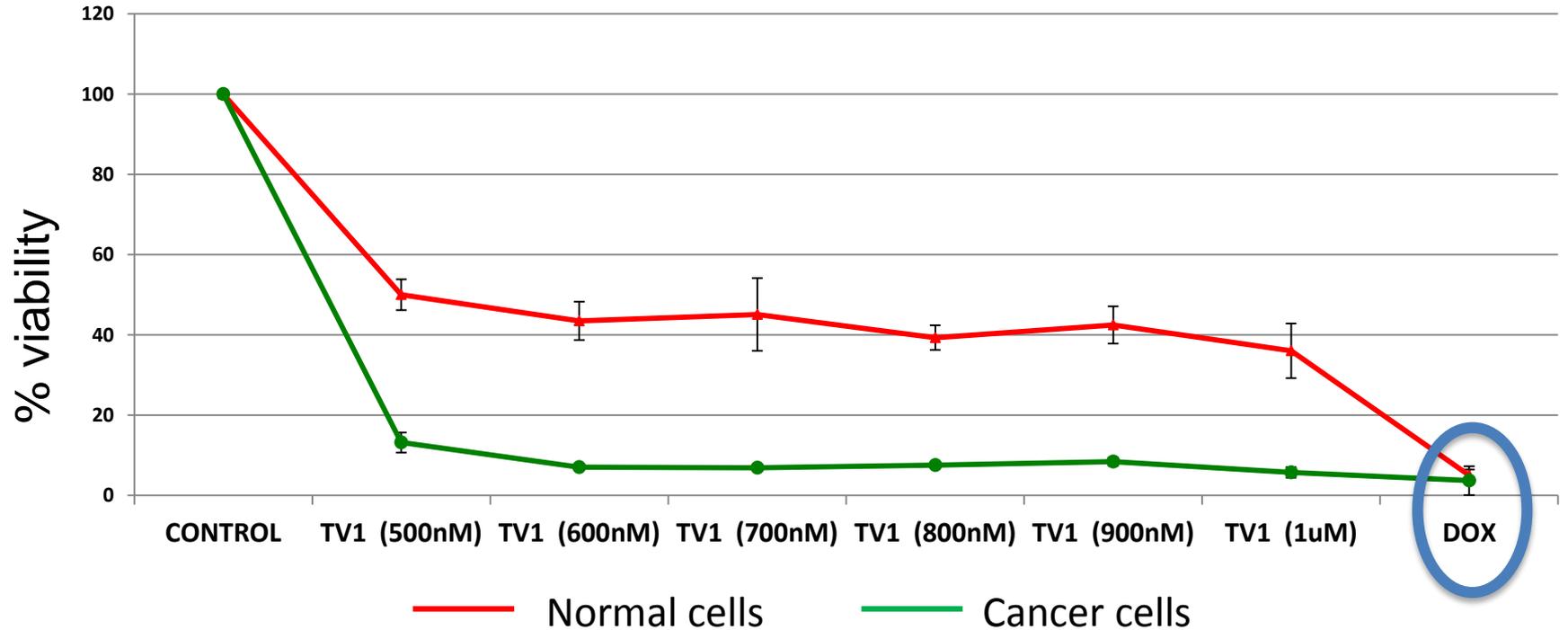
(ii) $>60\%$ sequence identity within the superfamily

(iii) pattern of cysteines different from the sister clade.

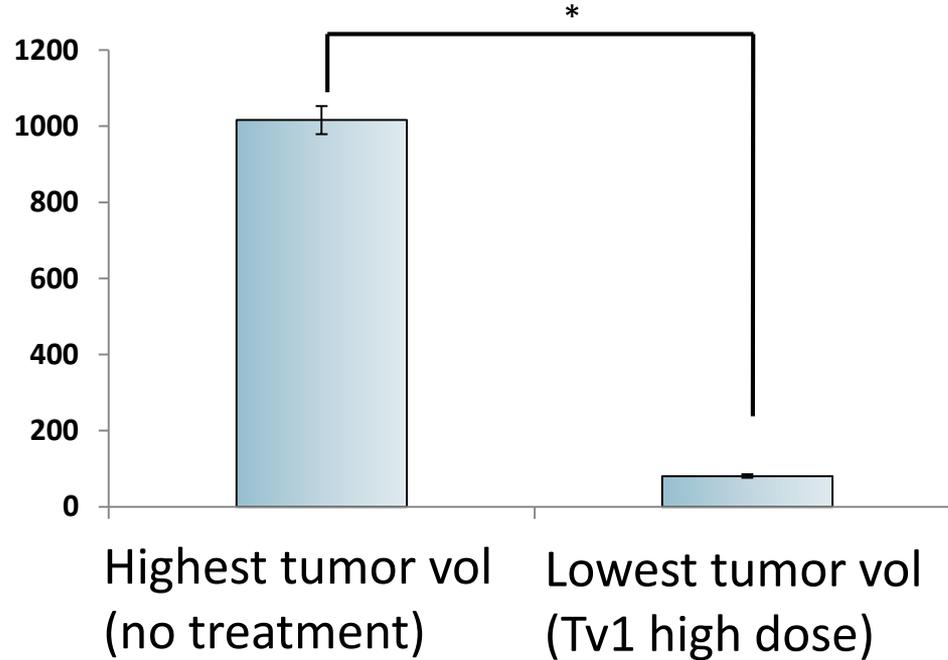
Proteomic Discovery and Characterization of Terebrid Toxin Tv1



Tv1 kills cancer cells



Comparison of tumor volume for 7day treatment



* $p < 0.0001$ using paired t-test

Tv1
peptide

liver cancer



10 mcg

NDC 66780-212-01

Byetta[®]
exenatide injection 250 mcg/mL, 2.4 mL

READ ENCLOSED BYETTA MEDICATION GUIDE FOR IMPORTANT SAFETY INFORMATION



Each prefilled pen will deliver 60 subcutaneous doses, 10 mcg per dose **Rx Only**

SUBCUTANEOUS USE ONLY **REFRIGERATE – DO NOT FREEZE**
DO NOT TRANSFER THIS MEDICATION TO A SYRINGE.

Pen needles not included

Ask your healthcare provider which pen needle length and gauge is best for you
Use 29 (thin), 30, or 31 (thinner) gauge disposable pen needles

*Gila monster
(diabetes)*



Chinese red-headed centipede

 Egis Ltd.

1 ml

prialt

(1 x 1 ml infúziószer) (1 x 1 ml injekciószer) (1 x 1 ml infúziószer) (1 x 1 ml injekciószer) (1 x 1 ml infúziószer)

100 mikrogrammos infúziószeres, szpongiós zicronál
100 mikrogrammos infúziószeres, szpongiós, zicronál
100 mikrogrammos, intravénás, szpongiós, zicronál
100 mikrogrammos infúziószeres, szpongiós, zicronál
100 mikrogrammos infúziószeres, szpongiós, zicronál

*Cone snail
(pain)*

Captopril
Captoprilum
tabletki **25** mg

30 tabletek

25

EGIS

Captopril
tabletki 25 mg

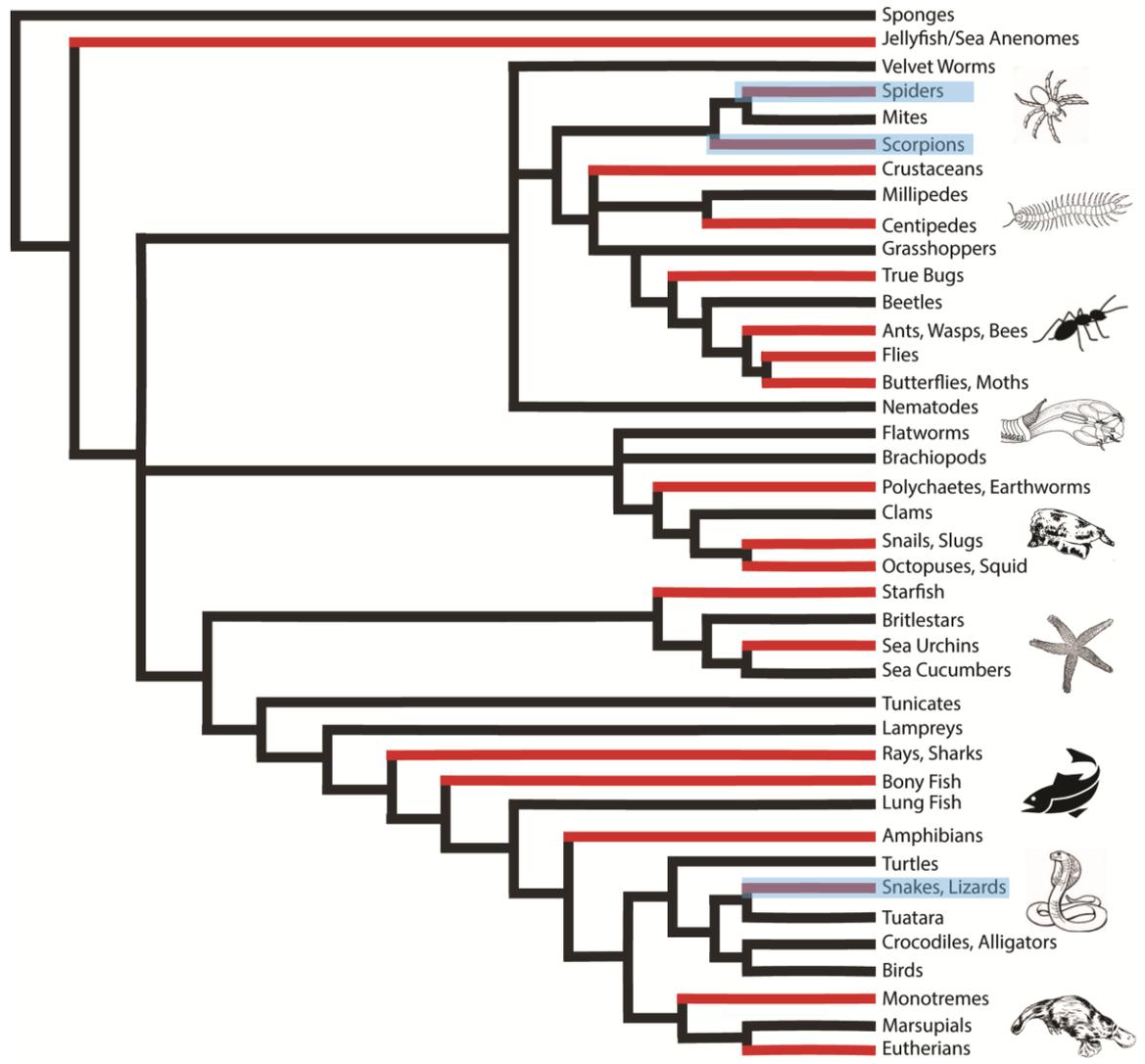
*Brazilian lancehead snake
(hypertension)*

VENOM evolution is convergent

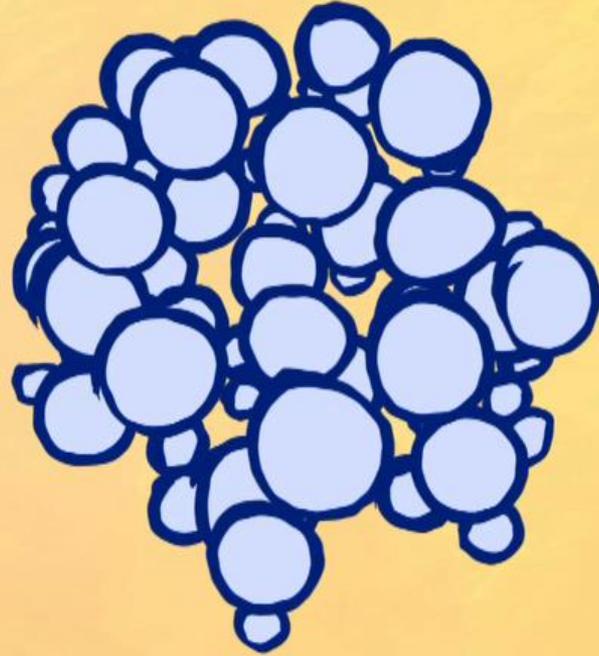
-Omics technology expanding reach to small

-Evolution of rapidly evolving genes

-Scaffolds that work



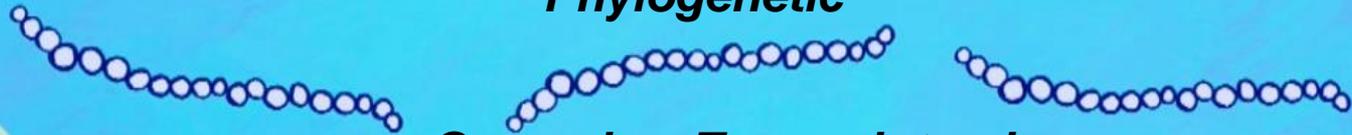
From Mollusks to Medicine



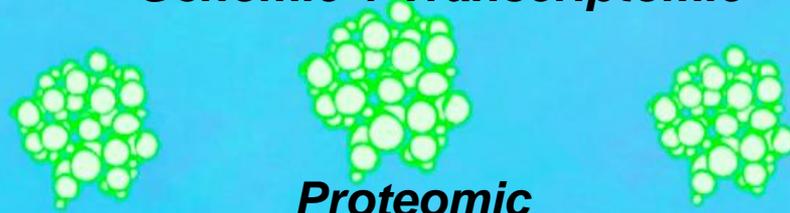
Integrated Roadmap to Identify Novel Venom Peptides



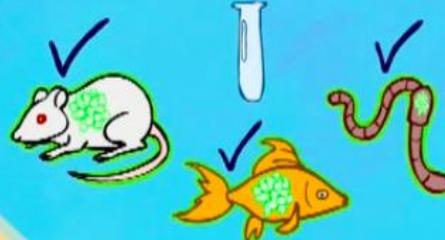
Phylogenetic



Genomic + Transcriptomic



Proteomic



Structure + Function

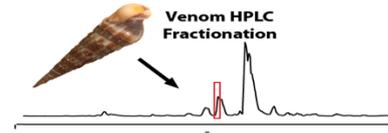
On to more testing!



Merci Beaucoup @ Philippe Bouchet & Malaco Team!



Acknowledgements



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