

Nobel prize to Briton, Japanese for stem cell work (Update 4)

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In this April, 2008 photo, Kyoto University Professor Shinya Yamanaka, left, and British researcher John Gurdon exchange words as they attend a symposium on induced pluripotent stem cell in Tokyo. Gurdon and Yamanaka of Japan won this year's Nobel Prize in physiology or medicine on Monday, Oct. 8, 2012 for discovering that mature, specialized cells of the body can be reprogrammed into stem cells - a discovery that scientists hope to turn into new treatments. (AP Photo/Kyodo News)

Two scientists from different generations won the Nobel Prize in

medicine Monday for the groundbreaking discovery that cells in the body can be reprogrammed into completely different kinds, work that reflects the mechanism behind cloning and offers an alternative to using embryonic stem cells.

The work of British researcher John Gurdon and Japanese scientist Shinya Yamanaka—who was born the year Gurdon made his discovery—holds hope for treating diseases like Parkinson's and diabetes by growing customized tissue for transplant.

And it has spurred a new generation of laboratory studies into other illnesses, including schizophrenia, which may lead to new treatments.

Basically, Gurdon, 79, and Yamanaka, 50, showed how to make the equivalent of embryonic stem cells without the ethical questions those very versatile cells pose, a promise scientists are now scrambling to fulfill.

Once created, these "blank slate" cells can be nudged toward developing into other cell types. Skin cells can ultimately be transformed into brain cells, for example.

Just last week, scientists reported turning skin cells from mice into eggs that produced baby mice, a possible step toward new fertility treatments.

Gurdon and Yamanaka performed "courageous experiments" that challenged scientific opinion, said Doug Melton, co-director of the Harvard Stem Cell Institute.

"Their work shows ... that while cells might be specialized to do one thing, they have the potential to do something else," Melton said. It "really lays the groundwork for all the excitement about stem cell biology."

Another Harvard stem cell researcher, Dr. George Daley said, "I don't think anybody is surprised" by the award announcement. "The fact that these two share it together is inspired."

In announcing the \$1.2 million award, the Nobel committee at Stockholm's Karolinska Institute said the work has "revolutionized our understanding of how cells and organisms develop."

Gurdon showed in 1962 that DNA from specialized cells of tadpoles, like skin or intestinal cells, could be used to clone more tadpoles. In 1997, the same process led to the cloning of Dolly the sheep, showing it would also work in mammals.

Gurdon told reporters in London that at the time of his discovery, it had "no obvious therapeutic benefit at all. ... It was almost 50 years before the value—the potential value—of that basic scientific research came to light."

Forty-four years after Gurdon's discovery, in 2006, Yamanaka and his team moved beyond tadpoles. They showed that a surprisingly simple recipe could turn mouse skin cells back into primitive cells, which in turn could be prodded into different kinds of mature cells. The work was later repeated with human cells.

In theory those primitive cells are "blank slates"—like embryonic stem cells that can be turned into any cell in the body.

Turning a skin cell into a stem cell takes weeks in a lab. Scientists introduce two to four genes that turn the cell's own genes on and off. It's a little like rebooting a computer, changing the cell from running the collection of genes that make it a skin cell into using another set that make it a stem cell.

Gurdon, who said his ambitions to become a scientist were dismissed as "completely ridiculous" by his headmaster when he was in his teens, has served as a professor of cell biology at Cambridge University's Magdalene College. He is currently at the Gurdon Institute in Cambridge, which he founded.

Yamanaka worked at the Gladstone Institute in San Francisco and Nara Institute of Science and Technology in Japan. He is currently at Kyoto University and also affiliated with the Gladstone Institute. Yamanaka is the first Japanese scientist to win the Nobel medicine award since 1987.

Asked how he planned to celebrate, Gurdon said he was invited to drinks at 6 o'clock.

"I intend to attend those drinks," he said dryly.

He described his skepticism when first getting the congratulatory call from Stockholm, saying that "the call came from someone in Sweden, and your immediate reaction is: 'Is this right? Is it true or is it someone pulling your leg?'"



British scientist John Gurdon speaks during a news conference in London, Monday, Oct. 8, 2012. Gurdon and a Japanese scientist, Shinya Yamanaka, won the Nobel Prize in physiology or medicine on Monday for discovering that ordinary cells of the body can be reprogrammed into stem cells, which then can turn into any kind of tissue—a discovery that may led to new treatments. (AP Photo/Matt Dunham)

Yamanaka said he was honored to share the award with Gurdon "because without his work, which he published 50 years ago, the same year I was born, without his work I would never done this and we would have never studied this project."

Yamanaka said he did not yet know what he was going to do to celebrate.

"I just need some beer," he said, speaking via videoconference from Japan to thank his colleagues in San Francisco for their support.

Choosing Yamanaka as a Nobel winner just six years after his discovery is unusual. The Nobel committees typically reward research done more than a decade earlier, to make sure it has stood the test of time.

However, in 2010, the Nobel Prize in physics went to two researchers whose discoveries were also published six years earlier. In 2006, two American scientists won the medicine prize eight years after their work was published.

Prize committee member Juleen Zierath said Gurdon and Yamanaka's discoveries, which also earned them a Lasker award for basic research in 2009, could hold "immense potential," including in developing treatments for Parkinson's disease and in making cells that produce insulin. However, she added that therapeutic implications are still far away.

Experts welcomed the Nobel announcement, praising the duo for their groundbreaking and influential discoveries in a field riddled with ethical debates.

President George W. Bush outlawed federal funding for work on embryonic stem cells that hadn't been derived by a particular date. President Barack Obama overturned that order, allowing access to many more lines of cells.

"Everyone who works on developmental biology and on the understanding of disease mechanisms will applaud these excellent and clear choices for the Nobel Prize," said John Hardy, professor of Neuroscience at University College London. "Countless labs' work builds on the breakthroughs they have pioneered."

The idea of reprogramming cells has been put to work in basic research on disease, through an approach sometimes called "disease in a dish."

The reprogramming allows scientists to create particular kinds of tissue they want to study, like lung tissue for studying cystic fibrosis, or brain tissue for Huntington's disease. By reprogramming cells from patients with a particular disease, they can create new tissue with the same genetic background, and study it in the lab. That can give new insights into the roots of the problem.

In addition, that approach allows them to screen drugs in the lab for possible new medicines.

The medicine award was the first Nobel Prize to be announced this year. The physics award will be announced Tuesday, followed by chemistry on Wednesday, literature on Thursday and the Nobel Peace Prize on Friday.

The economics prize, which was not among the original awards, but was established by the Swedish central bank in 1968, will be announced on Oct. 15.



Kyoto University Professor Shinya Yamanaka speaks during a news conference at Kyoto University in Kyoto, western Japan, Monday, Oct. 8, 2012, after learning that he and British researcher John Gurdon won this year's Nobel Prize in physiology or medicine. The prize committee at Stockholm's Karolinska Institute said the two won the prize for discovering that mature, specialized cells of the body can be reprogrammed into stem cells—a discovery that scientists hope to turn into new treatments. (AP Photo/Kyodo News)

Recent winners of the Nobel Prize in medicine

Recent winners of the Nobel Prize in physiology or medicine, and their research, according to the Nobel Foundation:

— 2012: Briton John Gurdon and Japan's Shinya Yamanaka for their discovery that mature cells can be reprogrammed into immature cells that can be turned into all tissues of the body, a finding that revolutionized understanding of how cells and organisms develop.

— 2011: American Bruce Beutler and French researcher Jules Hoffmann for their discoveries concerning the activation of innate immunity, sharing it with Canadian-born Ralph Steinman for his discovery of the dendritic cell and its role in adaptive immunity.

— 2010: British researcher Robert Edwards for the development of in vitro fertilization.

— 2009: Americans Elizabeth Blackburn, Carol Greider and Jack Szostak for their discovery of how chromosomes are protected by telomeres and the enzyme telomerase, research that has implications for cancer and aging research.

— 2008: Harald zur Hausen and Francoise Barre-Sinoussi and Luc Montagnier for discoveries of human papilloma viruses causing cervical cancer and the discovery of human immunodeficiency virus.

— 2007: Mario R. Capecchi and Oliver Smithies of the United States and Martin J. Evans of the United Kingdom, for their discoveries leading to a powerful technique for manipulating mouse genes.

— 2006: Andrew Z. Fire and Craig C. Mello, of the United States, for their work in controlling the flow of genetic information.

— 2005: Barry J. Marshall and Robin Warren, of Australia, for their work in how the bacterium *Helicobacter pylori* plays a role in gastritis and peptic ulcer disease.

— 2004: Richard Axel and Linda B. Buck, both of the United States, for their work in studying odorant receptors and the organization of the olfactory system in human beings.

— 2003: Paul C. Lauterbur, United States, and Sir Peter Mansfield, Britain, for discoveries in magnetic resonance imaging, a technique that reveals the brain and inner organs in breathtaking detail.

— 2002: Sydney Brenner and John E. Sulston, Britain, and H. Robert Horvitz, United States, for discoveries concerning how genes regulate organ development and a process of programmed cell death.

— 2001: Leland H. Hartwell, United States, R. Timothy Hunt and Sir Paul M. Nurse, Britain, for the discovery of key regulators of the process that lets cells divide, which is expected to lead to new cancer treatments.

— 2000: Arvid Carlsson, Sweden, Paul Greengard and Eric R. Kandel, United States, for research on how brain cells transmit signals to each other, thus increasing understanding on how the brain functions and how neurological and psychiatric disorders may be treated better.

— 1999: Guenter Blobel, United States, for protein research that shed new light on diseases, including cystic fibrosis and early development of kidney stones.

— 1998: Robert F. Furchgott, Louis J. Ignarro and Ferid Murad, United States, for the discovery of properties of nitric oxide, a common air pollutant but also a lifesaver because of its capacity to dilate blood vessels.

British, Japanese share Nobel Prize for medicine

WHO WON?

Britain's John Gurdon, 79, formerly of Magdalene College of Cambridge University and currently with the Gurdon Institute that he founded, and Japan's Shinya Yamanaka, 50, who worked at the Gladstone Institute in San Francisco and Nara Institute of Science and Technology in Japan. He is now at Kyoto University.

FOR WHAT?

In 1962, the year Yamanaka was born, Gurdon showed that the DNA from specialized cells of frogs, like skin or intestinal cells, could be used to generate new tadpoles. In 2006, Yamanaka showed that mature cells could be turned back into primitive cells, which in turn could be prodded into different kinds of mature cells.

SIGNIFICANCE

The discoveries showed that the body's mature, specialized cells can be reprogrammed into stem cells—a discovery that scientists hope to turn into new treatments without destroying human embryos. Scientists want to harness the reprogramming to create replacement tissues for treating diseases such as Parkinson's, cystic fibrosis and diabetes and for studying the roots of diseases in the laboratory.

WHAT THEY SAID

Yamanaka: "We still have a lot of work to do on our research, so I was really surprised. I have two feelings, gratitude and also responsibility. Even though we have received this prize, we have not really accomplished what we need to. I feel a deep sense of duty and responsibility." Gurdon:

"It is particularly pleasing to see how purely basic research, originally aimed at testing the genetic identity of different cell types in the body,

has turned out to have clear human health prospects."

More information: Nobel Prize website: nobelprize.org
'Blank slate' cells: [stemcells.nih.gov/info/Regener ...
ne/2006chapter10.htm](http://stemcells.nih.gov/info/Regeneration/2006chapter10.htm)

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