be to incorporate biomaterials into the design of this immunotherapy, as demonstrated by two preclinical studies from Fred Hutchinson Cancer Research Center in Seattle, WA.

Immunobioengineering is a young field, says senior author Matthias Stephan, MD, PhD, but it could make CAR T-cell therapy more widely applicable and “not such a big deal,” referring to the elaborate protocols currently required to manufacture these cells ex vivo.

In one study, Stephan and his team evaluated polymer-based nanoparticles that bind CD3 on T cells and deliver their cargo—a CAR gene for CD19—to be integrated into the cell nuclei (Nat Nanotech 2017 April 17 [Epub ahead of print]). When these biodegradable nanoparticles were injected into mice with acute lymphoblastic leukemia (ALL), circulating T cells were successfully converted, in situ, into CD19-targeting CAR T cells within 24 hours.

“We turned naïve T cells into serial killers that were already at their job site and could immediately eliminate tumors,” Stephan explains. The newly minted therapeutic cells’ huge proliferative capacity prompted their rapid self-expansion, he adds, so “although the [CAR] gene transfer process was fairly inefficient, we only needed an initial spark to start the fire.”

These in situ programmed CAR T cells eradicated ALL in seven of 10 mice; the rest experienced substantial disease regression and a median 58-day improvement in survival. The efficacy data were not significantly different from those for a control group of mice given conventionally generated CAR T cells, Stephan notes.

This “very novel approach may shake up the gene and cell therapy fields to think in new, fresh ways,” observes Crystal Mackall, MD, of Stanford University in Palo Alto, CA. “The results are preliminary but highly impressive, illustrating the untapped potential of marrying nanomedicine with genetic engineering.”

“Our goal is for CAR T-cell therapy to outcompete chemotherapy as a first-line treatment for leukemia/lymphoma, because it can be prescribed and administered just as easily,” Stephan says.

Meanwhile, to better apply CAR T-cell therapy to solid tumors, which are highly heterogeneous compared with hematologic malignancies, the team developed what Stephan describes as “a simple tool for surgeons” (J Clin Invest 2017;127:2176–91). It involves implanting alginate-based sponges within the cavity of a resected tumor, or directly on the surface of otherwise inoperable tumors. These dissolvable quarter-sized sponges serve as scaffolds that can be loaded with CAR T cells (conventionally manufactured ex vivo) plus an optimal mix of growth factors to stimulate proliferation.

Importantly, expansion of CAR T cells to destroy tumor cells expressing a given antigen—in this case, NKG2D—is “just the first wave,” Stephan says. The scaffold is designed to simultaneously deliver a STING agonist that primes a second, broader immune response by recruiting and stimulating dendritic cells capable of recognizing multiple other tumor antigens. STING agonists are “very potent vaccine adjuvants and too toxic to be given intravenously,” he adds, but these small sponges can safely deliver high local concentrations that synergize with CAR T cells in antitumor activity.

Biomaterials,” says Michael Goldberg, PhD, of Dana-Farber Cancer Institute in Boston, MA. “This platform is worthy of consideration for clinical translation—the data confirm that the efficacy of CAR T-cell therapy is vastly augmented if these cells are released in the presence of factors supporting both innate and adaptive immunity.”

“We need industry partners who are adventurous enough to combine bioengineering with immunotherapy,” Stephan says. Given the present focus among major CAR T-cell therapy players on crossing the FDA-approval finish line, he thinks smaller biotechs may be better positioned to advance both nanoparticle and scaffold strategies in the clinic. —Alissa Poh

Congress OKs $2 Billion Boost for the NIH

In May, President Donald Trump signed a $1.1 trillion spending bill for the remainder of fiscal year (FY) 2017, which includes a $2 billion increase for the NIH. The move comes as a relief to many in the biomedical research community, which is gearing up to fight massive cuts in FY 2018 in the wake of a White House budget proposal to reduce the agency’s funding by nearly 20%.

The funding increase expands the NIH’s total annual budget by 6.2% to $34.1 billion. The NCI will be allocated $5.69 billion of this amount—an overall boost of $476 million, of which $300 million was appropriated in
Comprehensive Cancer Research

Institute in Atlanta, GA, has been

Emory’s Winship Earns Comprehensive Status

Emory University’s Winship Cancer Institute in Atlanta, GA, has been granted Comprehensive Cancer Center status, the NCI’s highest designation. It is one of 48 centers nationwide to achieve this distinction, which recognizes leadership in cancer research, education, and clinical care.

Winship became Georgia’s first and, to date, only NCI-designated center in 2009. It has since added new faculty and enhanced its research programs, says executive director Walter Curran Jr., MD. Currently, Winship’s four research programs—Cancer Cell Biology; Cancer Prevention and Control; Cancer Genetics and Epigenetics; and Discovery and Developmental Therapeutics—encompass 440 grants totaling $110 million in funding annually. “To earn comprehensive status, we had to demonstrate that our research, education, and training impact the burden of cancer across the entire state of Georgia,” says Curran. “We’ve added eight new faculty members in the area of population science who have helped us make significant advances in cancer prevention and control.”

For example, Michelle Kegler, DrPH, MPH, director of the Emory Prevention Research Center, recruited a group of low-income adults who either smoked or lived with a smoker to participate in a randomized trial. They received three mailings and one coaching phone call on how to create smoke-free homes (Am J Public Health 2015;105:530–7). After 6 months, 40% of participants who received this intervention reported a full ban on smoking in the home, compared with 25% of control subjects.

The study’s findings are helping to change secondhand-smoke policies and practices statewide, including a current effort to promote smoke-free apartment communities, says Kim Kerstann, PhD, Winship’s senior director for cancer research administration. Kegler’s intervention strategy has been implemented by 2-1-1 referral and information phone services in Georgia and several other states—including Alabama, Oklahoma, Texas, Ohio, Florida, and North Carolina—as well as several community organizations in California.

Winship has also pioneered new imaging techniques to better visualize tumors, says Curran. Studies led by radiologist Mark Goodman, PhD, resulted in the FDA approving fluciclovine (Axumin; Blue Earth Diagnostics), a radiolabeled synthetic analog of the amino acid leucine, in 2016 for PET imaging of prostate cancer.

As well, the NCI recognized Winship’s efforts to expand patient access to experimental treatments. The Discovery and Developmental Therapeutics program operates a phase I clinical trials unit; in addition, Winship is a lead academic participating site for the NCI’s National Clinical Trials Network, which focuses on phase II and III trials. In total, Winship researchers oversee about 250 clinical trials enrolling almost 800 patients annually, says Kerstann.

“A major contributing factor to our new designation is the depth and breadth of our clinical trials and translational research,” she says. “We are developing a network and formal mechanism to partner with community oncologists and expand clinical research into the community setting to help lessen the burden of cancer in our state.” –Janet Colwell

Immune Atlases Created for Kidney, Lung Cancers

Researchers from the University of Zurich in Switzerland and Mount Sinai School of Medicine in New York, NY, have generated the first comprehensive “immune atlases” of clear cell renal cell carcinoma (ccRCC) and early lung adenocarcinoma, respectively. Their simultaneously published work better illuminates the tumor immune microenvironment and may lead to more effective immunotherapy strategies.

Both groups used mass cytometry—which enables rapid, fine-grained scrutiny
CANCER DISCOVERY

Congress OKs $2 Billion Boost for the NIH

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