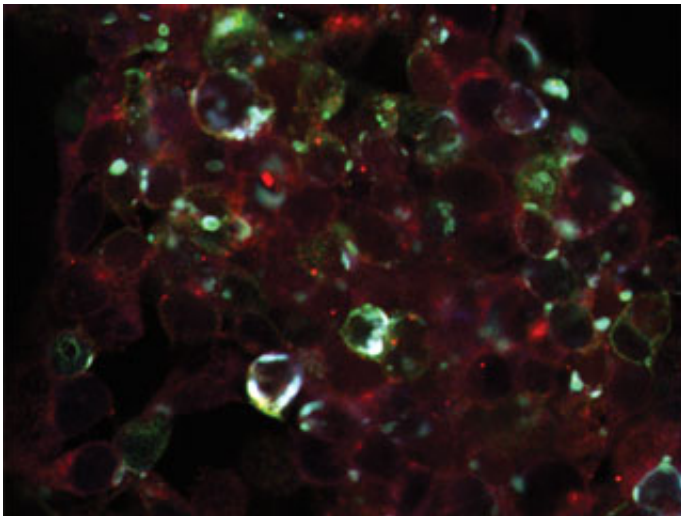


'Radiogenetics' seeks to remotely control cells and genes

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Researchers experimented with different configurations for their remote control system, and they found the best relies on an iron nanoparticle (blue), which is tethered by a protein (green) to an ion channel (red). Above, all three appear within cell membranes.

It's the most basic of ways to find out what something does, whether it's an unmarked circuit breaker or an unidentified gene—flip its switch and see what happens. New remote-control technology may offer biologists a powerful way to do this with cells and genes. A team at Rockefeller University and Rensselaer Polytechnic Institute is developing a system that would make it possible to remotely control biological targets in living animals—rapidly, without wires, implants or drugs.

Today (December 15) in the journal *Nature Medicine*, the team describes successfully using electromagnetic waves to turn on insulin production to lower [blood sugar](#) in diabetic mice. Their system couples a natural iron storage particle, ferritin, to activate an ion channel called TRPV1 such that when the metal particle is exposed to a radio wave or magnetic field it opens the channel, leading to the activation of an insulin producing gene. Together, the two proteins act as a nano-machine that can be used to trigger gene expression in cells.

"The method allows one to wirelessly control the expression of genes in a living animal and could potentially be used for conditions like hemophilia to control the production of a missing protein. Two key attributes are that the system is genetically encoded and can activate cells remotely and quickly," says Jeffrey Friedman, Marilyn M. Simpson Professor head of the Laboratory of Molecular Genetics at Rockefeller. "We are now exploring whether the method can also be used to control neural activity as a means for noninvasively modulating the activity of neural circuits." Friedman and his Rensselaer colleague Jonathan S. Dordick were co-senior researchers on the project.

Other techniques exist for remotely controlling the activity of cells or the expression of genes in living animals. But these have limitations. Systems that use light as an on/off signal require permanent implants or are only effective close to the skin, and those that rely on drugs can be slow to switch on and off.

The new system, dubbed radiogenetics, uses a signal, in this case low-frequency radio waves or a magnetic field, to heat or move ferritin particles. They, in turn, prompt the opening of TRPV1, which is situated in the membrane surrounding the cell. Calcium ions then travel through the channel, switching on a synthetic piece of DNA the scientists developed to turn on the production of a downstream gene, which in this study was the insulin gene.

In an earlier study, the researchers used only radio waves as the 'on' signal, but in the current study, they also tested out a related signal – a magnetic field –to activate insulin production. They found it had a similar effect as the radio waves.

"The use of a radiofrequency-driven magnetic field is a big advance in remote [gene expression](#) because it is non-invasive and easily adaptable," says Dordick, who is Howard P. Isermann Professor of Chemical and Biological Engineering and vice president of research at Rensselaer. "You don't have to insert anything—no wires, no light systems—the genes are introduced through gene therapy. You could have a wearable device that provides a [magnetic field](#) to certain parts of the body and it might be used therapeutically for many diseases, including neurodegenerative diseases. It's limitless at this point."

The choice to look at [insulin production](#) was driven by the equipment they used to generate the [radio waves](#) and magnetic fields. Because the coil that generates these signals is currently small i.e; only three centimeters in diameter, it was necessary to anesthetize the mice to keep them still. Since anesthesia can repress the production of insulin, the hormone that reduces blood sugar, Stanley and her colleagues designed the genetically encoded system to replace the insulin that is normally reduced by anesthesia in mice.

"Ferritin, a protein-coated iron storage molecule, is normally found throughout the mouse and human body, but in our experiments, we modified it, placing the ferritin particles in different positions to see if we could improve our results," says co-first author Sarah Stanley, a senior research associate in Friedman's lab. "We found tethering the ferritin to the channel to be most effective."

The team's positive results suggest other applications for the system. In late September, Stanley received a first-round BRAIN grant from the

ambitious federal initiative seeking to create a dynamic map of the brain in action. Stanley and colleagues plan to adapt this system to switch neurons on and off, and so examine their roles within the brain.

"In this current study, we've shown that by opening the TRPV1 channel to allow [calcium ions](#) to enter the cell, we can turn on a gene. Since neurons can be depolarized by calcium and other positively charged ions, such as those the TRPV1 channel controls, we hope that this system may be effective at regulating neural activity."

More information: "Remote regulation of glucose homeostasis in mice using genetically encoded nanoparticles." *Nature Medicine* (2014)
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