CHEMISTRY

Nobel for test-tube evolution

Controlling protein evolution in the lab has led to greener technologies and new medicines.

BY ELIZABETH GIBNEY, RICHARD VAN NOORDEN, HEIDI LEDFORD, DAVIDE CASTELVECCHI & MATTHEW WARREN

Ways to speed up and control the evolution of proteins to produce greener technologies and new medicines have won three scientists the 2018 Nobel Prize in Chemistry.

Chemical engineer Frances Arnold, at the California Institute of Technology in Pasadena, is just the second woman to have won the prize in the past 50 years. She was awarded half of the 9-million-Swedish-krona (US$1-million) pot. The remaining half was shared between Gregory Winter at the MRC Laboratory of Molecular Biology in Cambridge, UK, and George Smith at the University of Missouri in Columbia.

Arnold carried out pioneering work in the 1990s on the 'directed evolution' of enzymes — proteins that catalyse chemical reactions. She devised a method for inducing mutations in enzyme-producing bacteria and then screening and selecting the bacteria to speed up and direct enzyme evolution. These enzymes are now used in the production of biofuels and drugs.

"Biology has this one process that's responsible for all this glorious complexity we see in nature," she told *Nature* shortly after the prize announcement on 3 October. But whereas nature operates blindly, Arnold's techniques accelerate natural selection towards producing enzymes with known properties. "It's like breeding a racehorse," she says.

In 1985, Smith pioneered a technique that uses a bacteriophage — a virus that infects bacteria — as a host that displays a protein on its outer coat, allowing researchers to find other molecules that interact with the protein. Winter developed and improved this technology, called phage display, and invented ways to use it to evolve antibodies adapted for use as therapeutics. Today, antibodies evolved using this method can neutralize toxins and counteract autoimmune diseases.

Nobel laureates Gregory Winter (left), Frances Arnold and George Smith.

L–R: AGA MACHAJ; CALTECH; UNIV. MISSOURI-COLUMBIA

The first humanized antibody, called adalimumab (Humira), was discovered by Cambridge Antibody Technology — a company that Winter co-founded in 1989 — and was approved for treating rheumatoid arthritis in 2002. It is also used to treat psoriasis and inflammatory bowel diseases. In 2017, it was the world's top-selling drug, generating revenues of $18.4 billion.

Scepticism abounded when the company was launched, says co-founder David Chiswell, and it struggled to find investors. "Nobody in the world believed that antibodies were really good," says Chiswell, who is now chief executive of Kymab, an antibody company in Cambridge.

Arnold also faced a battle when she put forward the idea of evolving proteins in the lab, says Dane Wittrup, a protein engineer at the Massachusetts Institute of Technology in Cambridge. Researchers thought then that they would be able to sit down at a computer and rationally design proteins to carry out specific functions. "But now, by and large, directed evolution is how the work is done."

Winter says that a woman with cancer who had received an early, experimental version of one of his humanized antibodies against a cancer-related protein drove him to push his research out of the laboratory and into the clinic. When Winter warned her that the effects of the therapy might not last, she told him she only needed to live for a few more months, so that she could help her dying husband. "I was so choked by that," Winter says.

Before Arnold, the last woman to win the Nobel Prize in Chemistry was Ada Yonath, a crystallographer at the Weizmann Institute of Science in Rehovot, Israel, who won in 2009 for mapping the structure of the ribosome, which generates proteins from the genetic code in cells. Before her, the most recent woman to win was crystallographer Dorothy Hodgkin, in 1964. Arnold is just the fifth female winner in the prize's history. ■

EUROPE

Tiny space fleet could track CO_2

Project could help to show whether nations are meeting pledges to cut emissions.

BY ALEXANDRA WITZE

European researchers are developing a miniaturized instrument that could precisely measure carbon dioxide coming from cities and power plants. If it works, the device could fly aboard a constellation of small satellites starting in the late 2020s, helping to track daily fluctuations in greenhouse-gas emissions.

Developers with the 3-year, €3-million (US$3.5-million) project envisage it complementing more-expansive efforts to monitor CO_2 from space, such as a proposed set of new Sentinel Earth-observing satellites from the European Space Agency. If approved, those might also come online in the late 2020s.

Several satellites currently monitor CO_2 emissions, including Japan's GOSAT, the United States's Orbiting Carbon Observatory-2 (OCO-2) and China's TanSat. But none of them launched with the explicit goal of tracking compliance with global treaties.

In 2015, before the signing of the Paris