CRS INSIGHT

CRISPR: A Revolutionary Tool for Editing the Code of Life?

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Genes, the fundamental code of life, are written in DNA (deoxyribonucleic acid). Before DNA was even discovered, humans sought to manipulate it through selective breeding. Since its discovery, scientists, science fiction writers, philosophers, and others have speculated on the implications of being able to modify DNA. Over the last half century, billions of dollars and immeasurable effort have been devoted to understanding, characterizing, and controlling DNA. These efforts produced early gene editing tools and, in 2003, the completion of the Human Genome Project. Similar sequencing has been completed on thousands of other species.

Current gene editing tools have allowed scientists to edit the genomes of agricultural crops (e.g., improving insect resistance) and to create animal research models (e.g., transgenic mice). However, shortcomings in gene editing technologies have hindered even wider use.

What Is CRISPR?

CRISPR-cas9 (CRISPR for short) is a new gene editing tool that offers the potential for substantial improvements in ease of use, speed, efficacy, and cost. Many in the scientific, engineering, and business communities believe CRISPR may offer revolutionary advances in the investigation, prevention, and treatment of diseases; understanding of gene function; crop yields and varieties; production of chemicals used in biofuels, adhesives, and fragrances; and control of invasive species. CRISPR has already been used to modify the genomes of a variety of species—ranging from mice and fruit flies to corn and yeast. Some scientists believe the relative simplicity and lower cost of CRISPR represents the democratization of genetic engineering.

The technology traces its foundations to the 1970s, when scientists investigating bacteria discovered repeating sequences of DNA (Clustered Regularly Interspaced Short Palindromic Repeats, CRISPR) with unknown function. Further research revealed that these sequences separated DNA that the bacteria stored from viruses as part of an immunity system. The bacteria use this stored information, along with CRISPR-associated proteins, to identify and

destroy invading viruses using "molecular scissors" to cut their DNA. During 2012 and 2013, scientists adapted this system to cut DNA at precise locations, enabling removal or replacement of targeted DNA in the genomes of microorganisms, plants, and animals.

Potential of CRISPR

The perceived potential of the technology is reflected in market projections (ranging from 14% to 31% annual growth over the next 5-6 years) and public and private investments. Several CRISPR-based startups had initial public stock offerings in 2016. These include Editas Medicine ($94.4 million), Intellia Therapeutics ($112.9 million); and CRISPR Therapeutics ($56 million). Caribou Biosciences raised $30 million in private financing in May 2016. In addition, pharmaceutical, agricultural, and other firms—including Novartis, Bayer AG, Monsanto, DuPont Pioneer, Juno Therapeutics—are conducting CRISPR research; have secured licenses to CRISPR patent rights; or have invested in, engaged in partnerships with, or formed joint ventures with CRISPR-based startups.

The potential of CRISPR is further reflected in increases in CRISPR-related federal research funding, scientific publications, and patents. National Institutes of Health funding for CRISPR-related research grew from $5.1 million in FY2011 to $463 million in FY2016.

Applications of CRISPR

CRISPR has been used to create wheat and rice that are resistant to disease, sweet oranges that are enriched with vitamins, corn with higher starch content, and cattle without horns. The use of CRISPR by U.S. agricultural companies rather than other gene editing technologies may allow some crops to bypass U.S. regulations faced by other genetically modified organisms (GMOs). Most traits (e.g., drought tolerance) that have been added to plants using other technologies have introduced bacterial DNA into the plant's genome along with the desired trait. The incorporation of bacterial DNA triggers regulation by the U.S. Department of Agriculture (USDA). CRISPR, however, is able to disable or cut out genes without the potential introduction of bacterial DNA. Recently, USDA determined that a CRISPR-edited mushroom did not fall within the agency's regulatory framework because it did not include bacterial DNA.

CRISPR-enabled approaches are being considered by some public and private researchers in efforts to reduce or eliminate malaria, one of the most widespread and lethal illnesses in the world. Effective modification, reduction, or elimination of the *Anopheles* mosquito—the primary vector for transmission of malaria—could save lives and substantially reduce costs associated with the prevention and treatment of malaria. Research approaches include the use of a gene drive, a genetic tool that results in a gene being preferentially passed to all offspring rather than part of them. This might offer a means by which all *Anopheles* mosquitoes could be made infertile or all offspring male, which in time could drastically reduce or possibly even eliminate the malaria vector. Other research seeks to make the mosquito resistant to the malaria parasite or more susceptible to pesticides.

Potential Concerns with CRISPR

Some scientists have raised ethical questions and expressed concerns over the potential ecological consequences of using CRISPR to eliminate a species or introduce a GMO into the wild.

Another significant area of ethical concern is the use of CRISPR to edit human germline cells (i.e., eggs and sperm) given that such changes would affect not only the immediate patient but future generations who would inherit, without choice, these genetic changes. Some researchers have also raised concerns about who would have access to CRISPR-based treatments and enhancements. Some scientists have called for a global moratorium on the editing of human germline cells. Nevertheless, in 2015, Chinese scientists used CRISPR to eliminate a gene that causes a deadly blood disorder. While the experiment used nonviable human embryos it sparked further ethical debate and calls for establishment of international norms and harmonization of regulations.

CRISPR may be a disruptive technology—one that spawns new products, activities, firms, and industries; and potentially displaces current market leaders. Such disruptions often have ethical, legal, and societal implications that have consequences for public policy in areas such as research and development; environmental, health, and safety regulations; trade; and workforce education and training. Disruptive technologies can also have implications for U.S.

industrial competitiveness, job creation, economic growth, health, the environment, and national security. As CRISPR-based gene editing technologies mature, policymakers may want to explore these policy dimensions.