Medical Xpress

Complex channels

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The messages passed in a neuronal network can target something like 100 billion nerve cells in the brain alone. These, in turn communicate with millions of other cells and organs in the body. How, then, do whole cascades of events trigger responses that are highly specific, quick and precisely timed? A team at the Weizmann Institute of Science (Israel) has now shed light on this mysterious mechanism.

Their discovery could have important implications for the future development of drugs for epilepsy and other nervous system diseases. These findings were recently published in the journal *Neuron*.

The secret is in the control over electrical signals generated by cells. These signals depend on ion channels – membrane proteins found in excitable cells, such as nerve cells – that allow them to generate electrical signals, depending on whether the channels are opened or closed. Prof. Eitan Reuveny, together with Ph.D. students Inbal Riven and Shachar Iwanir of the Weizmann Institute's Biological Chemistry Department, studied channels that work on potassium ions and are coupled to a protein called the G protein, which when activated, causes the channel to open. Opening the channel inhibits the conductance of electrical signals, a fact that might be relevant, for example, in the control of seizures.

The G protein itself is activated by another protein, a receptor, which gets its cue to carry out its task from chemical messengers known as neurotransmitters. But neurotransmitters are general messengers – they can inhibit as well as excite, and the receptors can respond to either message. How, the scientists wanted to know, is the G protein targeted so quickly and precisely to activate the channel?

Reuveny and his team found that the receptor and G protein are physically bound together in a complex, allowing the process to be finely tuned. When the receptor receives a chemical message from the neurotransmitter, it is already hooked up to the correct G protein. After being activated by the receptor, the G protein changes shape, opening the ion channel. The evidence for this complex structure came from special technique called FRET (Fluorescence Resonance Energy Transfer) that can measure the distance between two molecules. The scientists observed that even without stimulation, there is a lot of energy transfer between the G protein and the potassium channel, suggesting that they are very close together.

Mutations in ion channels are likely to be involved in epilepsy, chronic pain, neurodegenerative diseases and muscular diseases, and ion channels are the target of many drugs. Understanding the basic biological phenomena behind the way proteins organize themselves and orchestrate biological processes may allow scientists to design better or more efficient drugs.

Source: American Committee for the Weizmann Institute of Science