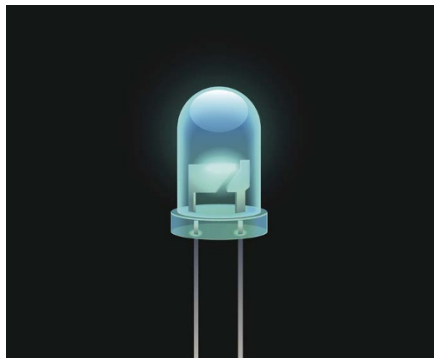
A new light switch for optogenetics

The ability to manipulate specific neurons and their circuits in awake-behaving animals would have been considered science fiction just a decade ago. With the advent of optogenetics, a technique that allows expression of light-activated proteins in defined populations of neurons, scientists can directly activate or silence neural activity with millisecond timing and cell-type precision. When combined with mice performing behavioral tasks, optogenetics can provide a causal link between neural activity and animal behavior.

Despite the successful use of optogenetics in many studies, technical constraints have limited its application. To deliver light into the brain and control optogenetically 'tagged' neurons during behavior, animals are often implanted with bulky optical devices and long cables connected to light sources, such as lasers and light-emitting diodes (LEDs). These can impair an animal's natural movements and limit the environmental conditions under which behavior can be studied.

To address this limitation, Ada Poon and colleagues at Stanford University (CA) developed a miniature and wirelessly powered optogenetic implant (*Nat. Methods* **12**, 969–974; 2015). Consisting of a small power coil and micro-LED, the device is only 4 mm in diameter and 50 mg in weight, a fraction of the size and weight of previous optogenetic implants. The device is fully biocompatible and can be implanted subcutaneously under the scalp or skin of mice without any protruding components. Because the implants are powered wirelessly and have a built-in LED, optical cables and power connectors are eliminated, leaving mice untethered and free to move naturally. Poon and colleagues tested the ability of their new implants to manipulate neural activity in mice under a variety of conditions that would be too difficult with bulkier and tethered implants. Using immunostaining and behavioral measurements, they confirmed successful optogenetic activation of neurons as mice maneuvered through enriched environments with tunnels and other enclosures, and under social conditions with multiple mice interacting in the same testing chamber.



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The study provides proof of concept for a novel optogenetic implant and gives a glimpse into the future of optogenetics. Without the constraints of bulkier implants, optogenetics could be unleashed to study how specific neurons and brain circuits drive complex behaviors, such as social decisions and communication. In a press release, Poon and colleagues say they also hope the implant will open the door to new treatments for movement disorders and other mental health conditions.

Dustin M. Graham

UNDERSTANDING THE HEARTS OF MICE AND MEN

During a myocardial infarction, or heart attack, cardiac tissue is deprived of oxygenated blood, which causes cardiomyocytes, the muscle cells of the heart, to die. This death of tissue impairs the heart's ability to function efficiently, and adult cardiomyocytes renew themselves at a low rate that effectively precludes regeneration of mature cardiac muscle. For this reason researchers studying cardiovascular disease are particularly interested in determining the age and conditions within which cardiomyocytes do proliferate. In humans it has been shown that most cardiomyocytes are generated during early childhood, but it was not known if or how this pattern of growth applies to other models of cardiovascular disease, including the mouse.

To address this question, Olaf Bergmann of Karolinska Institutet (Solna, Sweden) and colleagues isolated and examined hearts from mice, collected at different points during the first three weeks after birth. Bergmann's team used stereology, flow cytometry and immunohistochemistry in a variety of applications to determine cardiomyocyte counts, DNA synthesis and cell cycle activity change during early postnatal development in mice (*Cell* **163**, 1026–1036; 2015).

From these different approaches the researchers came to the conclusion that "in the uninjured neonatal mouse heart, up to 30% of all cardiomyocytes are generated even after postnatal day 2, and the full complement of cardiomyocytes (>95%) is reached after 11 days." This pattern of growth and development is similar to that seen in humans, with some minor differences. For instance, following early cell proliferation and DNA synthesis, approximately 60% of cardiomyocyte nuclei are polyploid in mature humans, whereas only 10% of cardiomyocyte nuclei are polyploid in mature mice. However, the authors note, the process by which cardiomyocytes become polyploid takes place at a similar stage in both species (during preadolescence). The researchers noted that in mice, this polyploidization occurs mainly during the second and third weeks after birth.

With these findings, Bergmann's team has improved upon the use of mice to study cardiovascular growth and regeneration, confirming essential similarities and distinguishing important differences between the murine cardiovascular model and the human heart. In doing so, they have also advanced research toward understanding the regenerative capabilities of the murine and human hearts. "The next step is to understand why most heart muscle cells stop dividing so early in life," Olaf Bergmann asserted in a press release. "Our aim is to help the adult heart to generate new muscle cells to replace lost heart tissue after injuries."

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