

A Cell's Private Life: Researchers Peer Inside a Hidden Protein

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(PhysOrg.com) -- To understand the molecular machinery of the human body, scientists have to be able to observe the structure of cellular proteins. This has been particularly challenging for those proteins embedded in cellular membranes. Now researchers from the Yale School of Medicine have established a novel way to peer inside this hidden universe, obtaining the first close-up look at a membrane-embedded potassium ion channel that, when defective, can cause high blood pressure or epilepsy. The research appears August 30 in *Nature's* Advance Online Publication.

The Yale team was able to visualize the so-called "BK" channel protein by using single-particle reconstruction. In this technique, individual protein molecules are imaged in an electron microscope, and



information from thousands of images is combined to produce a threedimensional map of the <u>protein structure</u>. This was the first time this reconstruction technique was extended to proteins embedded in membranes.

The researchers were able to see the BK channel protein's voltage sensors, the calcium-sensing domains and other aspects of this critical cellular component. "The technique opens up a new way to study the many important molecular machines of cellular membranes," said Fred Sigworth, Ph.D., of the Department of Cellular and Molecular Physiology at the Yale School of Medicine. "These machines include pumps, transporters and receptors as well as ion channels like the one visualized here."

Although the first map did not have high resolution, Sigworth and his coauthor Liguo Wang, Ph.D., say they are optimistic that better 3-D visuals will be obtained in the future. Furthermore, this technique will now allow the proteins to be caught in the act as they respond to cellular signals and transport their molecular cargoes across membranes.

Provided by Yale School of Medicine

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