

RESEARCH NOTES: Venom-Immune Acetylcholine Receptors

Cells speak to each other in the language of electricity and chemistry. Electrical impulses travel down the long cable-like extensions of nerve cells and trigger the release of special chemicals (neurotransmitters) at their tips. These chemical messengers diffuse across a narrow gap to the adjacent tip of a neighboring nerve cell. There they bind to a special receptor protein in the cell membrane, and trigger a new electrical signal that speeds on. If the next cell is a muscle cell, the receptor's binding of the chemical messenger can trigger molecular contraction. In many cases, the neurotransmitter is acetylcholine, a small molecule which exactly fits its receptor like a key fits its lock.

The venom of cobras and several other poisonous snakes is deadly in extremely small amounts because it contains toxin molecules which can bind to acetylcholine receptors on the muscle cell's surface, preventing the body's own chemical "Contract!" messages from getting through. This is particularly vital in the case of heart and diaphragm muscles. But if the toxins are so deadly, why don't they kill the snakes themselves?

Israel NSF grantee Prof. S. Fuchs and colleagues have found subtle, but crucial, differences between

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modified snake receptors.

These findings also solve another puzzle. The cat-size, Indian mongoose routinely fights, kills and lunches on cobras with no ill effects. A detailed study of the acetylcholine receptors on the surface of mongoose muscle cells show that they have four toxin-rejecting chemical variations at their binding sites. These differ from the highly conserved acetylcholine binding region in all other mammals, but resemble those of the cobra themselves, giving these plucky mammals equal immunity.

Point mutation studies show that two prolines at the binding site are essential (and two aromatic amino acids are useful) for toxin binding. Toxin-resisting mutations lead to phosphorylation and protection in both snakes and

mongooses, albeit at different positions. Since snakes are biologically very far from mammals, whereas mongooses are quite similar to rats and other rodents, the mongoose represents a more useful, not to mention far safer, model for future studies on acetylcholine interactions at the molecular level.

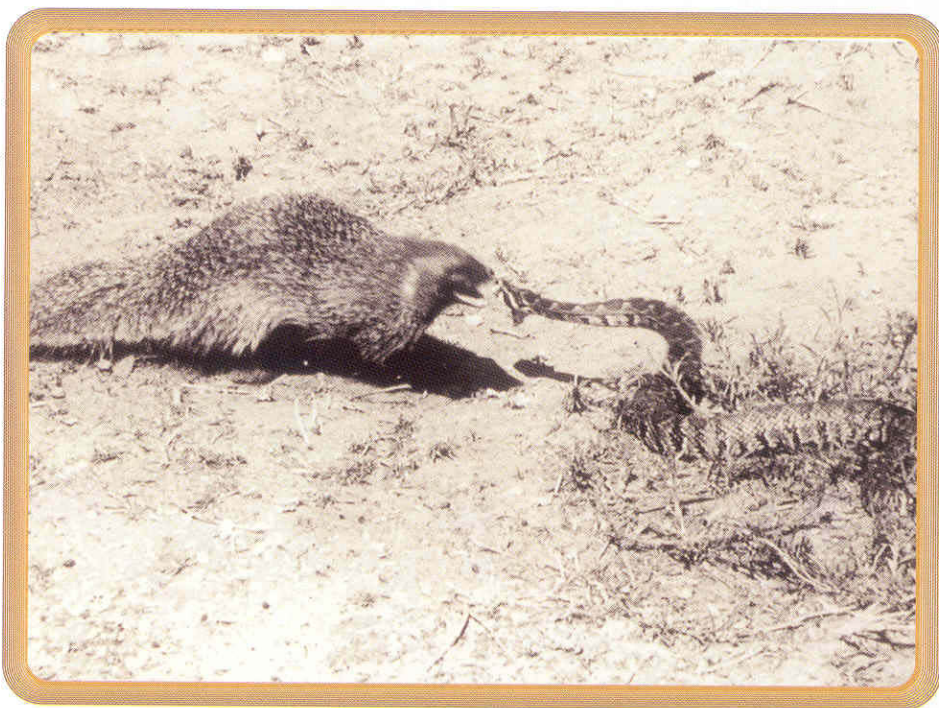


Photo Credit: A. Shoob, Tel Aviv University

Mongoose and soon to be eaten cobra square-off.

the amino acid sequences that make up the acetylcholine receptors of the snakes and those of their victims. In fact, four amino acids, all located near the acetylcholine binding site, are different and determine the resistance of these snakes to their own toxins. The results? Only acetylcholine, and not its toxin competitor, can bind these