Title: Venom: To Kill or Cure?

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Abstract:
In this case study, students will explore concepts of evolution, protein structure and function, taxonomy, and methods of scientific inquiry in a real-world way. Students will use 3D images, on-line resources, and published scientific papers to explore these topics related to venom while making inferences and evaluating their thinking related to taxonomic relationships and evolution. The case study should open lines of inquiry with additional questions that students can explore as an extension.

Subject, Grade, Level:
AP Biology

Learning objectives:
AP Biology-

- L.O.1.2- The student is able to evaluate evidence provided by data to qualitatively and quantitatively investigate the role of natural selection in evolution
- L.O.1.16- The student is able to justify the scientific claim that organisms share many conserved core processes and features that evolved and are widely distributed among organisms today
- L.O.1.13- The student is able to construct and/or justify mathematical models, diagrams, or simulations that represent processes of biological evolution
- L.O.1.16- The student is able to evaluate evidence provided by a data set in conjunction with phylogenetic tree or a simple cladogram to determine evolutionary history and speciation
- EVO-3.C - Explain how a phylogenetic tree and/or cladogram can be used to infer evolutionary relatedness.
- SYI-3.D- Explain how the genetic diversity of a species or population affects its ability to withstand environmental pressures.
- S.P.1.C- Explain biological concepts, processes, and/or models in applied contexts.
- S.P.2.A- Describe characteristics of a biological concept, process, or model represented visually.
- S.P.6.C- Provide reasoning to justify a claim by connecting evidence to biological theories.
- S.P. 6.E.b- Predict the causes or effects of a change in, or disruption to, one or more components in a biological system based on a visual representation of a biological concept, process, or model.

Timeframe:

- Instructor preparations varies. Consider access to internet resources and choice of printing or doing the activity digitally when determining the time for preparation. No physical materials are required.
- Estimated class time is 2-weeks with a 45-minute period daily.

List of materials:

- Computers and computer access
- Printed student guides (if not doing the responses digitally)
- Chart paper and markers

Procedure and general instructions (for instructor):
Day 1

Introduction:

1. Project the 3-D image of the snake skull with moving fang. Ask students to consider the following informally:
    a. What is the selective advantage for venomous snakes to be able to move their fangs?
    b. What is it about snakes that might make it beneficial for them to have venom to kill their prey?
    c. Do all venomous animals have similar fang structures?
2. Lead class discussion where students share out their thoughts to the above questions.
3. Read through case study situation together
4. Have students share out questions they have related to the case study and post these on a large poster in the room (chart paper)

Procedure and general instructions (for students).
[Provide a student version of the instructions if applicable. Include any student handouts here.]

OPTIONAL SECTIONS (other sections you can add if applicable)
Suggestions and materials for assessing student learning
Student data

Student assignments related to the activity
Any other appendices appropriate for your particular activity

Reference list

Mexican Beaded Lizard Scan
https://www.morphosource.org/Detail/MediaDetail/Show/media_id/11873

https://www.ncbi.nlm.nih.gov/pubmed/16292255

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5577576/

http://www.venomdoc.com/lizard-venom-system-evolution

https://www.nationalgeographic.com/science/phenomena/2005/11/21/which-came-first-the-snake-or-the-venom/

https://www.theatlantic.com/science/archive/2015/11/reptile-scientists-bear-their-fangs-in-debate-over-venom/413485/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC551567/

https://www.nature.com/articles/nature04328

https://allyouneedisbiology.wordpress.com/2016/05/02/venomous-lizards/

https://www.newscientist.com/article/dn8331-lizards-poisonous-secret-is-revealed/

https://en.wikipedia.org/wiki/Toxicofera

Venom in gland of rattlesnake- https://www.ncbi.nlm.nih.gov/sra/ERX2690652[accn] and https://www.ncbi.nlm.nih.gov/sra/ERX2690653[accn]

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4516934/

Evolution of Venom https://en.wikipedia.org/wiki/Squamata

Shrews
https://www.researchgate.net/publication/43352028_Salivary_Gland_Adaptations_Modification_of_the_Glands_for_Novel_Uses

https://www.google.com/imgres?imgurl=https%3A%2F%2Fwww.researchgate.net%2Fprofile%2FAbigail_Tucker%2Fpublication%2F43352028%2Ffigure%2Ffig1%2FAS%3A267442836471841%401440774749506%2FSchematic-of-the-lower-jaw-of-a-Solenodon-

Arrow-indicates-flow-of-venomous-saliva.png&imgrefurl=https%3A%2F%2Fwww.researchgate.net%2Ffigure%2FSchematic-of-the-lower-jaw-of-a-Solenodon-Arrow-indicates-flow-of-venomous-saliva_fig1_43352028&docid=BPAYY8ZDclOpgM&tbnid=Mjb5hpZr4SW9_M%3A&vet=10ahUKEwjtn6WFjvbiAhXGxFkKHYyyDt4QMwi7AShcMFw..i&w=375&h=232&bih=610&biw=1280&q=solenodons%20teeth&ved=0ahUKEwjtn6WFjvbiAhXGxFkKHYyyDt4QMwi7AShcMFw&iact=mrc&uact=8

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0079092

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2690028/

Venom in medicine

https://www.sciencedaily.com/releases/2015/02/150224091828.htm

https://www.sciencedaily.com/releases/2016/02/160229082005.htm

Global perspective of snake bites https://www.idigbio.org/content/research-spotlight-september-2018

California Ground Squirrels are awesome

https://www.ucdavis.edu/news/feisty-squirrels-hold-clues-treatment-rattlesnake-bites

https://www.scientificamerican.com/article/squirrel-hot-tail-tell-snakes/

VENOM: TO KILL OR CURE?

In this case study, students will explore concepts of evolution, protein structure and function, taxonomy, and methods of scientific inquiry in a real-world way. Students will use 3D images, on-line resources, and published scientific papers to explore these topics related to venom while making inferences and evaluating their thinking related to taxonomic relationships and evolution. The case study should open lines of inquiry with additional questions that students can explore as an extension.

Case Narrative

Tamiko and Bridget were enjoying a walk through the woods near Tamiko's house on a warm evening in Florida. As they were walking through the brush, Bridget jumped and screamed in fear and pain. Tamiko looked down and saw a well-camouflaged snake that had struck out and bit Bridget on the ankle. By the time she'd spotted the venomous viper hidden under a bush, it was too late—the snake had already injected her with its deadly neurotoxins.

Within seconds, Bridget started feeling the effects: blurred vision and jelly-like legs. She started sweating profusely and had difficulty breathing. Tamiko could tell that Bridget was panicking and knew she had to keep her calm. Tamiko called her mother who came and took them immediately to the local hospital.

The Emergency Room took Bridget in immediately and asked me a lot of questions about what kind of snake bit her. I did my best to describe it since the nurses told me it was important to know the type of snake. After that, the doctors began administering vials of antivenin to Bridget.

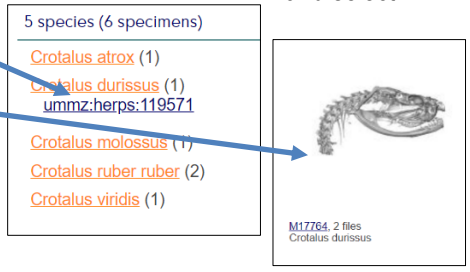
Tamiko wondered about how the snake was able to inject her friend with the venom so quickly and efficiently. She also wondered why the people at the emergency room needed to know what kind of snake bit Bridget. She began to do some research online about snakes and venom. At a site for the Florida Museum, she found an image that was like the snake she saw bite Bridget. It seemed to be an Eastern Diamondback Rattlesnake. The Florida Museum had a lot of information about that snake (https://www.floridamuseum.ufl.edu/herpetology/fl-snakes/list/crotalus-adamanteus).

Tamiko was thrilled to learn that the Blackburn Lab at the University of Florida was working on digitizing images of reptiles and amphibians and decided to look into the physical structures of the snake that allow it to inject venom. Tamiko used MorphoSource, one program that researchers at UF were using to share specimen data.

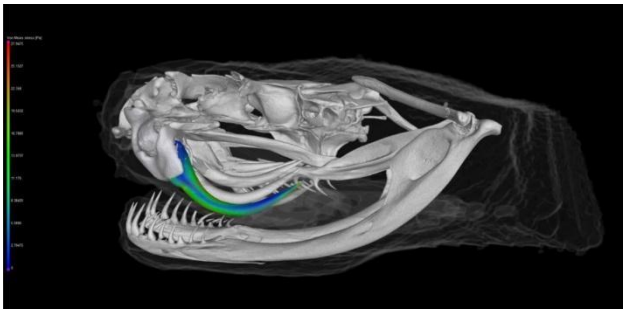
Image Source: https://en.wikipedia.org/wiki/Crotalus

I. SNAKE MORPHOLOGY

- Go MorphoSource at https://www.morphosource.org/Browse/Index
- Click "Browse" and "Taxonomy".
- Select "Chordata" and then "Reptilia" and then "Squamata" and then "Viperidae" and "Crotalus".
- On the right, you will see species listed. Click on "Crotalus durissus" and select the specimen number that appears below it in blue.
- Scroll down until you see the image of the specimen and click on it. Then, click on the same image again in the next screen.
- The image will then open as a 3D file that you can zoom and rotate. Take a few minutes to look at the snake skull.



1. **DESCRIBE** the structure of the bones around the fangs.



Crotalus adamantius, UF Specimen # UF103268, Stanley, E.

2. Go back to the page with the species options for Crotalus and select "Crotalus viridis". Look at the skull of this snake. **DESCRIBE** the similarities and differences between the two skulls.

3. Pit vipers (Species *Crotalus*) generally have fangs that work like hypodermic needles. (see image to the right) They are hollow and have a venom canal attached from a primary venom duct.

   However, other species of venomous snakes have different venom delivery systems. Read the Science Daily article "Biophysics of snakebites: How do venomous snakes inject venom into victim's wound?" at https://www.sciencedaily.com/releases/2011/05/110516121728.htm.

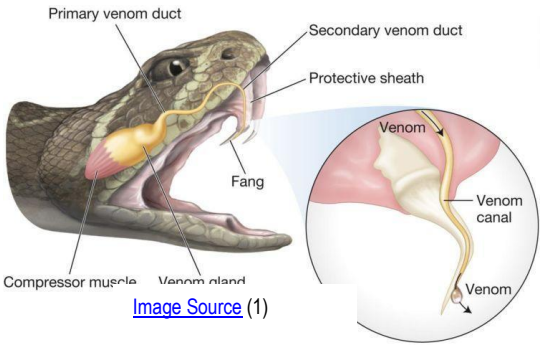


Image Source (1)

   Based on the text, **DESCRIBE** the other method of venom delivery.

   Based on the text, deeper grooves in teeth were an advantage in snakes that fed on birds. **IDENTIFY** why this was an advantage and **CONNECT** that idea to the idea of Descent with Modification/Evolution. Would snakes with longer fangs and/or deeper grooves be more likely to survive and reproduce?

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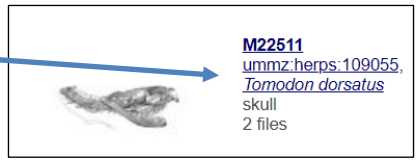
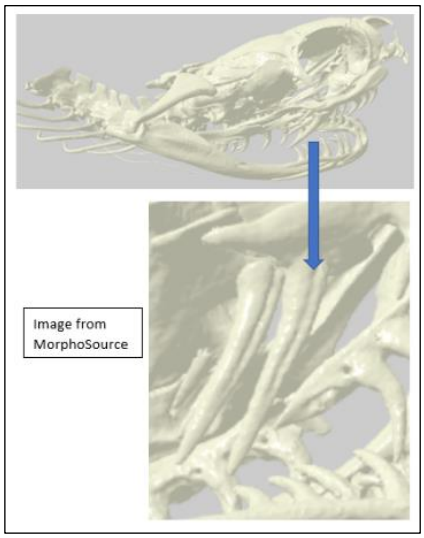
4. Go back to MorphoSource and in the search box at the top right, enter "Tomodon dorsatus" and click on the images to get to the 3-D model. Using the on-line 3D image or the image to the right, **DESCRIBE** how the teeth are similar and different to the rattlesnake.





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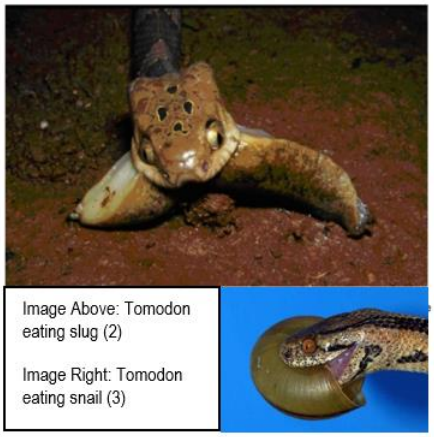

Image Above: Tomodon eating slug (2)

Image Right: Tomodon eating snail (3)

Tomodon is a snail and slug eater. Based on what the Tomodon and the Crotalus prey on, **DESCRIBE** the evolutionary advantage for each that might explain the difference in teeth structures.

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5. **DESCRIBE** characteristics of a common ancestor of both species of snakes based on the idea of Descent with Modification. _____

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6. **DESCRIBE** the method of organization of MorphoSource. What do the terms like "Chordata", "Reptilia", and Crotalus" tell you about the specimen you are searching for? _____

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7. **DEFINE** the term "morphology". **EXPLAIN** why the program that we were using is likely called *Morpho*Source.

II. VENOM

Tamiko considered what she had learned about different snakes and their morphology related to venom delivery. She realized that venomous snakes were classified by similarities, one of which is their morphology. In her research, she had also learned that snakes can have different venoms. "This is why the doctors were so intent on figuring out which snake bit Bridget- they had to get the right anti-venin", Tamiko thought.

In her research, Tamiko had also read about different types of venom. For example, hemotoxic venom works on the blood while neurotoxic venom works on the nervous system. Tamiko wanted to do more research on how venom works and how anti-venin is used. Tamiko started with an article she found on BiologyDiscussion.com entitled "*Poisonous Snakes: Biting Mechanism, Effect and Treatment*" where she found an informative chart.

1. Look at the first compound on the list in Table 29. Proteases are enzymes that break down proteins into individual amino acids. Using what you know about protein structure (or with research), **EXPLAIN** the primary and secondary structure of proteins. Be sure to use the terms polypeptide, amino acids, and peptide bonds.

Table 29: Showing the components of different snakes venom with occurence and effects on human beings (Sources from Deoras, 1965, Bellairs, 1969 and McFarland et al., (1985).

Name of the compounds	Occurrence	Effects
1. Proteases	All snakes	Necrosis; helps in the digestion of the tissues and blood coagution.
2. Hyaluronidase	All snakes	Increases tissue permeability and thus helps in the spreading of toxic substances.
3. Phospholipase A	All snakes	Hydrolyse lecithin to lysolecithin and cause haemolysis.
4. Cholinesterase	Elapids	Block the transmission of nerve impulses.
5. L-amino acid oxidase	Many colubrid snakes	Cause massive tissue destruction.
6. Phosphatases	All snakes	Destroy cell membranes and cause haemolysis.
7. Nucleases (Deoxyribonuclease and Ribonuclease)	All snakes	Cause hydrolysing phosphodiester bonds in DNA and RNA.
8. Neurotoxin	Cobra	Exerts actions on the nervous tissues and causes paralysis.
9. Haemolysin	All snakes	Release haemoglobin from RBC.
10. Crotamine	Tropical rattle snake	Produces paralysis in the posterior part of the body.
11. Cardiotoxin	Indian cobra	Produces a sharp fall in blood pressure and causes heart stop.

2. Proteases are enzymes. **DEFINE** the term enzyme. _____

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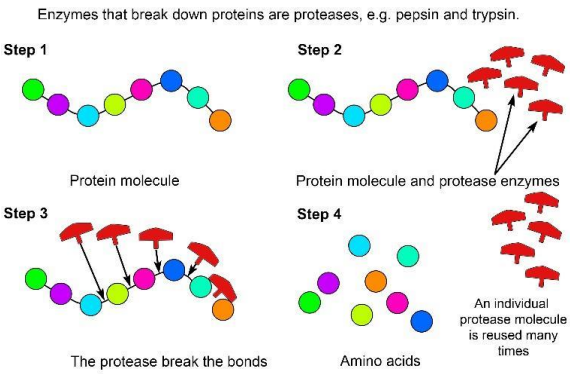
3. Proteases are found in saliva and are used in digestion by breaking bonds between molecules. Using the diagram to the right, **DESCRIBE** how proteases act as enzymes.



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4. Specifically, the protease in snake venom catalyze reactions that break down protein peptide bonds in tissues, causing blood-vessel wall damage and hemorrhaging. **DESCRIBE** how this catabolic process could be fatal.

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5. Evolution is decent with modification. **CONNECT** the idea that many compounds found in venom are also found in non-venomous organisms or used in other ways in living things. **EXPLAIN** how this supports the idea that organisms are descended from a common ancestor. _____

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MEDICINE AND SIGNALING

ADAPTATIONS FOR VENOM IMMUNITY IN PREY LIKE OPOSSUM AND CA GROUND SQUIRREL

BLAST?

CONVERGENT EVOLUTION OF VENOM- Genetics is important to classify vs just morphology/ morphology can give false relationships

INDIVIDUAL QUESTION AND RESEARCH

Venom Evolution

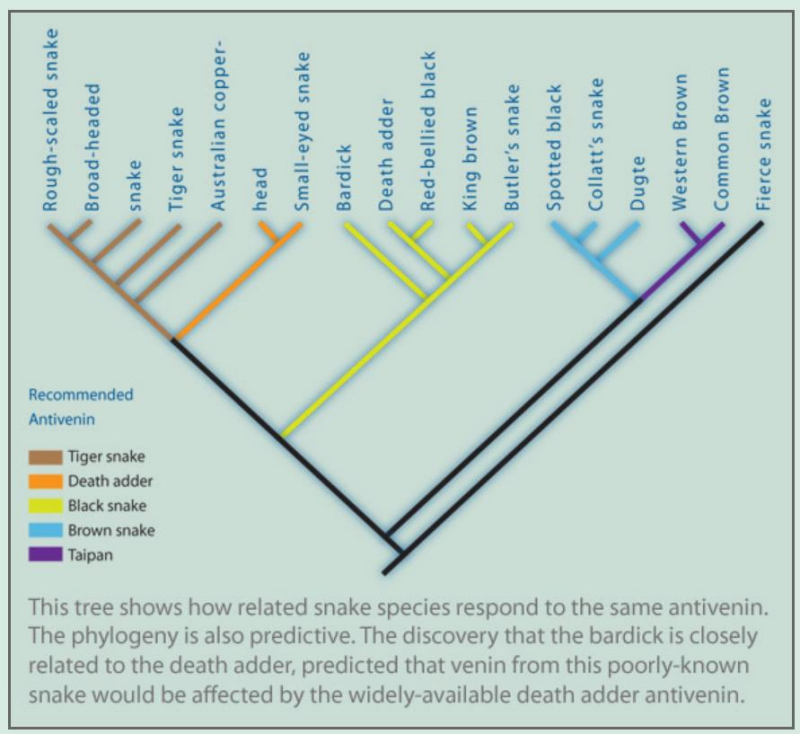
Adam Hargreaves explained: "Our work shows that genes which have gone on to duplicate and mutate to produce venom toxins were ancestrally expressed in lots of body tissues, including the salivary gland of non-venomous reptiles. This is different to the previously accepted idea that the genes were recruited from different body tissues to the venom gland. Our results give us a new insight into how venom toxins evolved in reptiles which we can use as a starting point to better understand the origins of this remarkable evolutionary adaptation, and also to aid research efforts into developing better treatments for victims of snakebite." (https://phys.org/news/2014-08-snake-venom.html)

From genome to “venome”: Molecular origin and evolution of the snake venom proteome inferred from phylogenetic analysis of toxin sequences and related body proteins Bryan G. Fry Australian Venom Research Unit, Level 8, School of Medicine, University of Melbourne, Parkville, Victoria 3010 Australia;

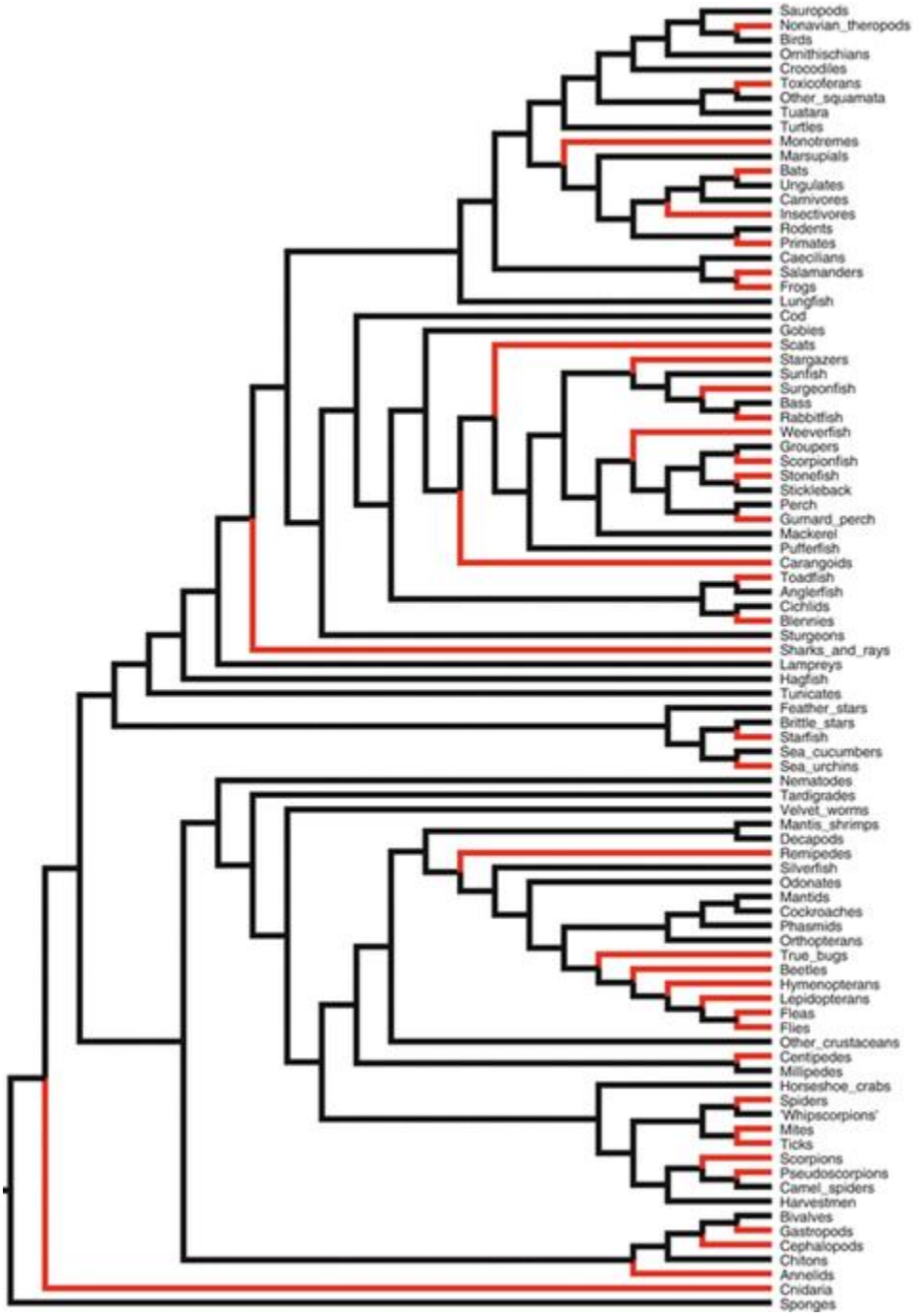
SWISS-PROT Group, European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SD, United Kingdom

III. Venomous Animal Taxonomy

Watch the video from the American Museum of Natural History on "Bites, Stings, Spines, and Spurs" at https://www.youtube.com/watch?v=BjVfZr8UlpE&feature=youtu.be and watch the video.



This tree shows how related snake species respond to the same antivenin. The phylogeny is also predictive. The discovery that the bardick is closely related to the death adder, predicted that venin from this poorly-known snake would be affected by the widely-available death adder antivenin.



Resources

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Image Sources:

(1) https://www.google.com/imgres?imgurl=https://cdn-image.hipwee.com/wp-content/uploads/2017/04/hipwee-kobra4-750x474.jpg&imgrefurl=https://www.hipwee.com/hiburan/katanya-digigit-ular-king-kobra-rasanya-kayak-digigit-serangga-kulitnya-terbuat-dari-apa-sih/&docid=zxW74q24EffJuM&tbnid=p8qEZvQn-QgvgM:&vet=1&w=750&h=474&hl=in-ID&source=sh/x/im