RESEARCH NOTES: Venom-Immune Acetylcholine Receptors

Cells speak to each other in the anguage of electricity and chemistry. Electrical impulses travel down the ong cable-like extensions of nerve ells and trigger the release of special hemicals (neurotransmitters) at their ips. These chemical messengers iffuse across a narrow gap to the djacent tip of a neighboring nerve ell. There they bind to a special eceptor protein in the cell membrane, nd trigger a new electrical signal hat speeds on. If the next cell is muscle cell, the eceptor's binding f the chemical nessenger can rigger molecular ontraction. In nany cases, the eurotransmitter is cetylcholine, a small nolecule which xactly fits its eceptor like a key ts its lock.

The venom of cobras nd several other oisonous snakes s deadly in xtremely small mounts because it ontains toxin nolecules which can bind to cetylcholine receptors on the muscle ell's surface, preventing the body's wn chemical " Contract!" messages om getting through. This is articularly vital in the case of eart and diaphragm muscles. But the toxins are so deadly, hy don't they kill the snakes emselves?

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

If the toxins are so deadly, why don't they kill the snakes themselves?

Photo Credit: A. Shoob, Tel Aviv University

Mongoose and soon to be eaten cobra square-off.

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.