Researchers found that activity of STAT3 (above) is higher in patients with CLL who experience a complete remission following CAR T-cell therapy.

studied 41 patients with advanced CLL who had received CAR T-cell therapy. Their initial analysis ruled out several possible factors, including patients’ age, prior therapy, and p53 status.

Next, patients were divided into four categories based on treatment results: complete remission, partial response, no response, or partial response after which the cancer evolved into aggressive B-cell lymphoma. The scientists then measured gene expression in T cells engineered to express the CAR protein and were ready to be infused into the patients.

T cells from patients who had complete remission and those whose cancer transformed into B-cell lymphoma showed increased expression of genes that favor early differentiation into memory cells. Why the response was so strong in patients whose cancers evolved isn’t clear. In patients who had partial responses or did not respond, however, expression of genes involved in effector T-cell differentiation went up. Also, the activity of genes that indicate exhaustion or that promote apoptosis and aerobic glycolysis, which provides much of the energy for effector cells, also increased. These differences in gene expression were not the result of the CAR T-cell manufacturing process, the researchers determined.

The scientists found further evidence that an early memory T-cell phenotype correlates with a stronger response when they analyzed STAT3, which spurs memory cell differentiation and maintenance. STAT3 activity was higher in patients who had a complete remission or whose cancers evolved into B-cell lymphoma than in patients with partial or no responses. “We think that STAT3 signaling is really important for the cells’ behavior in vivo,” says co-author Joseph Fraietta, PhD, also of Penn.

Another sign that the CAR T-cell treatment was likely to be successful was the presence of CD8+ T cells that carry CD27 but lack CD45RO, the scientists determined. These cells show characteristics of long-lived memory cells and were more than twice as abundant in patients who had complete remissions or whose disease evolved than in the other two groups.

The study is “a step forward in trying to understand what is a good CAR T product and what is a good starting [T-cell] population,” says Satava Neelapu, MD, of The University of Texas MD Anderson Cancer Center in Houston, who wasn’t connected to the research. “It provides some strategies to improve efficacy in CLL patients.”

Those strategies, Fraietta and Melenhorst note, could include testing patients’ T cells before they undergo CAR T-cell treatment to select the most likely responders. In addition, modifying CAR T-cell manufacturing might increase the number of cells that promote a response. For example, it might be possible to bolster this subpopulation by modifying the mixture of cytokines used to stimulate them. —Mitch Leslie

**President Signs STAR Act for Kids’ Cancers**

On June 5, President Donald Trump signed the Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act, comprehensive legislation that aims to broadly support pediatric cancer research by expanding the collection of patient biospecimens and records, improving surveillance, and investigating pediatric survivorship.

“It’s very exciting legislation. It’s not focused on small questions; it’s focused on building and improving our ability to do pediatric cancer research,” says Donald Parsons, MD, PhD, of Texas Children’s Hospital in Houston. He adds that the Act includes provisions for large-scale, long-term data and sample collection that “can be the foundation for all types of different pediatric cancer research—studying individual diseases, studying late effects of therapy, trying to correlate clinical outcomes with particular treatments or biological features of the patients.”

One such provision expands the NCI’s efforts to collect biospecimens for patients enrolled in NCI-sponsored clinical trials, and to compile clinical, biological, and demographic information on children, adolescents, and young adults with cancer. The Act also authorizes grants for state cancer registries to track pediatric cancer incidence, and for research on pediatric cancer survivorship.

Although overall survival rates are now greater than 80%, pediatric cancers remain difficult to study, says Tara Henderson, MD, MPH, of The University of Chicago in Illinois, because their relative rarity, combined with a large number of cancer subtypes, means there aren’t many patients with any particular type of cancer.

“We really need the NIH and the government to support the research in those patients,” she says, and to support continued collaboration among pediatric oncologists. “Part of the reason we’ve been able to make the advances we have is because we have a very high-functioning cooperative group called the Children’s Oncology Group, supported by the NIH.”

The STAR Act follows another piece of legislation in childhood cancer—last August, Congress passed the Research to Accelerate Cures and Equity (RACE) Act of 2017, which requires companies developing cancer drugs for adults to develop those drugs for children based on the drug’s molecular target rather than cancer type.

Henderson hopes the STAR Act will support research on the biology of long-term side effects of treatment—for example, why some patients and not others develop cardiomyopathy. She also emphasizes the need for more research on older pediatric patients, who haven’t benefited as greatly from new treatments as younger patients.

Additionally, Henderson and Parsons are excited about expanding the database of biospecimens collected from patients enrolled in NCI-sponsored clinical trials.

“Those samples are worth their weight in gold—they’re biological samples that are matched to rigorous clinical data for patients who have been uniformly treated on clinical trials, such that you can really dive into...
the practical aspects of the biology of childhood cancer,” Parsons says.

“If we can start collecting [data] in a centralized location, then any one researcher is not going to be limited to the patients that they see at their hospital,” Henderson adds. “This will enable scientists to ask very broad-reaching questions with access to biological samples where they can have good [statistical] power to answer these questions.” –Catherine Caruso

**Little Benefit to Breakthrough Cancer Drugs**

In 2012, the FDA created the breakthrough therapy designation to speed up the development and review of drugs intended to treat serious or life-threatening diseases when preliminary clinical evidence indicates a possible substantial improvement over existing therapies. However, a recent analysis of breakthrough-designated cancer drugs indicates that although they are approved more quickly, they are no more effective, safe, or novel than drugs approved via the traditional pathway.

Because 59% of cancer medicines approved since 2014 have received that designation, researchers wanted to assess the value of these drugs, explains Jonathan Darrow, SJD, JD, MBA, of Harvard Medical School and Brigham and Women’s Hospital in Boston, MA, and senior author of the study (J Clin Oncol 2018;36, no. 15 suppl;6504). Researchers analyzed data from the 2016 American College of Radiology’s Lung Cancer Screening Registry, which tracked screening at 1,796 sites throughout the country. Screening rates were highest in the Northeast (3.5%) and lowest in the West (1%).

Men and women may have different responses to immunotherapies (Lancet Oncol 2018;19:737–46). Researchers analyzed 20 trials involving 11,351 patients with advanced cancers who were treated with immune checkpoint inhibitors. They found that although the drugs improved overall survival in both men and women, the efficacy of the drugs, on average, was significantly better in men.

President Donald Trump signed “right-to-try” legislation that allows terminally ill patients to seek experimental drugs directly from pharmaceutical companies. Previously, patients could apply to the FDA for access via a process called expanded access or compassionate use, which approved 99.5% of more than 7 million current and former heavy smokers were screened for lung cancer in 2016 (J Clin Oncol 2018;36, no. 15 suppl;6504). Researchers analyzed data from the 2016 American College of Radiology’s Lung Cancer Screening Registry, which tracked screening at 1,796 sites throughout the country. Screening rates were highest in the Northeast (3.5%) and lowest in the West (1%).

**Women with BRCA-mutant advanced triple-negative breast cancer are twice as likely to respond to carboplatin as docetaxel** (Nat Med 2018;24:628–37).

In the phase III TNT trial, women with BRCA gene faults who were treated with carboplatin had an objective response rate (ORR) of 68%, compared with 33% in those treated with docetaxel. This difference was not present when researchers analyzed ORR across the entire trial population.

Elie Lilly is buying ARMO Biosciences for $1.6 billion. ARMO Biosciences specializes in immuno-oncology drugs. Its leading candidate is pegilodecakin, a PE-glylated form of IL10 under study in a phase III trial in pancreatic cancer, as well as earlier-stage trials in other solid tumor types, including melanoma and lung and renal cancers.

In the United States, only 1.9% of more than 7 million current and former heavy smokers were screened for lung cancer in 2016 (J Clin Oncol 2018;36, no. 15 suppl;6504). Researchers analyzed data from the 2016 American College of Radiology’s Lung Cancer Screening Registry, which tracked screening at 1,796 sites throughout the country. Screening rates were highest in the Northeast (3.5%) and lowest in the West (1%).

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