Moving cells with light holds medical promise

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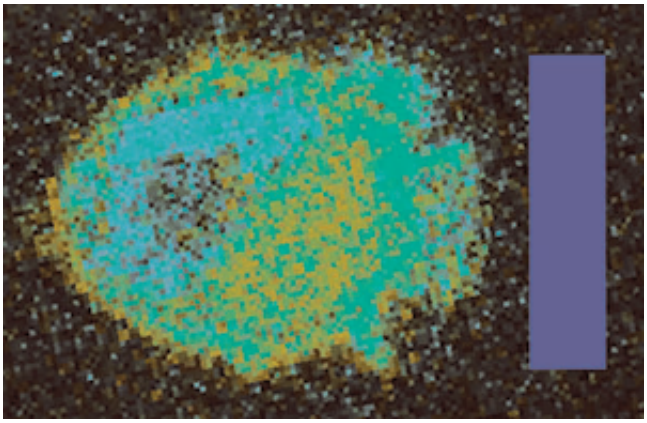

This image shows an immune cell moving toward a light beam (blue box). The opsin in the cell (red) senses light and triggers the formation of new structures of the cell skeleton (yellow) that allow the cell to move. Credit: Copyright *PNAS*, doi: 10.1073/pnas.1220755110

Scientists at Washington University School of Medicine in St. Louis have shown they can coax cells to move toward a beam of light. The feat is a first step toward manipulating cells to control insulin secretion or heart rate using light.

Their research is published April 8 in the *Proceedings of the National Academy of Sciences* Online Early Edition.

"We have succeeded in using light as a kind of on-off switch to control cells' behavior," says principal investigator N. Gautam, PhD, a professor of anesthesiology. "Much of the way cells behave is due to their ability

to sense signals in the environment. In these experiments, what the cells sense is the presence of light."

The new research focuses on immune cells. By adding a light-sensitive protein to the cells, the scientists could direct cells to move simply by shining a laser in the direction they wanted a cell to travel (see accompanying video).

"We were interested in the idea that you could activate receptors on a single area of a cell's exterior," says Gautam. "It's what happens naturally when an immune cell senses something amiss in its environment and then migrates toward that potential trouble, perhaps a bacterial infection or inflammation."

The researchers used genetic engineering techniques to introduce a light-sensing protein, called an opsin, into immune cells. Humans and other animals make opsins in the eye, and when activated by light, they allow cells in the eye to translate light signals into vision.

Gautam and the study's first author, Ajith Karunarathne, PhD, postdoctoral research associate in anesthesiology, introduced several different opsins into immune cells. After demonstrating that those cells had an affinity for light, the researchers performed the same experiment with nerve cells, with equal success. The idea is to "trick" the cells into thinking that the opsin is a normal receptor protein.

The light-sensing opsin they snuck into immune cells and nerve cells belongs to a family of receptors that recently has been in the spotlight. These are G protein-coupled receptors whose importance was recognized in the awarding of the 2012 Nobel Prize in Chemistry. The same receptors play a key role in vision, smell, behavior and mood, regulation of the immune system, heart rate and the spread of some tumors.

In another study also published recently in the *Proceedings of the National Academy of Sciences* Online Early Edition, Gautam's team made nerve cells grow branches, called neurites, when the cells were exposed to light. Currently, the laboratory is working with cardiac cells to test whether light signals can speed up or slow down the rate at which heart cells pulse.

"Eventually, we would like to introduce multiple light-sensing proteins into these cells," says Karunarathne. "The idea would be to use two different wavelengths of light. That way, when you shine one light for example, it could signal the first light-sensing protein to make the heart beat faster. Then a different wavelength of light could be used to slow down the heart rate."

In future studies, the researchers plan to use the same kind of strategy to learn whether light can influence insulin secretion and the regeneration of nerve cells. They also are using the approach to study signaling circuitry in cells to find out how networks of molecular pathways control cell behavior.

"This strategy can be valuable," Gautam says. "We can control migration of cells, which is important not only to the immune system but also during embryonic development to ensure that cells that make the heart, liver and other organs go to the right place. It's also key in cancer metastasis, when a tumor releases cells that migrate to other parts of the body. We are excited by the many possibilities."

More information: Karunarathne WKA, Giri L, Patel AK, Venkatesh KV, Gautam N. Optical control demonstrates switch-like PIP3 dynamics underlying the initiation of immune cell migration. *PNAS Early Edition*, published online April 8, 2013
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