Health

Towards “Off-the-shelf” Immune Cell Therapy for Cancer-ScienceDaily

robynford • 1 week ago

Immunotherapy, which uses the body’s natural defenses to combat disease, has revolutionized the treatment of aggressive and deadly cancers. However, in many cases, these therapies, especially those based on immune cells, need to be tailored to the individual patient, spending valuable time and pushing their price to hundreds of thousands of dollars.

Now, in the research published in the journal *Cell Reports Medicine*UCLA researchers have developed “off-the-shelf” cancer immunotherapy using rare but powerful immune cells that are mass-produced, stored for long periods of time, and have the potential to be safely used in a wide range of treatments. Reporting an important step in. Patients with various cancers.

“To reach the largest number of patients, we need cell therapies that can be mass-produced, frozen, and shipped to hospitals around the world,” said Lili Yang, a member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research. Says. Lead author of UCLA and research. “This allows us to prepare doses for these treatments and wait for the patient immediately if needed.”

For research, Yang and her colleagues focused on invariant natural killer T cells, or iNKT cells. These are unique not only because of their power and effectiveness, but also because of the risk of graft-versus-host disease. When transplanted cells attack the recipient’s body, that’s why most cell-based immunotherapies must be created patient-specific, Yang said.

Researchers have developed a new method for producing large numbers of these iNKT cells using hematopoietic stem cells that can self-replicate to produce all types of blood and immune cells. The team used stem cells from four donor cord blood samples and eight donor peripheral blood samples.

“Our findings suggest that a single cord blood donation can be treated up to 5,000 times, and a single peripheral blood donation can be treated up to 300,000 times.” Yang, an associate professor and member of microbiology, immunology, and molecular genetics, said. Of the UCLA Johnson General Cancer Center. “This yield can dramatically reduce the cost of manufacturing immune cell products.”

Researchers first used genetic engineering to program hematopoietic stem cells to increase their chances of developing into iNKT cells. These genetically engineered stem cells were then placed in artificial thymic organoids that mimic the environment of the thymus, a special organ in which T cells naturally mature in the body. After 8 weeks with organoids, each stem cell produced an average of 100,000 iNKT cells.

Next, Yang and her collaborators compared the ability of hematopoietic stem-engineered cells called iNKT cells or HSC-iNKT cells to fight cancer in natural killer cells or immune cells called NK cells. I tested it. In the laboratory dish, HSC-iNKT cells were much better than NK cells in killing multiple types of human tumor cells, including leukemia, melanoma, lung cancer, prostate cancer, and multiple myeloma cells. Was discovered by researchers.

More importantly, HSC-iNKT cells maintained their tumor-killing effect after freezing and thawing. This is an essential requirement for the widespread adoption of off-the-shelf cell therapies.

Next, the researchers equipped HSC-iNKT cells with a chimeric antigen receptor (CAR). It is a special molecule used in some immunotherapies to allow immune cells to recognize and kill certain types of cancer. In this case, they added CARs to HSC-iNKT cells that target the proteins found in multiple myeloma cells and tested the cells’ ability to fight human multiple myeloma tumors transplanted into mice.

HSC-iNKT cells equipped with these CARs eliminated multiple myeloma tumors, and the treated mice were tumor-free and showed no signs of complications such as graft-versus-host disease throughout their lives.

Researchers are currently working to improve manufacturing methods by eliminating sustentacular cells such as those used in thymic organoids and moving to a feeder-free system that helps blood stem cells generate iNKT cells. .. Yang hopes that this advance will enable mass production of therapies and ultimately their clinical and commercial development.

The co-lead authors of this paper are Yan-Ruide (Charlie) Li and Yang (Alice) Zhao, PhD students at UCLA. Other authors include UCLA professors Dr. Sarah Larson, Dr. Joshua Sasine, Dr. Xiaoyan Wang, Dr. Matteo Pellegrini, Dr. Owen Witte, and Dr. Antonio Ribas.

Genetic engineering of hematopoietic stem cell researchers leveraged the method developed by Dr. Donald Korn, and artificial thymic organoids were developed by all UCLA Broad Stem Cells, Dr. Gay Crooks, Dr. Chris Seet, and Amélie Montel-Hagen. rice field. Research Center.

The methods and products described in this study are patent applications filed by the UCLA Technology Development Group with Yang, Li, Yu Jeong Kim, Jiaji Yu, Pin Wang, Yanni Zhu, and Crooks on behalf of the Regent at the University of California, Los Angeles. Covered by. , Montel-Hagen and Seet are listed as co-inventors. The treatment strategy was used only in preclinical studies. It has not been tested in humans and has not been approved by the US Food and Drug Administration as safe and effective for human use.

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