



北京大学
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生命科学学院
School of Life Sciences

Gary's Self-Safe **Venom**: Biochemical Mechanisms of Snake Self-Resistance

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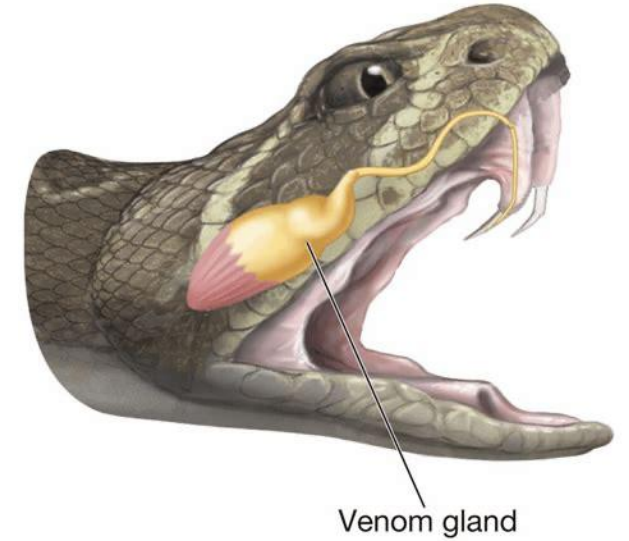


Zootopia 2
Gary De'Snake



Trimeresurus insularis
(海島竹叶青)

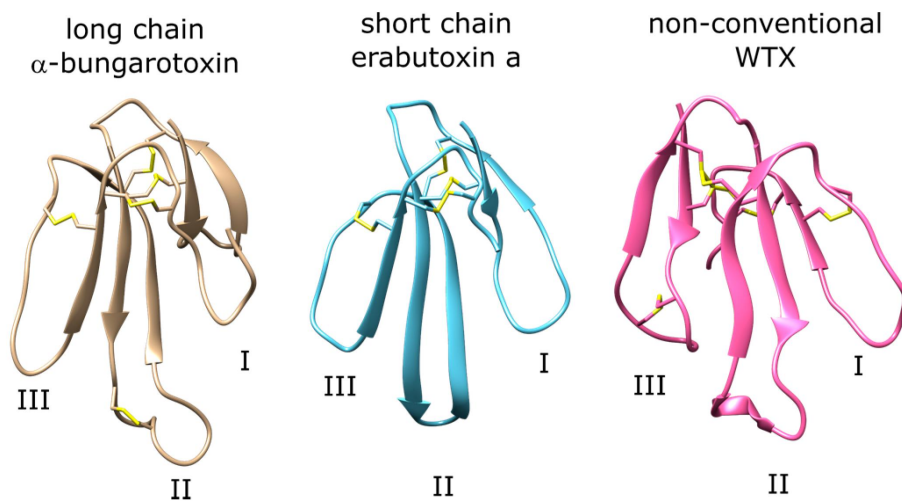
- Viperidae 蝰蛇科
- Crotalinae 蝮亚科
- Trimeresurus 竹叶青属



Why don't venomous snakes get poisoned by their own venom?

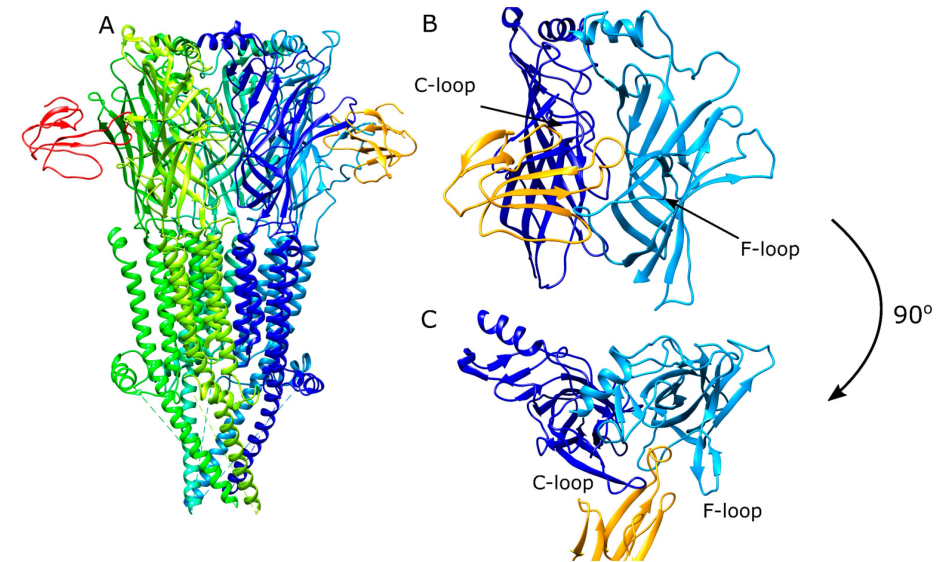
Type I: Neurotoxic venom

- Disrupts **synaptic transmission** via specific molecular targets
- Key toxins:
 - α -neurotoxins (3FTx) $\rightarrow$ nAChR**
 - β -neurotoxic sPLA₂ $\rightarrow$ presynaptic terminals
- Function: blocking nerve signaling, resulting in motor paralysis



α -neurotoxins

Gulsevin A, et.al. *Toxins (Basel)*. 2020

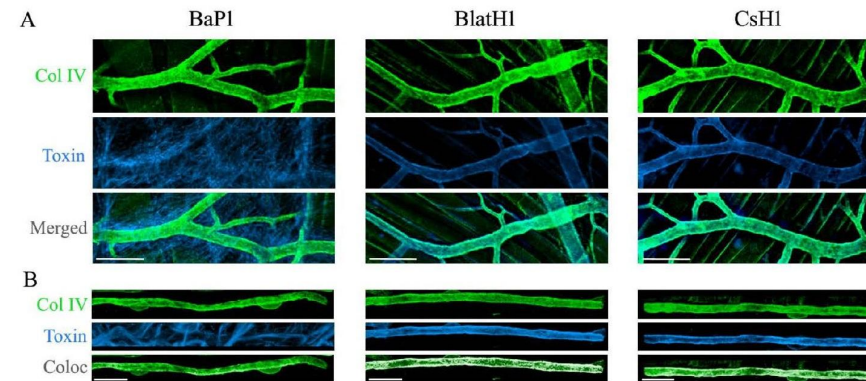
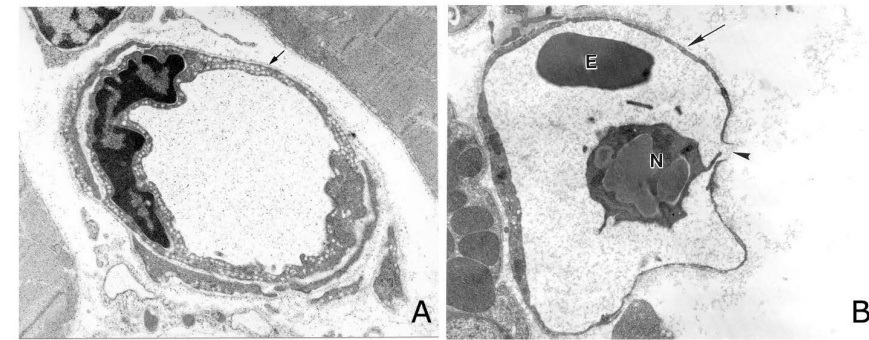
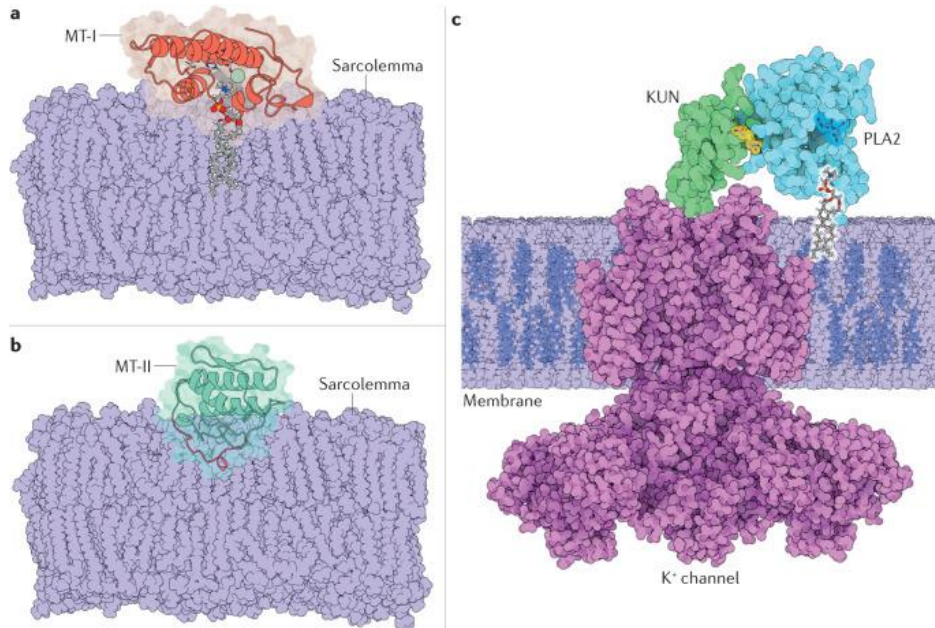


binding nAChR

Gulsevin A, et.al. *Toxins (Basel)*. 2020

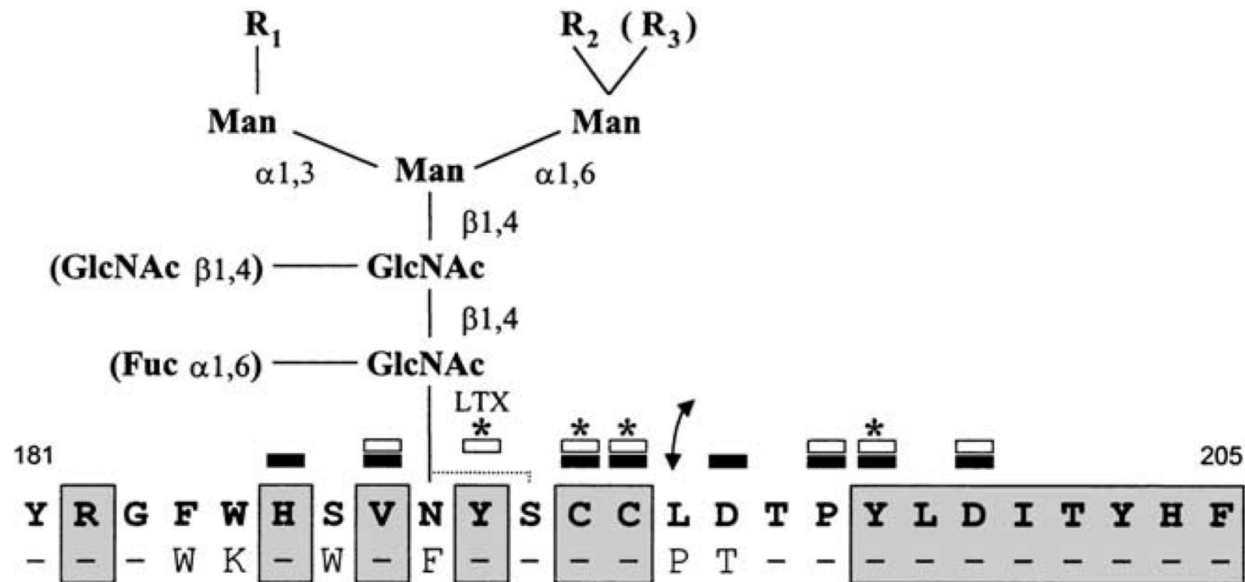
Type II: Hemotoxic venom

- Targets **coagulation + vessel integrity**
- Key toxins:
 - **SVMPs** (Zn^{2+} metalloproteases) → Capillary Collagen Type IV
 - **SVSPs** (serine proteases)
 - **PLA2** → cytomembrane



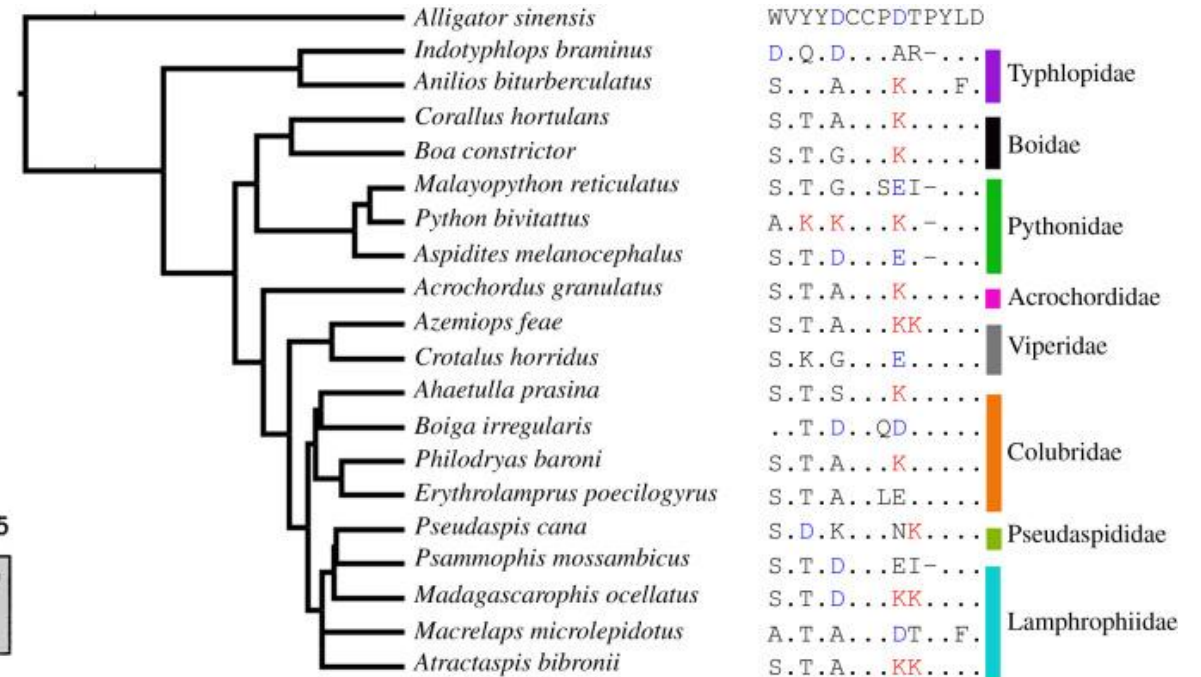
Neurotoxins: modify the receptor

Strategy: **target-site resistance** (reduce toxin binding, keep receptor function)



N-glycosylation shielding

Takacs Z, et.al. *J Mol Evol.* 2004



charge-altering mutations

Harris RJ, et.al. *Proc Biol Sci.* 2021

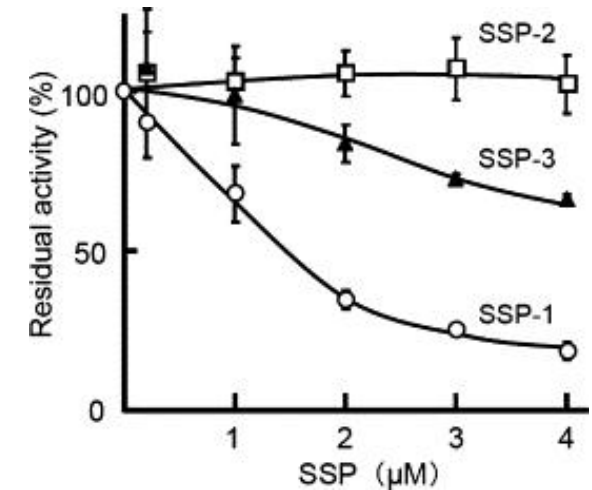
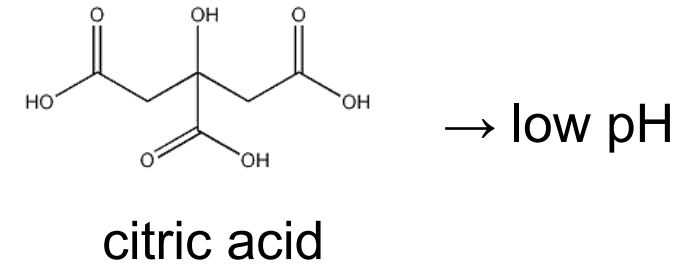
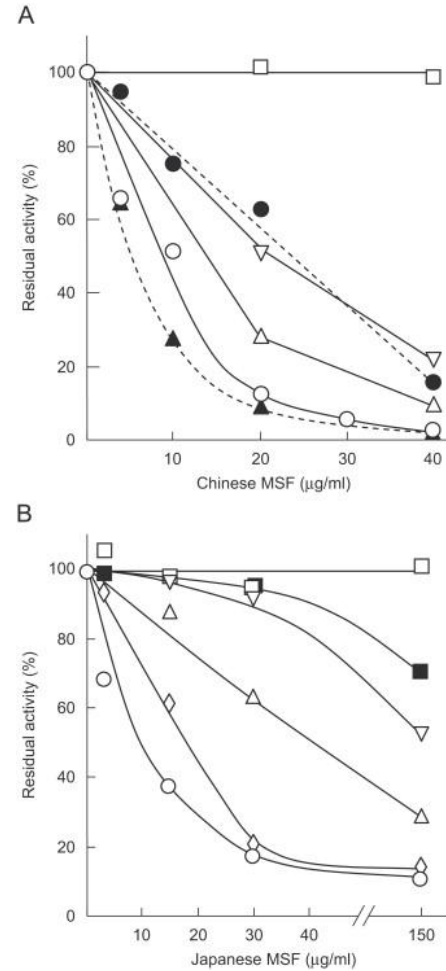
Hemotoxic enzymes: neutralize with serum inhibitors

Strategy: **endogenous antivenom proteins** in serum

Table 1 Snake blood PLA₂ inhibitors in the alpha structural class (sbaPLIs)

Family, species or subspecies	Common name	Reference
Colubridae		
<i>Elaphe climacophora</i>	Japanese ratsnake	[26]
<i>Elaphe quadrivirgata</i>	Japanese four-lined ratsnake	[27]
Viperidae		
<i>Bothrops alternatus</i>	Urutu (Portuguese)	[15, 31] ^a , [23]
<i>Bothrops asper</i>	Fer-de-lance, Terciopelo (Spanish)	[62]
<i>Bothrops erythromelas</i>	Caatinga lancehead	[23]
<i>Bothrops jararaca</i>	Jararaca (Port.)	[23]
<i>Bothrops jararacussu</i>	Jararacussu (Port.)	[14, 23]
<i>Bothrops moojeni</i>	Brazilian lancehead	[16]
<i>Bothrops neuwiedi</i>	Jararaca pintada (Port.)	[23]
<i>Cerrophidion godmani</i>	Honduras montane pit viper	[21]
<i>Crotalus durissus terrificus</i>	South American rattlesnake, tropical rattlesnake	[23]
<i>Gloydius brevicaudus</i>	Short-tailed mamushi, Japanese or Chinese mamushi,	[19] ^a , [63]
<i>Lachesis muta</i>	South American bushmaster	[23]
<i>Protobothrops flavoviridis</i>	Habu	[25, 64, 65], [66] ^a
<i>Protobothrops elegans</i>	Sakishima habu	[41]

^aRecombinant homolog



Small serum proteins (SSPs)

Phospholipase A₂ inhibitors (PLIs)

Anti-hemorrhagic factors Aoki N, et.al *Biochem Biophys Res Commun.* 2007

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2. Harris, R. J. & Fry, B. G. Electrostatic resistance to alpha-neurotoxins conferred by charge reversal mutations in nicotinic acetylcholine receptors. ***Proc Biol Sci*** 288, 20202703 (2021).
3. Aoki, N., Sakiyama, A., Deshimaru, M. & Terada, S. Identification of novel serum proteins in a Japanese viper: Homologs of mammalian PSP94. ***Biochemical and Biophysical Research Communications*** 359, 330–334 (2007).
4. Campos, P. C., de Melo, L. A., Dias, G. L. F. & Fortes-Dias, C. L. Endogenous phospholipase A2 inhibitors in snakes: a brief overview. ***J Venom Anim Toxins Incl Trop Dis*** 22, 37 (2016).
5. Takacs, Z., Wilhelmsen, K. C. & Sorota, S. Cobra (*Naja* spp.) Nicotinic Acetylcholine Receptor Exhibits Resistance to Erabu Sea Snake (*Laticauda semifasciata*) Short-Chain α -Neurotoxin. ***J Mol Evol*** 58, 516–526 (2004).
6. Gulsevin, A., Meiler, J., Gulsevin, A. & Meiler, J. An Investigation of Three-Finger Toxin—nAChR Interactions through Rosetta Protein Docking. ***Toxins*** 12, (2020).
7. Gutiérrez, J. M. et al. Hemorrhage Caused by Snake Venom Metalloproteinases: A Journey of Discovery and Understanding. ***Toxins*** 8, (2016).
8. Oliveira, A. L. et al. The chemistry of snake venom and its medicinal potential. ***Nat Rev Chem*** 6, 451–469 (2022).



*Thanks
For your
Listening!*

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