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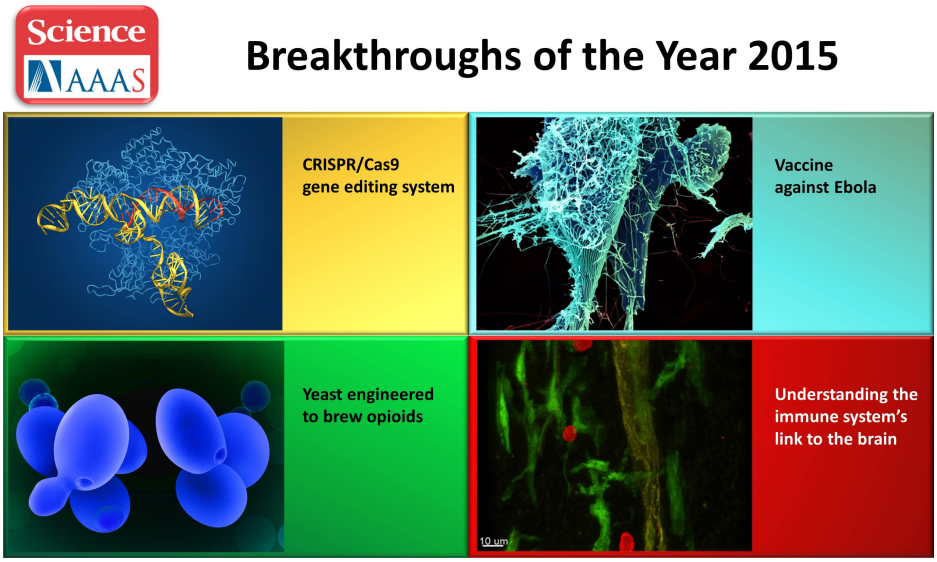
Happy New Year … and a Look Back at a Memorable 2015

Posted on January 5th, 2016 by Dr. Francis Collins



A new year has arrived, and it's going to be an amazing one for biomedical research. But before diving into our first "new science" post of 2016, let's take a quick look back at 2015 and some of its remarkable accomplishments. A great place to reflect on "the year that was" is the journal *Science's* annual Top 10 list of advances in all of scientific research worldwide. Four of 2015's Top 10 featured developments directly benefited from NIH support—including *Science's* "Breakthrough of the Year," the CRISPR/Cas9 gene-editing technique. Here's a little more on the NIH-assisted breakthroughs:

CRISPR Makes the Cut: I've highlighted CRISPR/Cas9 in several posts. This gene-editing system consists of a short segment of RNA that is attached to an enzyme. The RNA is preprogrammed to find a distinct short sequence of DNA and deliver the enzyme, which acts like a scalpel to slice the sequence out of the genome. It's fast and pretty precise. Although CRISPR/Cas9 isn't brand-new—it's been under development as a gene-editing tool for a few years—*Science* considered 2015 to be "the year that it broke away from the pack."

One way CRISPR/Cas9 earned its "breakthrough" status is through the demonstration of its ability to be used as a tool to create a "gene drive." A gene drive involves engineering an organism's genome in a way that intentionally spreads, or drives, a trait through its population much faster than is possible by normal Mendelian inheritance. CRISPR/Cas9 was successfully used in 2015 to create gene drives—in two model organisms and, in research with implications for malaria control, in mosquitoes.

Also contributing to the buzz about CRISPR/Cas9 are recent efforts by scientists in China to use non-viable human embryos to test the ability of CRISPR/Cas9 to edit germline cells and transmit the changes to the next generation of cells [1]. The study raised ethical concerns that science was fast approaching a red line of engineering human life. In December, representatives from some of the world's leading science academies met in Washington, D.C. to discuss the latest developments.They endorsed continued vigorous research on ways to use CRISPR/Cas9 to modify somatic cells for the treatment of genetic diseases, but concluded that any approaches that would alter the germline in a human individual should be prohibited: a cautious approach that NIH strongly endorses.

A Vaccine against Ebola: The Ebola outbreak that began two years ago in West Africa tragically has taken the lives of more than 11,000 people, but galvanized efforts to develop a vaccine for this horrible virus. Even as the epidemic waned, researchers pressed forward with trials of new vaccines that might prevent the next outbreak. A vaccine known as rVSV-ZEBOV was tested using a novel vaccination strategy in more than 7,600 people in Guinea [2]. Although NIH was not involved in this specific trial,

researchers from our National Institute of Allergy and Infectious Diseases (NIAID) and Clinical Research Center were involved in this vaccine's early Phase I clinical testing in collaborations with the Walter Reed Army Institute of Research [3]. The NIAID investigators also took part in the preclinical development of the vaccine and in Phase II clinical trials in Liberia.

NIAID scientists, led by Drs. Cliff Lane and Anthony Fauci, also conducted work in several other areas of great importance in our long-term battle against Ebola. They coordinated a randomized trial of two different Ebola vaccines in West Africa and set up a rigorous clinical trial to determine whether the monoclonal antibody strategy ZMapp plus medical support was more effective than medical support alone. In addition, they launched a follow-up study that to date has enrolled more than 1,000 individuals who survived the acute phase of Ebola infection and more than 700 of their close contacts, to assess the long-term consequences of the infectious disease.

Yeast Engineered to Brew Opioids: Yeast has many uses—including its role as a key ingredient in making leavened bread and brewing beer. Last September, a team of researchers at Stanford University, Palo Alto, CA, added another possibility: synthesizing drugs from scratch inside yeast cells—in their case opiates [4]. Doctors prescribe opiates to control many kinds of pain, but opiates are also a source of great current societal concern, with a steadily increasing incidence of U.S. deaths from unintentional overdoses. Currently, all opiates—even the semisynthetic ones—are derived from opium poppy plants. In the new work, the Stanford team engineered more than 20 genes from five different organisms (opium poppy, California poppy, goldthread plant, rat, and bacteria) into the genome of baker's yeast to cobble together a metabolic pathway that converts sugar into the semi-synthetic opioid hydrocodone or thebaine, which can be converted into a variety of opiate compounds. The opiate yield was very low, so this isn't about to become the next version of "Breaking Bad." But this approach could lead to a much more rational way to manage opioid production, and perhaps to produce new chemical entities that are less addictive. What's also exciting is this proof-of-principle work suggests that the technique can be adapted in yeast to make many other plant-derived compounds for fighting cancer, infectious disease, and a variety of chronic diseases.

The Brain's Well-Hidden Secret: It's long been thought that the brain isn't directly connected to the immune system. Last June, researchers at the University of Virginia, Charlottesville, discovered that's not the case [5]. It turns out the brain is indeed directly connected to the immune system by a network of lymphatic vessels that were hidden by major blood vessels. The discovery will allow researchers to take a more mechanistic approach to understanding how immune cells move in and out of the brain, promising to speed the discovery of possible targets to control the inflammation that may contribute to a range of neurological conditions, including multiple sclerosis, Alzheimer's disease, Parkinson's disease, and autism.

There are certainly other notable lists of research advances. *Science News*, for example, recently issued its Top 25 Science Stories of 2015, which included a number of additional biomedical research stories that are worth revisiting. But one end-of-the-year breakthrough list that really caught my eye was on the PLOS-hosted DNA Science Blog. That's where geneticist Ricki Lewis nominated the Precision Medicine Initiative (PMI) as the Breakthrough of the Year for 2015. Her enthusiasm for the upcoming launch of PMI is much appreciated.

As I look forward to seeing the biomedical breakthroughs that 2016 brings, I'm heartened by NIH's favorable support in the Fiscal Year 2016 Omnibus Bill—our most encouraging budget allocation in 12 years. The increase is well timed to take advantage of the many promising opportunities to improve human health, while helping to meet the needs of the biomedical research community to get the job done.

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***J.* says:**
January 13, 2016 at 6:45 am
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