



Jennifer Doudna and Emmanuelle Charpentier share the 2020 Nobel chemistry prize.

PIONEERS OF CRISPR GENE EDITING WIN CHEMISTRY NOBEL

Emmanuelle Charpentier and Jennifer Doudna share award for developing the precise technology.

By Heidi Ledford & Ewen Callaway

It's CRISPR. Two scientists who pioneered the revolutionary gene-editing technology are the winners of this year's Nobel Prize in Chemistry.

The Nobel committee's selection of Emmanuelle Charpentier, now at the Max Planck Unit for the Science of Pathogens in Berlin, and Jennifer Doudna, at the University of California, Berkeley, puts an end to years of speculation about who would be recognized for their work developing the CRISPR–Cas9 gene-editing tools. The technology allows precise edits to the genome and has swept through laboratories worldwide since its inception in the 2010s. It has countless applications: researchers hope to use it to alter human genes to eliminate diseases; create hardier plants; wipe out pathogens; and more.

"The ability to cut DNA where you want has revolutionized the life sciences," said Pernilla Wittung Stafshede, a biophysical chemist and member of the Nobel chemistry committee, at the prize announcement. "The 'genetic scissors' were discovered just eight years ago, but have already benefited humankind greatly."

Doudna and Charpentier and their colleagues did crucial early work characterizing

the system, but several other researchers have been cited – and recognized in other high-profile awards – as key contributors in the development of CRISPR. They include Feng Zhang at the Broad Institute of MIT and Harvard in Cambridge, Massachusetts, George Church at Harvard Medical School in Boston, Massachusetts, and biochemist Virginijus Siksnys at Vilnius University in Lithuania.

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Doudna was "really sound asleep" when her buzzing phone woke her and she took a call from a *Nature* reporter, who broke the news. "I grew up in a small town in Hawaii and I never in 100 million years would have imagined this happening," says Doudna. "I'm really stunned, I'm just completely in shock."

"I know so many wonderful scientists who will never receive this, for reasons that have nothing to do with the fact that they are wonderful scientists," Doudna says. "I am really kind of humbled."

CRISPR, short for clustered regularly interspaced short palindromic repeats, is a microbial 'immune system' that prokaryotes – bacteria and archaea – use to prevent infection by viruses called phages. At its core, the CRISPR system gives prokaryotes the ability to recognize precise genetic sequences that match those of a phage or other invader, and to target these sequences for destruction using specialized enzymes.

Previous work had identified these enzymes, known as CRISPR-associated proteins (Cas), including one called Cas9. But Charpentier, working first at the University of Vienna and later at the Umeå Centre for Microbial Research in Sweden, identified another key component of the CRISPR system – an RNA molecule that is involved in recognizing phage sequences – in the bacterium *Streptococcus pyogenes*, which can cause disease in humans.

Charpentier reported the discovery in 2011 and that year struck up a collaboration with Doudna. In a landmark 2012 paper (M. Jinek *et al. Science* **337**, 816–821; 2012), the duo and their teams isolated the components of the CRISPR–Cas9 system, adapted them to function in the test tube and showed that the system could be programmed to cut specific sites in isolated DNA. The programmable gene-editing system has inspired a gold rush of applications in medicine, agriculture and basic science – and work continues to tweak and improve CRISPR and to identify other gene-editing tools.

"We were hoping that we could really translate this into a technology for rewriting the genetic code of cells and organisms," says Martin Jinek, a biochemist at the University of Zurich who was a postdoc in Doudna's lab and a co-author of the pivotal *Science* paper. "What we didn't quite appreciate was how quickly the technology would be adopted by others in the field and then pushed forward."

Race to commercialize

In less than a decade, researchers have used CRISPR–Cas9 to develop genome-edited crops, insects, genetic models and experimental human therapies. Clinical trials are under way to use the technique to treat sickle-cell anaemia, hereditary blindness and cancer. Doudna, Charpentier and others in the field have launched a generation of biotechnology companies aimed at developing the technique to achieve these goals.

But the technology has also generated controversy – in particular for its nascent applications in human cells. In November 2018, Chinese biophysicist He Jiankui announced that twin girls had been born from embryos that he and his colleagues had edited using CRISPR–Cas9. The news sparked an outcry: editing embryos raises a host of ethical, social and safety concerns, and many researchers worldwide quickly condemned He's work.

In September, an international panel

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convened by leading US and UK scientific societies concluded again that the technology is not ready for use in human embryos that are destined for implantation.

The work also sparked a fierce patent battle – mainly between the Broad Institute and Berkeley – that rumbles on to this day over who owns the lucrative intellectual-property rights to CRISPR–Cas9 genome editing.

Still, Church agrees with how the award was divvied up. Although he is proud of the work in his lab and in Zhang’s – which adapted the system to work in mammalian cells, opening

the door to modelling and potentially treating human diseases – Church says that this work could be classified as engineering and invention, rather than scientific discovery. “I think it’s a great choice,” he says.

It is always difficult to single out a discovery for a prize, says geneticist Francis Collins, head of the US National Institutes of Health in Bethesda, Maryland. But one unique aspect of CRISPR–Cas9 genome editing has been the ease and versatility of the technique, he adds. “There is no molecular-biology laboratory that I know of that hasn’t started to work with CRISPR–Cas.”

the Milky Way, said the Royal Swedish Academy of Sciences, which awards the prize.

Astrophysicist Monica Colpi at the University of Milan Bicocca in Italy says the prizes are highly deserved. “The observational data by Genzel and Ghez are splendid and truly unique in their ability to monitor star motions around this object.”

Penrose, meanwhile, is “a giant in theoretical physics”, who has influenced generations of scientists, says Carole Mundell, an astrophysicist at the University of Bath, UK. He is “a genuinely creative thinker with immense imagination, sense of fun and a passion for curiosity in everything he does”, she adds.

PHYSICISTS WIN NOBEL PRIZE FOR BLACK-HOLE DISCOVERIES

Mathematical physicist Roger Penrose shares award with astronomers Andrea Ghez and Reinhard Genzel.

By Elizabeth Gibney & Davide Castelvecchi

A mathematical physicist and two astronomers have won the 2020 Nobel Prize in Physics for discoveries relating to the most massive and mysterious objects in the Universe – black holes.

British mathematical physicist Roger Penrose receives half the prize for theoretical work that showed how Albert Einstein’s general theory of relativity should result in black holes.

US astronomer Andrea Ghez and German astronomer Reinhard Genzel, share the other half of the 10-million-Swedish-kronor (US\$1.1-million) award for discovering the Universe’s most famous black hole – the supermassive object at the centre of the Milky Way.

Since the 1990s, Ghez and Genzel have each led groups that have mapped the orbits of stars close to the Galactic Centre. These studies led them to conclude that an extremely massive, invisible object must be dictating the stars’ frantic movements. The object, known as Sagittarius A*, is the most convincing evidence yet of a supermassive black hole at the centre of

General relativity to geometry

In a seminal 1965 paper, Penrose demonstrated how, according to general relativity, black holes could form given the right conditions – the formation of a surface that traps light (R. Penrose *Phys. Rev. Lett.* **14**, 57; 1965). Inside this surface, mass enters an irreversible gravitational collapse, producing a region of infinitely dense energy called a singularity. Previous researchers had demonstrated this inevitability only under conditions that were considered physically unrealistic.

Penrose’s contributions span many areas of mathematics and physics. He communicated with the graphic artist M. C. Escher and inspired some of his drawings of impossible geometrical objects. In the 1970s, he developed a geometrical theory: a non-repeating 2D pattern now called Penrose tilings. These patterns occur in nature in ‘quasicrystals’, which were the subject of the 2011 Nobel Prize in Chemistry.

Penrose introduced sophisticated mathematical techniques into several branches of physics, says Matilde Marcolli, a mathematical physicist at the California Institute of Technology in Pasadena. “It was a completely new way of thinking,” she says.

Whereas Penrose laid the theoretical foundations for the existence of black holes, Ghez and Genzel’s teams produced powerful evidence that such a void sits at our Galaxy’s heart.

Since the 1960s, astronomers had suspected that a supermassive black hole – with a mass more than one million times that of the Sun – might lie at the centre of most galaxies. The Milky Way was a prime candidate: radio observations had revealed energetic emissions from its centre. But peering closely was a challenge, because gas and dust obscured emissions from the stars. Beginning in the 1990s, rival teams led by Ghez and Genzel used some of the world’s biggest telescopes – the Keck Observatory on Mauna Kea, Hawaii, and the Very Large Telescope on Cerro Paranal, Chile, respectively – and cutting-edge observational techniques, to overcome this challenge.

Crucial to their work was finding ways to boost resolution and sensitivity to the faint light, says Andreas Eckart, an astrophysicist at



Roger Penrose, Andrea Ghez and Reinhard Genzel (left to right) received the 2020 Nobel physics prize for their research on black holes.

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