Discovery of the Function of Ion Channels in Cells

1991 Nobel Prize Medicine

In the year 1991, Erwin Neher and Bert Sakmann were awarded the Nobel Prize in Medicine or Physiology for their seminal discovery of the functions and mechanisms behind an ion channel in cells.

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Background

Cells are the basic building blocks of a living organism. Our bodies are composed of billions and billions of cells with varying forms and functions. Cells from the same type cluster together to form a tissue; tissues with similar function forms an organ; and different organs acting together in a coordinated manner forms a living organism.

This means that each cell has a designated function that it must accomplish to sustain the life of the organism. To be able to perform their specific functions, the cells must be capable of communicating with other cells within the same tissue to execute a coordinated action. Moreover, cells must also have the capability to communicate with cells from a different type of tissue to execute a coordinated action in the organ level. Furthermore, cells from an organ must communicate with cells from another organ to execute a coordinated action of the living organism.

The question now is how do cells communicate? Each cell is bounded by a membrane that isolates it from its environment, the extracellular environment. However, the cell membrane has channels that link the extracellular environment with the interior of the cell. This is the way by which cells communicate with each other.

The Minds Behind the Discovery

Erwin Neher was born on the 20th of March 1944 in Landsberg, Bavaria. In the fall of 1963, he took up physics at the 'Technische Hochschule' in Munich and finished in 1966. After finishing physics, he earned a scholarship to study biophysics in the US at the University of Wisconsin at Madison. In 1967, he went back to Munich to start Ph.D. projects in Biophysics and he met Dr. Lux who was investigating synaptic mechanisms in motor neurons and ion currents in snail neurons. During the years when he worked with Dr. Lux, he met Bert Sakmann who was working on a Ph.D. project in the same laboratory facility. The two scientists met again in 1973 in Gottingen where they started to work together on a research project.

Bert Sakmann was born on the 12th of June 1942 in Stuttgart, Swebia. His family initially thought that he will be an engineer due to his interest in motors and aeroplanes. In the final years of his early schooling, he learned about cybernetics and its possible application to biology. He then enrolled at the medical school faculty of Tubingen University. After passing all his medical exams, he became fascinated with neurological synaptic connections. He was convinced that he needed more knowledge on cellular physiology to understand synaptic connections. To gain more knowledge, he joined Dr. Dieter Lux’s laboratory and met Erwin Neher who taught him voltage clamping. Due to the great similarity between their interests, Neher and Sakmann decided to venture into a new research study as a pair.

The Discovery

The cell membrane is impermeable to ions, so ionic currents are carried through the membrane by specialized protein molecules called ion channels that span the membrane. Upon sensing a chemical stimulus, the ion channels change shape creating a pore in the cell membrane through which ions can flow. Such an idea of ion channels already existed during the 1950's especially when Bernard Katz at University College London worked on synaptic transmission from motor nerve to muscle. By the early 1970's there was enough indirect evidence about the channels to guess that a current of a few picoamps must flow through each channel. However, the machines during those days were not capable of measuring such tiny currents.

The world was stunned when Neher and Sakmann were able to observe the currents through

a single ion channel by means of their new method called patch clamp technique.

The new method allowed them to watch the activity of a single molecule, a technology that was considered fiction during those times. The method entails touching a micropipette with a tip diameter of about a thousandth of a millimeter against the external surface of the cell membrane in such a way that a high resistance seal is formed between the glass and the membrane, thus isolating a very small area of membrane.

When an ion channel opens in this patch of membrane, ions will move through the channel as an electric current, the current flows up the micropipette and can be measured with a sensitive ammeter. It was through this technique that the presence of ion channels was confirmed with sufficient physical evidence and the processes that take place within a single ion channel were uncovered.

Succeeding Studies

Neher was also able to elucidate the mechanisms behind the secretory process. He showed that different secretory agents are stored in secretory vesicles within the cell and when the cell is stimulated, the vesicles move closer to the cell membrane. The membrane of the vesicles then fuses with the cell membrane to release the secretory agents. He was able to show this by measuring the changes in the electric property of the cell membrane during its fusion with the secretory vesicle’s membrane by using a refined patch clamp technique.

Clinical Implications

The major contribution of this discovery was the enormous use of the patch clamp technique. This technique was combined with the new methods to study the different parts of the ion channels in cells. Through this procedure, it has been possible to identify what makes an ion channel select only one type of ion, or be sensitive to a particular type of chemical transmitter. Through this technique, our standard research procedures to study ion channels have been changed and became more efficient, more valid and more specific.

Researches are now being conducted about the participation of ion channels during the secretion of insulin by the pancreas, when the heart is contracting, or when we think or remember something. Drugs now are being developed to target specific types of ion channel, which are of importance in disease like anxiety, cardiovascular disease, epilepsy, and diabetes.
