Emmanuelle Charpentier, PhD (left), and Jennifer Doudna, PhD, were awarded the 2020 Nobel Prize in Chemistry for pioneering CRISPR-based genome-editing technology, a molecular tool that can precisely cut DNA. The system has myriad uses: It could, for example, be used to treat inherited diseases and develop immunotherapies for cancer.

In the years since Charpentier's and Doudna's landmark discovery, CRISPR technologies have become staples of basic research laboratories in all fields, with countless scientists adopting the simple and inexpensive tool to manipulate DNA in unprecedented ways. Cancer researchers have used the tool to precisely disrupt tumor suppressor genes or activate oncogenes to build more accurate disease models, discover drug targets, reveal basic mechanisms of tumor development, and much more.

"CRISPR really made genetic engineering methods a lot more convenient, easier, faster, and cheaper," says Jerry Li, MD, PhD, of the NCI's Division of Cancer Biology.

"For now, the most impactful outcome of this CRISPR technology is in the cancer biology world," he says, "but it's trickling into the therapeutic world," with several CRISPR-based interventions already in human testing. Some take aim at rare blood disorders, others at an inherited form of blindness. Leading the way, however, are trials of gene-edited T cells for cancer.

The first such U.S.-based trial launched in 2018 at the University of Pennsylvania in Philadelphia, where Edward Stadtmauer, MD, and his colleagues treated three patients—two with myeloma and one with liposarcoma—with an autologous NY-ESO-1–directed T-cell product in which they had disabled genes encoding T-cell receptors (TCR) and PD-1 receptors. "CRISPR was essential for the performance of our first-in-human attempt to enhance the function and activity of engineered T cells," says Stadtmauer, who reported earlier this year that the cells were well tolerated and showed durable engraftment (Science 2020;367:eaba7365).

CRISPR Therapeutics, a company cofounded by Charpentier, is also testing three allogeneic chimeric antigen receptor T-cell therapies that use the gene-editing technique to eliminate the TCR and MHC I molecules from donor cells and to precisely insert the genetic construct equipped with antigens for either CD19, BCMA, or CD70, depending on the therapy. Meanwhile, Intima Bioscience is studying whether knocking out an intracellular immune checkpoint gene called *CISH* from a patient's own tumor-infiltrating lymphocytes can enhance TCR avidity, improve neoantigen recognition, and lead to tumor regression. A phase I trial in metastatic gastrointestinal cancers kicked off earlier this year at the University of Minnesota's Masonic Cancer Center in Minneapolis.

Clinicians in China have also launched at least nine other trials of CRISPR-engineered T-cell therapies since 2017.

The various T-cell therapies under evaluation all involve gene editing *ex vivo*, but Eric Kmiec, PhD, of ChristianaCare's Gene Editing Institute in Newark, DE, hopes to soon begin testing an *in vivo* CRISPR-based treatment. He plans to disable *NRF2*—a gene involved in tumor progression and chemotherapy resistance—in patients with advanced non–small cell lung cancer to try to stall cancer growth and make tumors more susceptible to platinum-based chemotherapeutics.

Earlier this year, Kmiec's team described a unique stretch of tumor-specific DNA that allows for targeting *NRF2* in cancer cells without affecting the gene in normal tissues—and he credits Charpentier and Doudna, who helped define the various pieces of the CRISPR machinery, for making that strategy possible (Mol Cancer Res 2020;18:891–902). "Without this fundamental molecular information," Kmiec says, "it would've taken us much longer to develop our tumor-specific selective protocol for the disablement of the *NRF2* gene in squamous cell carcinoma cells." *–Elie Dolgin* ■

For more news on cancer research, visit *Cancer Discovery* online at http://cancerdiscovery.aacrjournals.org/CDNews.

NOTED

Exact Sciences will acquire Thrive Earlier Detection for $1.7 billion up front and up to $450 million more in milestone payments. Exact will gain CancerSEEK, Thrive's liquid biopsy cancer-screening test that combines genomic screening with protein analysis. Exact will also acquire Base Genomics, an epigenetics company developing technology for DNA methylation sequencing.

CRISPR Therapeutics announced positive results but concerning side effects with CTX110 in patients with relapsed/refractory B-cell malignancies. In the phase I CARBON trial, the allogeneic anti-CD19 chimeric antigen receptor T-cell therapy elicited complete responses in four of 11 patients. However, three patients developed cytokine release syndrome, one experienced immune effector cell–associated neurotoxicity syndrome, and one died due to side effects.

The FDA approved Bristol Myers Squibb's nivolumab (Opdivo) plus ipilimumab (Yervoy) for patients with newly diagnosed, inoperable malignant pleural mesothelioma. The approval was based on the phase III CheckMate-743 trial, in which patients treated with the PD-1–CTLA4 inhibitor combination had a median overall survival of 18.1 months, compared with 14.1 months in patients who received standard chemotherapy.

People living in U.S. counties with persistent poverty may have a higher risk of dying from cancer than those living in areas with less poverty (Cancer Epidemiol Biomarkers Prev 2020;29:1949–54). Between 2007 and 2011, the cancer mortality rate was 201.3 deaths per 100,000 people in counties with persistent poverty (those with poverty rates of at least 20% in Census data since 1980), compared with 179.3 deaths per 100,000 people in counties without persistent poverty.

The COVID-19 pandemic has dramatically cut cancer screenings, diagnoses, and treatments (JCO Clin Cancer Inform 2020 Oct 21 [Epub ahead of print]). Researchers analyzed 6,227,474 Medicare claims and found significant decreases in screening when comparing April 2019 with April 2020: Screening dropped by 85% for breast cancer, 75% for lung cancer, 74% for colon cancer, and 56% for prostate cancer. There were also declines in biopsies, chemotherapy treatments, and surgery.