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For Immediate Use

UCLA RESEARCHERS IDENTIFY LEUKEMIA STEM CELLS AND THE ALTERATIONS THAT CAUSE STEM CELLS TO BECOME CANCEROUS

Stem cell researchers at UCLA have identified a type of leukemia stem cell and uncovered the molecular and genetic mechanisms that cause a normal blood stem cells to become cancerous.

The discovery may lead to new therapies that target these leukemia stem cells, attacking the disease at its very root and killing the early cells that give rise to the mature cancer cells. The study appears in the May 22, 2008 issue of the journal Nature.

Scientists now believe stem cells are responsible for the origin of many cancers and their ability to become drug resistant and spread throughout the body. Current cancer therapies don't target cancer stem cells, only the cancer cells that are generated by them. Scientists theorize that the cancer stem cells – a very small population when compared with mature cancer cells - lay dormant while the cancer cells are killed. Later, sometimes years later, the cancer stem cells begin to self-renew and differentiate into malignant cells, causing a recurrence of the disease.

If scientists could understand the biology of cancer stem cells and find a way to kill them, it might provide what the oncology research community never talks about – a potential cure for certain cancers. If the cancer stem cells could be sought out and eliminated from the body, the cancer could not re-grow.

Led by Dr. Hong Wu, a professor of medical and molecular pharmacology and a scientist with the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research, the UCLA team has for the first time identified and isolated the stem cells responsible for a type of leukemia known as T-cell or acute T-lymphoblastic leukemia, an aggressive and deadly cancer that , can occur in both children and adults. The team also discovered the mechanisms by which blood stem cells – the cells that become the various cells in the blood supply – are converted to malignant leukemia stem cells, providing potential targets for therapies to home in on and attack those stem cells.

SUGGESTED QUOTE BY HONG WU

“One of the main challenges in cancer biology is to identify cancer stem cells and define the molecular and genetic events required for transforming normal cells into cancer stem cells,” said Wu, who also is a researcher at UCLA’s Jonsson Comprehensive Cancer Center and senior author of the Nature study. “With this study, we’ve been able to do that in one type of leukemia.”

In mouse models that developed T-cell leukemia, the team studied the cancerous cells and, using a sorting method that sought out certain cell surface markers, was able to identify the leukemia stem cells. Those cells were isolated and then transplanted into other mouse models to see if they developed T-cell leukemia, a sign that the team had been successful in finding the leukemia stem cells.

The team also wanted to know how blood stem cells become cancerous and studied the cells at the molecular and genetic level to uncover those mechanisms.

“We thought that multiple genetic or molecular alterations would have to occur for cancer to develop,” said Wei Guo, a postdoctoral student in Wu’s lab and the first author of the study. “In this case, we were able to find those alterations.”

The alterations found that collaboratively contribute to leukemia stem cell formation were the deletion of the PTEN tumor suppressor gene, a chromosomal translocation involving c-myc, a gene known to result in cancer that is usually regulated and kept in line, and the activation of a cell signaling pathway called beta catenin. **PLEASE HELP ME EXPLAIN THIS BETTER AND MORE ACCURATELY. WEI WAS GREAT AT THE EXPLANATION BUT I DIDN’T UNDERSTAND IT AS WELL AS I COULD HAVE.**

Wu and her team currently are testing therapies that target the alterations they discovered, hoping to interrupt the process that causes the blood stem cells to become leukemia stem cells, thereby preventing the cancer. They’re also looking for other alterations that might be at play in transforming the normal stem cells into cancerous stem cells.

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 150 members, the Eli and Edythe Broad Center for 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 institute 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/>.