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## **UCLA STEM CELL SCIENTISTS AWARDED \$20 MILLION GRANT TO DEVELOP NEW MELANOMA TREATMENT AND TEST IT IN CLINICAL TRIALS**

### **Project Calls for the Genetic Engineering of Blood Stem Cells to Fight Cancer**

A team of scientists led by Dr. Antoni Ribas, a member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research Center at UCLA and a professor of medicine, were awarded a \$20 million grant today to take leading-edge stem cell science from the laboratory and translate it into a new treatment for metastatic melanoma, a deadly form of skin cancer.

In all, eight such grants totaling more than \$150 million were awarded by the California Institute for Regenerative Medicine (CIRM), the state's stem cell agency. To date, scientists with the UCLA stem cell center have been awarded 54 grants totaling nearly \$174 million since 2005 for human pluripotent and adult stem cell research.

Up to \$20 million per applicant, the grants are awarded to teams of researchers in both academia and industry who have been working on projects that represent the best possible chances of producing therapies for deadly and disabling diseases and disorders.

The four-year grants are part of CIRM's Disease Team Initiative, which seeks to explore new ways to integrate and organize the highest quality basic, translational and clinical research with the aim of developing new therapies and diagnostic tools. As part of the approval process, disease teams must submit an investigational new drug application, or IND, to the U.S. Food & Drug Administration within four years in an effort to fast-track stem cell-related drug development.

Dr. Ribas and his team propose to develop an IND and open and fully enroll a Phase I clinical trial to genetically engineer the patient's immune response to specifically attack the melanoma starting from their blood stem cells. The specialized immune cells use a protein called the T-Cell Receptor (TCR) to seek out and recognize the melanoma. Evaluation of immune system reconstitution, effectiveness and immune response during treatment will be monitored using Positron Emission Tomography scans.

"This award will allow us to take to patients an approach devised by the Nobel laureate David Baltimore from Caltech and successfully tested in preclinical models," Ribas said. "It has been a long process to translate an advance in basic biology into patients with an aggressive cancer. The approach is complex and requires a large infrastructure and highly skilled expertise, which can now be facilitated by the CIRM award."

The proposed treatment approach has been validated in extensive studies in a UCLA laboratory. Ribas and his team recently initiated a clinical trial where adult immune cells obtained from blood are genetically modified with a TCR to become specific killer cells of melanoma cells. The cells were given back to patients, and early data is encouraging, Ribas said. The cells can be generated, safely administered back to patients and result in a clinical benefit. However, the adult immune cells genetically redirected to attack cancer slowly decrease over time and lose their killer activity, mainly because they do not have the ability to self-renew.

The advantage of the proposed blood stem cell method over adult blood cells is that the genetically modified blood stem cells will continuously generate new melanoma-targeted immune system killer cells. This approach, hopefully, will provide prolonged protection against the cancer.

The IND filing will test the modified blood stem cells in advanced stage melanoma patients. By the end of year four, Ribas and his team will have fully accrued the early phase clinical trial and assessed the value of genetic modification of blood stem cells to provide a stable reconstitution of a cancer-fighting immune system. Ribas said the therapeutic principles and procedures developed will be applicable to a wide range of cancers and transferrable to other centers that perform bone marrow and blood stem cell transplants.

More than 160,000 new cases of melanoma are diagnosed each year worldwide. The majority are caught early and can be treated with surgery. But when the cancer becomes metastatic – spreads throughout the body – it is highly resistant to most conventional therapies and results in about 50,000 deaths worldwide each year. In the U.S., melanoma has the fastest rising incidence of any cancer.

In October of 2009, three Broad center scientists received \$49.2 million in the first round of disease team grants. That funding is being used to translate basic science discoveries into new therapies for such devastating diseases as sickle cell, HIV/AIDS and brain, ovarian and colorectal cancers.

“UCLA has long been a leader in translational research, taking the best science from the bench to the bedside to provide novel, more effective therapies,” said Dr. Owen Witte, the director of the UCLA stem cell center and a Howard Hughes Medical Institute Investigator. “The fact that UCLA has received an additional disease team grant is an acknowledgement of our leadership in the field, and it will provide a much needed new treatment for metastatic melanoma.”

The stem cell center was launched in 2005 with a UCLA commitment of \$20 million over five years. A \$20 million gift from the Eli and Edythe Broad Foundation in 2007 resulted in the renaming of the center. With more than 200 members, the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research is committed to a multi-disciplinary, integrated collaboration of scientific, academic and medical disciplines for the purpose of understanding adult and human embryonic stem cells. The center supports innovation, excellence and the highest ethical standards focused on stem cell research with the intent of facilitating basic scientific inquiry directed towards future clinical applications to treat disease. The center is a collaboration of the David Geffen School of Medicine, UCLA’s Jonsson Cancer Center, the Henry Samueli School of Engineering and Applied Science and the UCLA College of Letters and Science. To learn more about the center, visit our web site at <http://www.stemcell.ucla.edu>.

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