**Breakthrough to genome editing**

A, T, G, C: the alphabet code for the nucleotides that are the building blocks of life. Minor, but consequential, changes in this DNA coding can change gene function. Researchers have long sought better ways to edit the genetic code in cultured cells and laboratory organisms to silence, activate, or change targeted genes to gain a better understanding of their roles. This, in turn, could open the door to beneficial applications, from ecological to agricultural to biomedical.

Over the years, several editing methods have been developed, but they have suffered from a lack of specificity, difficulty in assembling the molecular constituents, or concerns about off-target effects. Recently, accomplishments in genome editing across biological disciplines have been so remarkable that the method known as clustered regularly interspaced short palindromic repeats—or CRISPR—is *Science*’s 2015 Breakthrough of the Year (see p. 1456).

The 2015 advances using CRISPR that warrant this recognition have been on multiple fronts. Researchers have now delivered on the method’s promise to, for example, disable retroviruses encoded in the pig genome that had posed a safety concern for organ transplantation from pigs to humans. Concurrently, CRISPR was used to develop a potent gene drive, a system that allows the rapid transmission of an introduced gene throughout insect populations faster than natural selection would permit. CRISPR should make it easier to study human genetic diseases, because it can quickly create cell and animal models for study and for the testing and screening of drugs. For certain diseases, genome editing of somatic cells may lead to potential therapy. Because CRISPR is poised to revolutionize research, the international community gathered earlier this month to address the implications of this technique for modifying human germ cells and embryos, articulating guidelines that clarify the ethical bounds for researchers, funders, and publishers.

Many other achievements in 2015 gave CRISPR tough competition. One that came too late to be considered is last week’s agreement in Paris by nearly 200 nations on a pact to fight climate change. Of those that made the short list, most notable are the stunning images from the New Horizons mission as it swept past Pluto; the mission is *Science*’s “People’s Choice” for the Breakthrough. Also startling was the discovery that the mammalian lymphatic system extends the immune system’s reach into the brain, opening up possible new routes to treatment. In a form of modern-day alchemy, yeast was engineered to produce opiates. We gained experimental confirmation of the correlation in the quantum state of two widely separated particles, a process called “entanglement.” Improvements in seismic imaging provided long-sought confirmation of the existence of mantle plumes, responsible for midplate volcanoes such as Hawaii. Our line of defense against Ebola virus has been bolstered with the successful development of a vaccine. Psychologists led the charge in research reproducibility. And affirming that there is still serendipity in science, a new member of the human family was revealed from a hidden cave in South Africa harboring 1500 human fossils. DNA sequencing has now settled the origin of Kennewick Man: Native American, with Asian ancestors.

Choosing the Breakthrough is easy when new research resolves a long-standing question, such as the experimental confirmation of the Higgs particle in 2012. More commonly, the road to success is marked by glimmers of hope, setbacks, and uncertainty as to whether time will prove the value of a new finding or technique. *Science* has been tracking genome editing since the initial successes with zinc fingers; in 2012, we named transcription activator–like effector nucleases (TALENs) as a runner-up Breakthrough. By 2013, researchers were embracing CRISPR, enough so that it too was a runner-up Breakthrough. The Breakthrough nod in 2013 went to cancer immunotherapy, still in early clinical trials at the time. Our hope is that in 2 years’ time, CRISPR will have brought to many diverse fields in biology the enduring level of excitement and optimism that immunotherapy has brought to cancer patients.

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