Unraveling the mysteries of poison

April 13 2006

Researchers from the Max Planck Institite for Biophysical Chemistry and other German and French colleagues have combined magnetic resonance spectroscopy (solid-state NMR) with special protein synthesis procedures to uncover how potassium channels and toxins combine and change in structure. This work could make it possible to develop medications for high blood pressure and many other diseases connected to potassium channel failure (*Nature*, April 13, 2006).

Our body's cells have membranes, and "ion channels" are embedded in them. Ion channels are special proteins which let only certain ions through the membrane. The channels build an electro-chemical gradient, allowing nerve and heart muscle cell signals to pass. The nerve or heart muscle cell is excited, and the ion channel structure changes, developing pores which let the ions through. Different channels are open to different specific ions; for example, potassium channels only allow potassium ions through. Poisonous animals use very specific toxins to target channels; the toxins block the channels and make it impossible for electric signals to move through the membrane – often killing the cell.

These kind of interactions had not been well investigated at a structural level – even though scientists had made great strides studying ion channels, using x-ray crystallography. Scientists from the Max Planck Institute for Biophysical Chemistry in Göttingen, working together with researchers from the Institute for Neural Signal Processing in Hamburg and French colleagues from the University of Marseille, combined a new method of solid-state NMR with particular protein synthesis procedures and looked at the example of poison from the north African scorpion

Androctonus mauretanicus mauretanicus, to determine how bacterial potassium channels interact with toxins at an atomic level.

The researchers first examined the electrophysiological characteristics of the "poisoned" channel protein. The scientists "spin-marked" some of them and investigated them with solid-state NMR. Spin-marked proteins contain carbon and nitrogen atoms with an intrinsic magentic moment (spin) which strengthens the NMR's signals. Looking at spectroscopic data before and after the toxin affected the channel, it turned out that the poison attaches to a particular area of the channel – the pore region – and changes the area's structure. The poison is thus only effective when it recognises a particular amino acid sequence in the ion channel. It is also important how intrinsically flexible the binding partner is; for a strong interaction to take place, the molecules of both partners have to be able to change their structures.

Applying these new spectroscopic methods, scientists are now better understanding the pharmacology and physiology of potassium channels. This could lead to better, more specific medications.

Source: Max-Planck-Gesellschaft