UCLA researcher receives largest award in latest round of funding from California's stem cell agency

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The immune system is equipped to fight many types of invasions by germs or viruses, but often is unable to fight against deadly diseases such as cancer. Lili Yang, a member of the UCLA Broad Stem Cell Research Center, is working to change that. With new funding awarded by the California Institute for Regenerative Medicine (CIRM), Yang hopes to engineer the body's immune system to give it the ability to attack and kill cancerous cells, while leaving the body's healthy tissues unharmed. By genetically engineering blood-forming stem cells, Yang will generate a special kind of white blood cell that can both directly kill tumor cells and activate other immune cells to eradicate cancerous tumors.

Yang's grant of $7,659,309, is the largest of the seven awards funded by CIRM's governing Board on March 16, 2016, under the 2.0 Translation Program. This program supports projects that will be ready for entering clinical trials in 30 months.

"Dr. Yang's research is a perfect illustration of our center's bench to patient bedside stem cell program," said Dr. Owen Witte, director of the UCLA Broad Stem Cell Research Center.

"We are grateful for this new funding opportunity from CIRM, which will allow us to bring to the clinic a novel stem cell-based immunotherapy that has the potential to treat a broad range of cancers and a large population of cancer patients," said Yang, an assistant professor in the UCLA Department of Microbiology, Immunology and Molecular Genetics.

The novel approach genetically modifies blood-forming "hematopoietic" stem cells to create specialized cells that have the capacity to kill cancer tumor cells. Hematopoietic stem cells create every type of blood cell in the body, including the white blood cells called T cells that fight against disease-causing invaders. Among these T cells is a much smaller group of powerful cells called "invariant natural killer T cells" (or iNKT) that have the capacity to immediately respond to diseases and are important to the immune system's regulation of cancer, infections, allergies and autoimmune diseases. One drop of human blood contains around 10 million total blood cells, about 5,000 T cells and only around 10 iNKT cells; cancer patients typically have even less iNKT cells.

Yang's CIRM-funded research seeks to modify cancer patients' own hematopoietic stem cells in order to create an increased number of iNKT cells once transplanted back into the patient. This new stem cell-based iNKT cell therapy could potentially provide cancer patients with life-long therapeutic levels of iNKT cells needed to fight the disease.

The grant team consists of 15 scientists and clinicians from a wide variety of disciplines at UCLA such as the College of Life Sciences, the David Geffen School of Medicine, the Jonsson Comprehensive Cancer Center, the Molecular Biology Institute and the Center for AIDS Research.

Yang's project is an extension of ongoing efforts by the Engineering Immunity Consortium, a partnership between UCLA, Caltech, University of Southern California, Children's Hospital Los Angeles and City of Hope. The

consortium seeks to promote translational research centering on the genetic modification of the human immune system through T cell and stem cell engineering.

The initial work that led to the novel concept of stem cell-based iNKT cell therapy was funded by a CIRM Basic Biology V Exploratory Concepts Award and a National Institutes of Health Director's New Innovator Award (DP2), both received by Yang in 2014. Additional funding that supported Yang's initial therapeutic concept include a UCLA Broad Stem Cell Research Center-Concern Foundation Research Award, a SPORE in Prostate Cancer Career Development Award from the NIH, and a Research Career Development Award from the STOP CANCER Foundation

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