Optogenetics -- Combination switch turns neurons on and off

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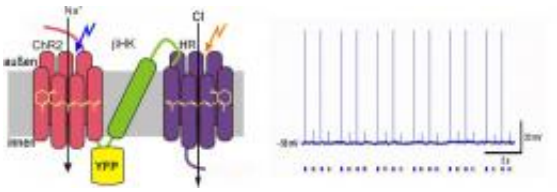

Molecular combination switch: two light-sensitive membrane proteins - here red and purple - are linked via a connecting piece (green) and anchored into the cell wall (left). When the cell is illuminated with blue light, it allows positively charged ions in. Orange light has the opposite effect, allowing negatively charged ions into the cell. The cell is activated or deactivated, respectively (right). © MPI of Biophysics

(PhysOrg.com) -- Flies that display courtship behaviour at the press of a button, worms made to wriggle by remote control: since the dawn of optogenetics, scientists can turn nerve cells on and off using pulses of light. A research team at the Max Planck Institute of Biophysics in Frankfurt am Main has developed a molecular light switch that makes it possible to control cells more accurately than ever before. The combination switch consists of two different light-sensitive membrane proteins – one for on, the other for off. The method used by the scientists to connect the two components can be used with different protein variants, making it highly versatile.

Optogenetics is a new field of research that aims to control cells using

light. To this end, scientists avail of light-sensitive proteins that occur naturally in the cell walls of certain algae and bacteria. They introduce genes with the building instructions for these membrane proteins into the DNA of target cells. Depending on which proteins they use, they can fit cells with on and off switches that react to light of different wavelengths.

For accurate control, it is important that the cell function can be switched off and on equally well. This was exactly the problem until now: when the genes are introduced separately, the cell produces different numbers of copies of each protein and one type ends up dominating.

A group of scientists headed by Ernst Bamberg at the Max Planck Institute of Biophysics has now developed a solution that is both elegant and versatile: they have located the genes for the on and off proteins on the same portion of DNA, along with an additional gene containing the assembly instructions for a connection piece. This interposed protein links the two switch proteins and anchors them firmly in the cell membrane. “In this way, we can ensure that the on and off switches are built into the cell wall side by side, and always in a ratio of 1:1. This allows us to control the cell with great accuracy”, explains Ernst Bamberg.

The combination light switch conceived by the researchers consists of the membrane proteins channelrhodopsin-2 and halorhodopsin. Channelrhodopsin-2 originally comes from the single-celled green alga Chlamydomonas reinhardtii. It reacts to blue light by making the cell wall permeable to positively charged ions. The resulting influx of ions triggers a nerve impulse that activates the cell. Halorhodopsin, isolated by scientists from the bacterium Natromonas pharaonis, has the opposite effect: when the cell is illuminated with orange light, it allows negatively charged ions in, suppressing nerve impulses.

Since channelrhodopsin-2 and halorhodopsin react to light of different wavelengths, together they comprise a useful tool for switching cells on and off at will. The scientists have shown that the method they used to connect the two molecules is also suitable for use with other proteins. “By linking different proteins as required, we will be able to control cells with much greater accuracy in future”, affirms Bamberg.

More information: Sonja Kleinlogel, Ulrich Terpitz, Barbara Legrum, Deniz Gökbuget, Edward S Boyden, Christian Bamann, Philip G Wood & Ernst Bamberg, A gene-fusion strategy for stoichiometric and co-localized expression of light-gated membrane proteins, *Nature Methods*, Vol. 8(12); DOI:10.1038/NMETH.1766

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