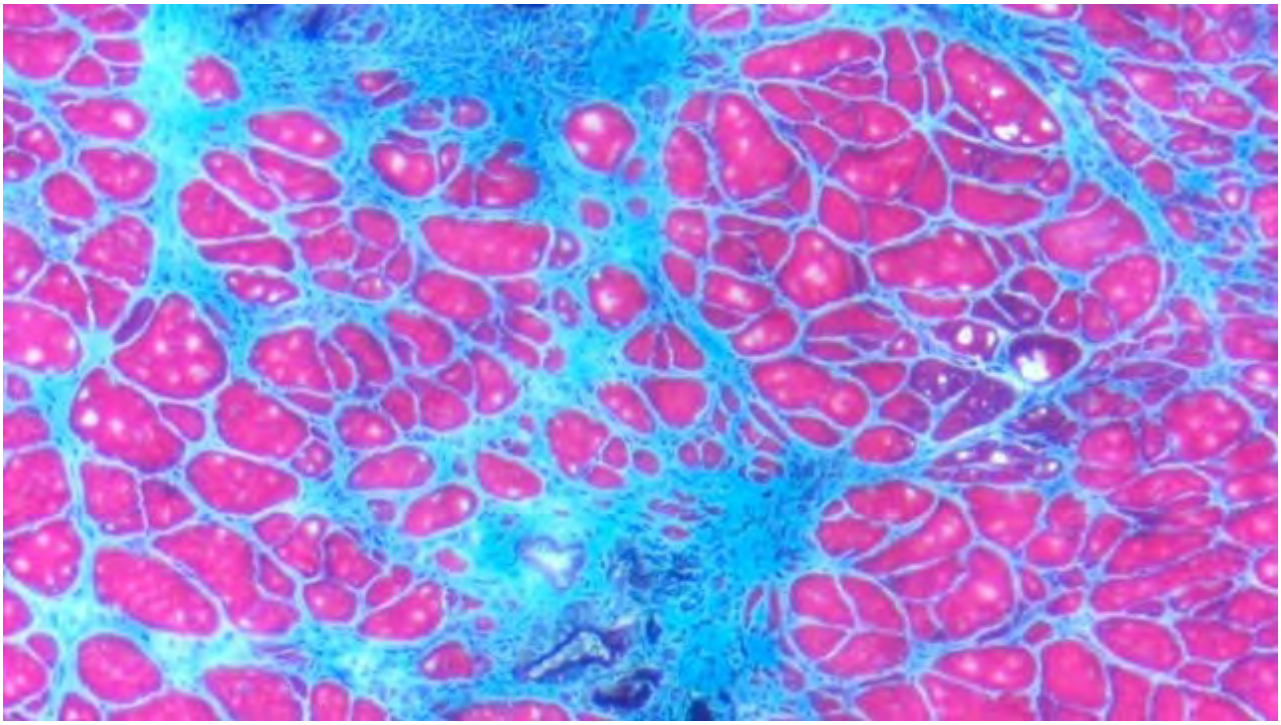
Top Technical Advances in 2017

The year's most impressive achievements include new methods to extend CRISPR editing, patch-clamp neurons hands-free, and analyze the contents of live cells.

By Shawna Williams | December 25, 2017

Amping up CRISPR-Cas



CONBOY LAB AND MURTHY LAB

Researchers aren't just finding new applications for this precise and relatively easy-to-use gene-editing technique, they're also tweaking it to give it new powers. Among this year's developments:

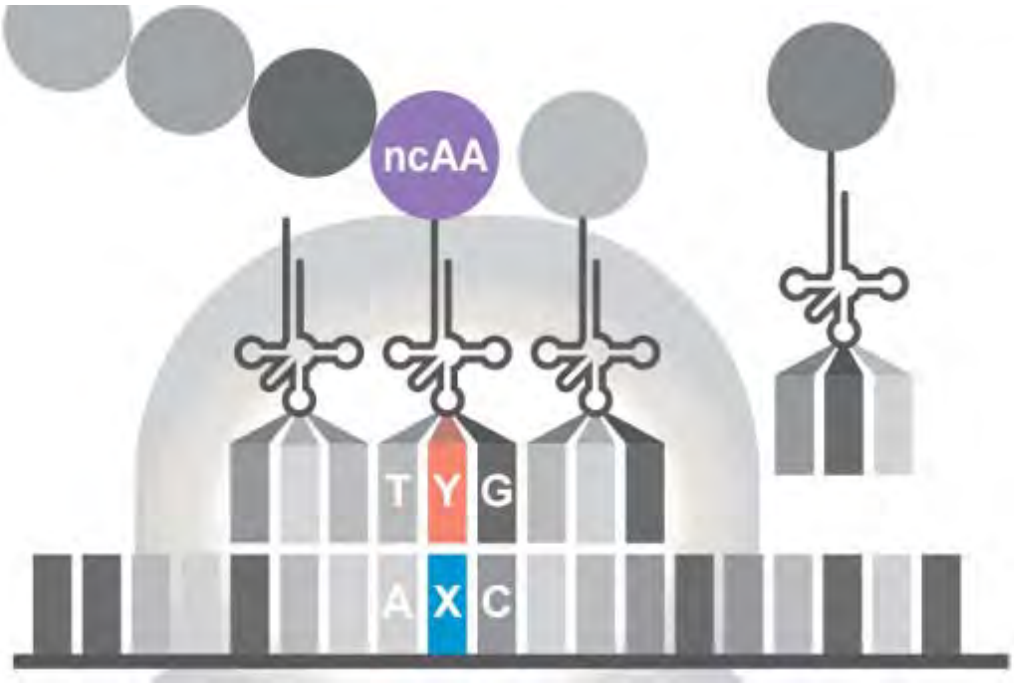
RNA editing: A research team led by Feng Zhang of the Broad Institute fused an RNA-editing enzyme to

an RNA-targeting Cas protein, enabling users to edit specific nucleotides within RNA molecules in human cells. The technique, called RNA Editing for Programmable A-to-I Replacement (REPAIR), is expected to help researchers investigate phenomena such as alternative splicing mechanisms and translation. The study's authors suggest it could one day even be used therapeutically.

Base-editing human embryos: A team from Sun Yat-Sen University in China reported correcting, in living human embryos, the single-nucleotide mutation that leads to the blood disorder β thalassemia. The base-editing does not cut the DNA when it makes an edit, so it potentially has fewer harmful side effects than classic CRISPR-Cas editing would.

Nanoparticle delivery: While research applications of CRISPR-Cas abound, one challenge of applying it therapeutically is finding a safe, effective delivery system. Researchers at the University of California, Berkeley, and GenEdit recently reported using gold nanoparticles to shuttle a CRISPR system into mouse cells to correct a Duchenne muscular dystrophy–like condition.

Synthetic base pairs get to work inside cells



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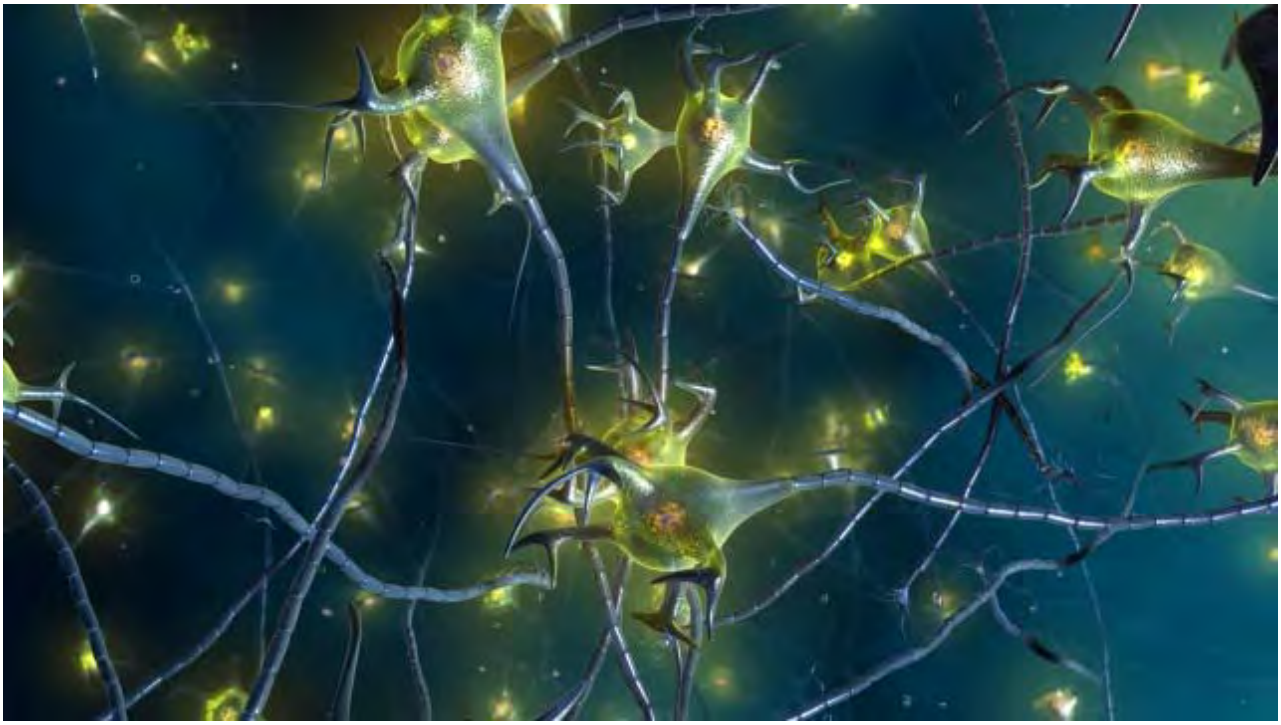
Why have four DNA base pairs when you could have six? A team at the Scripps Research Institute not only invented two new base pairs, X and Y, but got them to function inside living bacteria. The cells were able to transcribe DNA incorporating the new base pairs and translate the resulting RNA, producing an alternative synthetic codon—GXC, and a non-canonical amino acid called pAzF. The ability to incorporate new amino acids may make it easier for biochemists to devise proteins with novel functions.

Robotic patch clamping

It's possible to monitor the electrical activity of a selected neuron in the brain of a live mouse using a technique known as two-photon targeted patching (TPTP), but only a handful of people in the world are able to perform the tricky technique. Earlier this year, groups at MIT and Imperial College London independently reported developing an automated version of TPTP, which guides a pipette to a neuron of interest and monitors it. "This whole-cell patch method is really the gold standard for looking at synaptic and other events that make a neuron compute," MIT bioengineer Ed Boyden told *The Scientist* at the time. "We're trying to take this art form and turn it into something that's fully automated."

DNA origami





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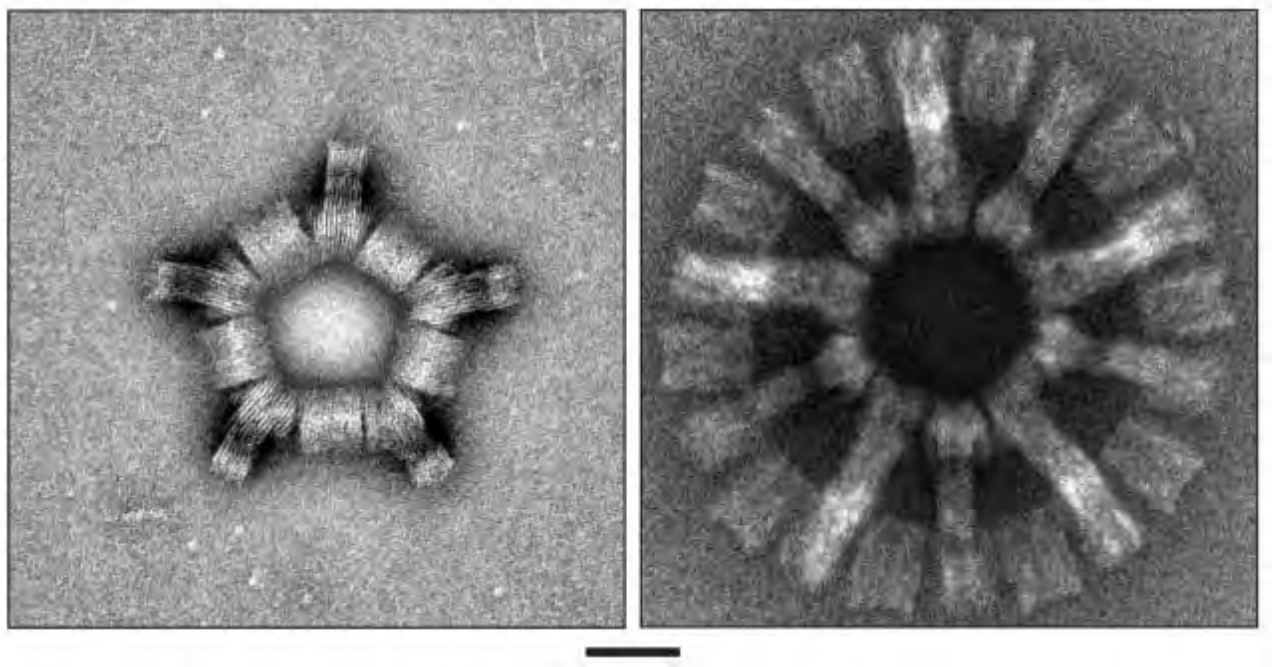
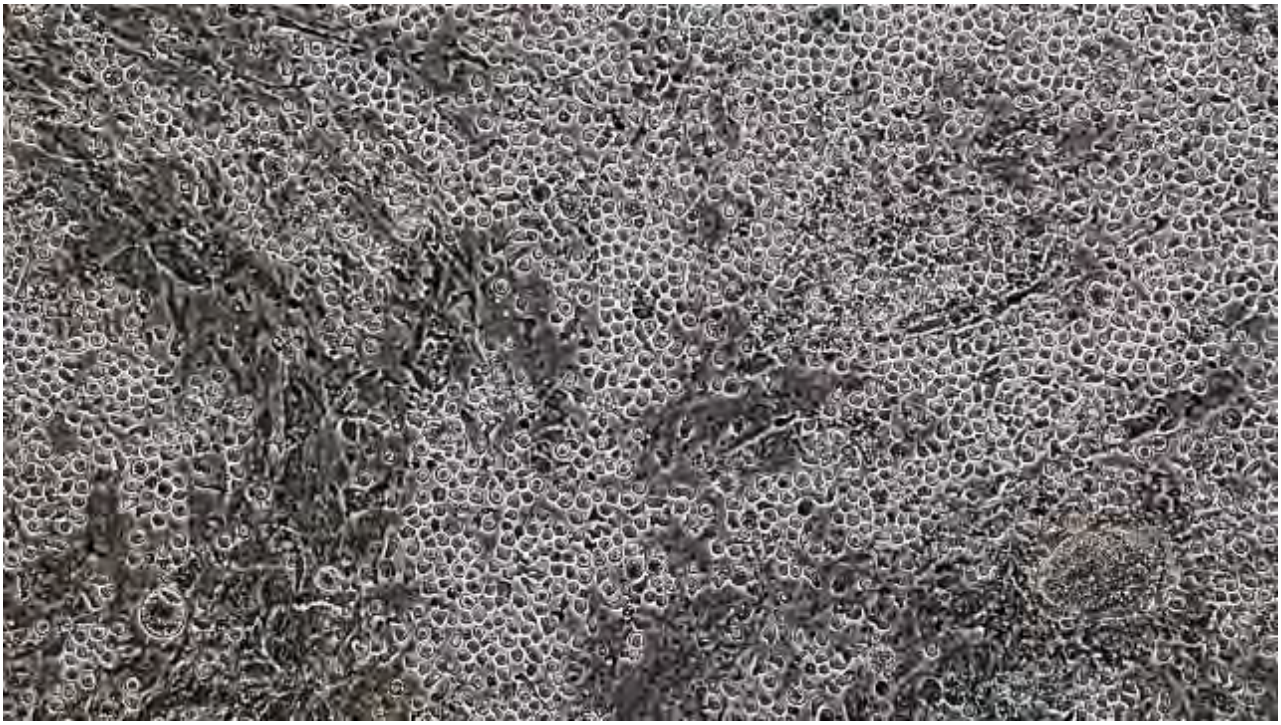


NATURE, 2017, WAGENBAUER ET AL.

Building nanoscale structures with DNA is no mere curiosity—these synthetic mega-molecules could one day have applications in biosensing, drug delivery, biomolecular analysis, and molecular computation, among other areas. This year saw the advent of new techniques that enabled researchers to build structures ranging from a teddy bear to fractals to the Mona Lisa.

Lab-grown blood stem cells

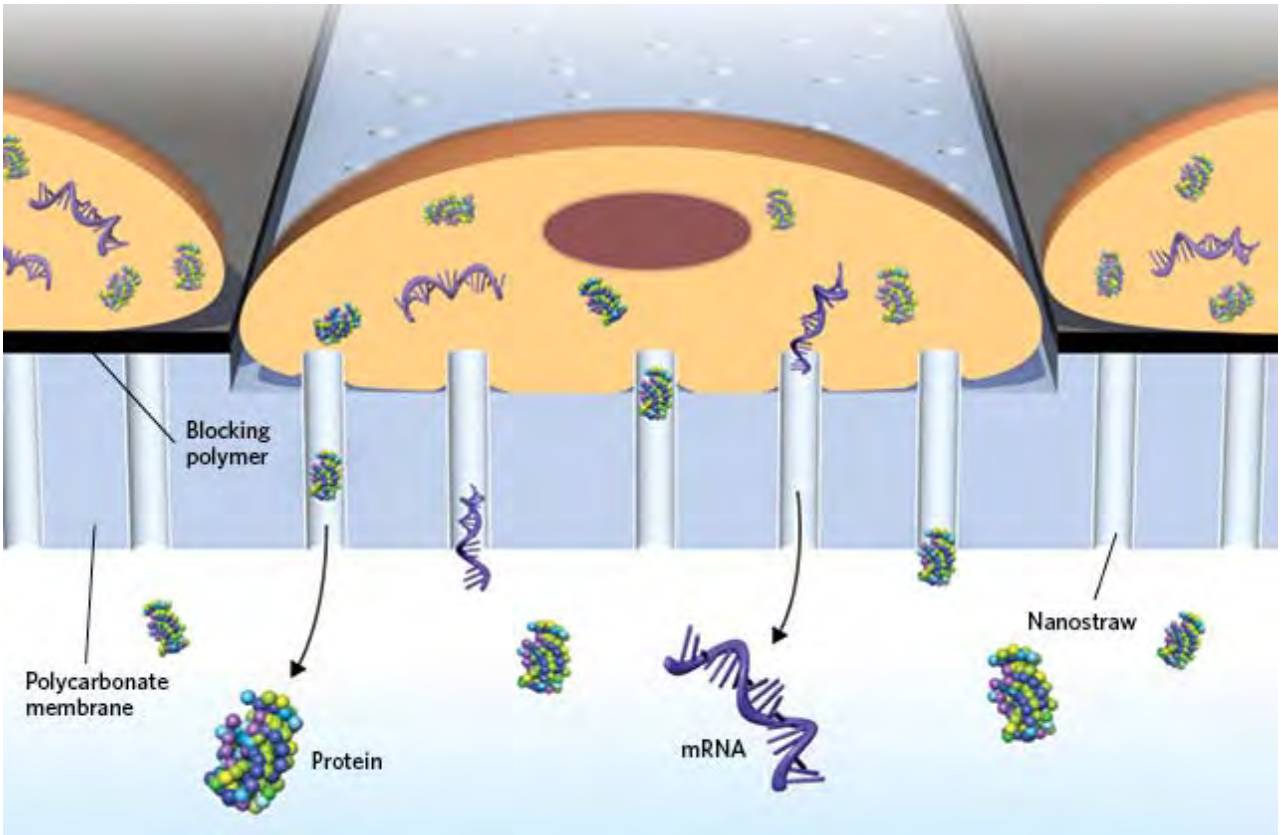
In two studies published this spring, groups in Massachusetts and Wisconsin reported reprogramming mouse or human cells to generate hematopoietic stem cells, which produced blood cells when implanted into mice. Key to both studies was finding the right mix of transcription factors and environmental cues to coax the cells toward the desired identity. Progress had been slow in reprogramming cells to become blood progenitors, but these results could help overcome obstacles, increasing the odds of moving the



RIO SUGIMURA

research from the lab to the clinic.

Sampling live cells



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With today's laboratory and computational technology, researchers can garner gene expression and other types of data at the single-cell level, but there's a catch: the cells have to be killed in order to analyze their contents. A new method called nanostraw extraction, developed by Nicholas Melosh of Stanford

University, aims to avoid that. Cells are grown atop a polycarbonate membrane with aluminum oxide nanostraws that protrude into the cell membrane. When an electric current passes through the straws, they briefly open pores in the cell membrane, allowing contents such as protein and mRNA to flow out.

Correction (Dec. 27): An earlier version of this article misidentified one of the institutions where a robotic patch clamping method was developed. It was Imperial College London, not University College London. The Scientist *regrets the error.*

Tags

techniques, synthetic biology, Patch clamping, nanotechnology, nanostraws, methods, hematopoietic stem cells, DNA origami, CRISPR/Cas and CRISPR

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December 30, 2017

Gee, with all these wonderful research developments, one would expect miraculous cures for diseases in 2018! Kudos to all you researchers, don't give up.

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