MedicalXpress

Spread of human melanoma cells in mice correlates with clinical outcomes in patients

November 7 2012

UT Southwestern Medical Center scientists led by Dr. Sean Morrison, director of the Children's Medical Center Research Institute at UT Southwestern, have developed an innovative model for predicting the progression of skin cancer in patients.

In a new study published today in *Science Translational Medicine*, Stage III human melanoma cells from 20 patients were implanted into specially selected mice with compromised immune systems. Using this xenograft model, in which tissue is transplanted from one species to another, the institute's team observed reproducible differences in the rate at which the cancer spread in the mice, or metastasized, that correlated with clinical outcomes in patients.

Dr. Morrison said human melanomas that metastasized efficiently in the mice eventually progressed to advanced, Stage IV disease in patients – spreading to distant organs, such as the brain, liver, or lungs. When the melanoma did not metastasize efficiently in the mice, it also did not form distant metastases in patients.

This xenograft model will make it possible to study the mechanisms that regulate disease progression and distant metastasis of melanomas in patients. The researchers said they hope that their system will lead to new prognostic markers that identify patients at highest risk of disease progression as well as new therapies.

"We believe this is the only time in cancer biology that anyone has

developed a xenograft model in which disease progression correlates with what happens in the patient," said Dr. Morrison, senior author of the investigation and a Howard Hughes Medical Institute investigator at UT Southwestern. "The highly immune-compromised state of the mice makes it possible to observe the metastasis of human melanomas, and to study intrinsic differences among melanomas in their metastatic potential."

Previous studies of cancer metastasis were limited by a lack of workable models in which scientists could study the progression of a patient's cancer cells in laboratory animals in a way that correlated with clinical outcomes, he said.

But such correlation was clear in this study by the research institute, an innovative collaboration that melds the leading clinical resources of Children's Medical Center with the outstanding research resources of UT Southwestern. Melanomas that spread slowly and could not be detected in the blood of mice did not form distant tumors within 22 months in patients. Melanomas that spread rapidly in mice did form distant tumors in patients within the same time frame, giving rise to circulating melanoma cells in the blood of the mice. This finding suggests that entry of melanoma cells into the blood is a step that limits the rate of distant metastasis.

"Ultimately we want to identify new drug targets," Dr. Morrison said. "There are promising ideas coming out of this work that we hope will lead to clinical trials in melanoma."

The research arose from the Morrison laboratory's innovative techniques for studying neural crest stem cells – work that was recognized in 2004 with a Presidential Early Career Award for Scientists and Engineers. Neural crest stem cells make melanocytes, a type of cell that can mutate into melanoma if exposed, for example, to excessive sunlight.

The Children's Research Institute focuses on the interface of stem cell biology, cancer, and metabolism and will eventually include approximately 150 scientists in 15 laboratories. The work of Dr. Morrison, who also leads the Hamon Laboratory for Stem Cell and Cancer Biology, focuses on adult stem cell biology and cancers of the blood, nervous system, and skin.

"We're trying to do transformational science that not only changes scientific fields, but also creates new strategies for treating diseases," Dr. Morrison said. "The goal is for our work to have a direct impact on the patient."

Other UTSW researchers involved in the study were Drs. Elena Piskounova and Ugur Eskiocak, both postdoctoral researchers in the Children's Research Institute. This work originated with lead author Dr. Elsa Quintana and Dr. Mark Shackleton in Dr. Morrison's former lab at the University of Michigan. Other key collaborators from the University of Michigan were Dr. Douglas R. Fullen, director of dermatopathology, and Dr. Timothy Johnson, director of the Multidisciplinary Melanoma Clinic.

"This animal model offers unprecedented opportunities for discovery efforts that could be translated into patient care," Dr. Johnson said. "Dr. Morrison and I share a core mission to effectively treat melanoma, and that shared belief is the basis of the past, present, and future collaboration between UT Southwestern and the University of Michigan."

Provided by UT Southwestern Medical Center