LEMELSON-MIT

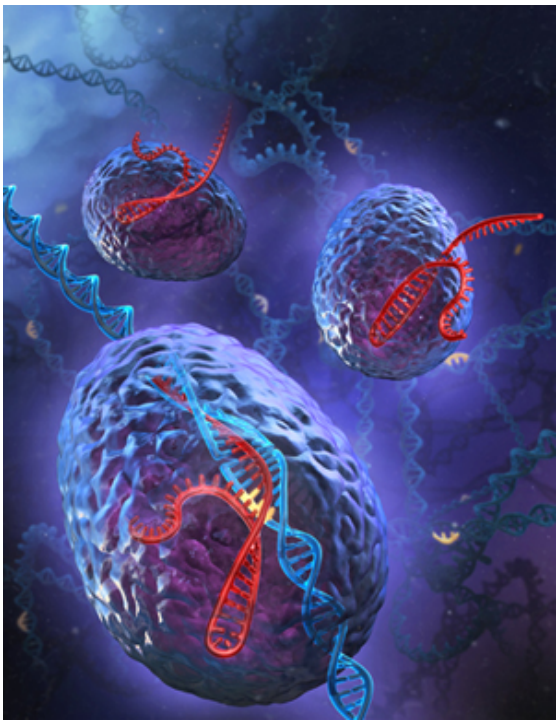
Winner of the 2017 $500,000 Lemelson-MIT Prize – Feng Zhang, PhD

Feng Zhang, core member of the Broad Institute of MIT and Harvard, an investigator at the McGovern Institute for Brain Research, James and Patricia Poitras Professor in Neuroscience at MIT, and associate professor in the departments of Brain and Cognitive Sciences and Biological Engineering at MIT, is a pioneer in genome editing technologies.

CRISPR-Cas9

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) first came to the attention of researchers in the mid-1990s. Over the next decade scientists discovered that CRISPR is a microbial adaptive immune response to invading viruses – essentially, a bacterium's immune system.

Scientists still don't know everything about CRISPR, but they do know how some of them work. Repeating sequences of genetic code (the Short Palindromic Repeats) that give CRISPR its basic form and function are interrupted (Regularly Interspaced) by "spacer" sequences copied from past invaders, forming a genetic memory. The spacers are transcribed into short pieces of RNA guides to detect matching DNA sequences in the genome of invading viruses. This RNA guide directs a naturally produced enzyme called Cas9 to the target site, which is then cut by Cas9 -- killing the invading virus.



Depiction of CRISPR system in action. Image courtesy of BroadInstitute.org. Illustration by Stephen Dixon

Feng Zhang, a core member of the Broad Institute of MIT and Harvard, was the first to demonstrate how CRISPR-Cas9 can be used to edit genomes in living mouse and human cells. Researchers can now design a guide RNA to direct Cas9 to a specific genetic target for gene editing or epigenetic manipulation.

After that breakthrough, Zhang and his team's commitment to sharing the technology widely and subsequent advances have turned CRISPR technologies into a practical platform of editing and epigenetic manipulation tools. Now researchers can modify Cas9 to activate a gene rather than cut it, or they can insert a new gene by delivering a repair template to the site of the fresh cut. The whole process -- often compared to the "find-and-replace" function in a word-processing program -- is simpler and more versatile than previous gene-editing technologies. Ultimately, precisely editing a living cell's genome holds enormous promise to accelerate life-science research, improve biotechnology, and treat or even eliminate human diseases. Zhang's open-source philosophy has already given the research community tools to accelerate research around the world.

Optogenetics and TAL Effectors

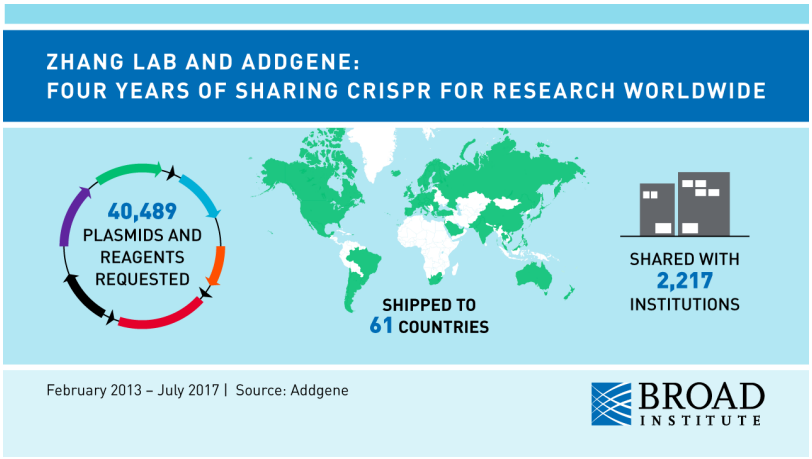
When Zhang entered graduate school at Stanford in 2004, he joined Karl Deisseroth's newly formed lab where he worked as part of a team to establish the new field of optogenetics, which involves inserting genes from light-sensitive proteins into specific brain cells and enabling scientists to precisely control their activity with light signals. Over the next five years, Zhang coauthored some 30 publications and was the primary author of several others focusing on optogenetics.

Upon earning his PhD, Zhang turned to genome editing. Researchers were already working on a new class of DNA-binding proteins that alter gene expression in plants. Transcription activator-like effectors (TALEs) had potential to form the basis of a gene-editing toolbox, but synthesizing new custom variants that could target a specific site in the genome was difficult. As a Junior Fellow at the Harvard Society of Fellows, Zhang overcame some of the technical challenges blocking development of libraries of "programmable" reagents.

Zhang kept working on TALEs and optogenetics after arriving at MIT and the Broad Institute in 2011. CRISPR caught his attention almost immediately as potentially offering improvements over existing systems, and his background positioned him to develop the CRISPR system for conducting genome editing in living mammalian cells.

Applications and Commercialization

Zhang has received numerous patents, most notably the first issued patent for CRISPR mammalian genome editing in the United States. His lab has trained thousands of researchers to use CRISPR-Cas9 and openly shared more than 40,000 samples of CRISPR tools with academic labs in more than 60 countries. Among many other applications, Zhang and his colleagues recently used another CRISPR system's RNA-recognition powers to search human bodily fluids for evidence of an array of viral and bacterial pathogens using a Cas13-mediated technology dubbed SHERLOCK; the same technology could potentially find cancer-causing mutations.



In 2013, Zhang cofounded Editas Medicine along with other leading researchers in genome editing. Editas Medicine is a leading genome editing company working on therapies for treating genetically-defined diseases, and its mission is to translate the promise of genome editing science into a broad class of transformative genomic medicines to benefit the greatest number of patients.

Beyond treating genetic diseases in individuals, CRISPR-based technologies can also be used in other areas, such as making crops more drought resistant and enabling planting in broader geographies to help solve the food scarcity problem.