

Remote-controlled genes trigger insulin production

Nanoparticles heated by radio waves switch on genes in mice

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Researchers have remotely activated genes inside living animals, a proof of concept that could one day lead to medical procedures in which patients' genes are triggered on demand.

The work, in which a team used radio waves to switch on engineered insulin-producing genes in mice, is published today in *Science*¹.

Jeffrey Friedman, a molecular geneticist at the Rockefeller University in New York and lead author of the study, says that in the short term, the results will lead to better tools to allow scientists to manipulate cells non-invasively. But with refinement, he thinks, clinical applications could also be possible.

Friedman and his colleagues coated iron oxide nanoparticles with antibodies that bind to a modified version of the temperature-sensitive ion channel TRPV1, which sits on the surface of cells. They injected these particles into tumours grown under the skins of mice, then used the magnetic field generated by a device similar to a miniature magnetic-resonance-imaging machine to heat the nanoparticles with low-frequency radio waves. In turn, the nanoparticles heated the ion channel to its activation temperature of 42 °C. Opening the channel allowed calcium to flow into cells, triggering secondary signals that switched on an engineered calcium-sensitive gene that produces insulin.

After 30 minutes of radio-wave exposure, the mice's insulin levels had increased and their blood sugar levels had dropped.

Radio stars

"The great thing about this system is that radio-wave heating can penetrate deep tissue, and TRPV1 can focus that stimulus very locally to just where you have the nanoparticles," says David Julius, a physiologist who studies TRPV1 at the University of California, San Francisco.

Friedman says that his team did not develop the method as a way of managing diabetes; insulin and blood sugar levels simply provide convenient physiological readouts for checking that the remote control is working. "There are many good treatments for diabetes that are much simpler," he says. However, the system could potentially be engineered to produce proteins to treat other conditions.

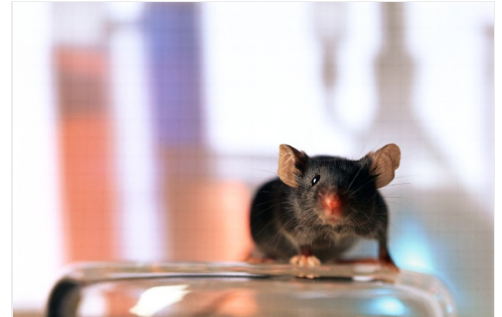
In control experiments, the researchers showed that the radio waves heated only cells that contained nanoparticles, and the heat neither killed the specialized cells nor spread to neighbouring, unmodified ones. "Magnetic fields are a good way to develop enough energy without doing harm," says Arnd Pralle, a biophysicist at the State University of New York at Buffalo, who has worked on stimulating neurons using nanoparticles heated by radio waves². However, he says, more research is needed to characterize fully how the nanoparticles absorb, retain and distribute heat.

Genetic therapy

The researchers also experimented with cultured cells genetically engineered to make their own nanoparticles, and found that they could stimulate a weaker insulin secretion in these cells, too. "What I found most novel about this is there's no need for any chemicals or small molecules to be administered," says Ed Boyden, a neurobiologist at the Massachusetts Institute of Technology in Cambridge, who helped to pioneer a method of using fibre optics to control neural activity with light³.

Friedman's current method is not practical for use in the clinic because it is not ethical to grow tumours in humans, so the researchers are planning to test alternative delivery systems for the nanoparticles.

"I think people intuit that someday nanotechnology will have an impact on human medicine," says Friedman. "We've extended the



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Radio waves remotely triggered the release of insulin in mice.

repertoire of what the particles can do in living animals.”

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References

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