

Research Highlights

Among the hundreds of publications by our researchers in 2007, two studies by scientists associated with Huntsman Cancer Institute (HCI) revealed important discoveries about a type of sarcoma and breast cancer. Both studies explored fundamental questions about the origin and behavior of cancer, and the answers they found can be applied to develop new treatments for the disease. In addition, both studies demonstrated the power of the mouse as a model system for cancer that closely resembles human disease. In the mouse “model system,” scientists can easily create experiments to test ideas about the origins of cancer and potential new treatments.

Origins of Synovial Sarcoma

An article in the journal *Cancer Cell* reports that synovial sarcoma develops in muscle cell precursors known as myoblasts. Synovial sarcomas arise in tissues near joints such as the knee or elbow. They can metastasize to the lungs, lymph nodes, and bone marrow. The disease most often strikes adolescents and young adults, and the five-year survival rates can be as low as 25 percent.

The cancer was once thought to arise in the membrane lining joints (synovium), but that idea fell from favor in recent years, and scientists now search to discover cells in which the cancer originates. Members of HCI’s Nuclear Control of Cell Growth and Differentiation Program, including co-authors Mario Capecchi, PhD, distinguished professor and co-chair of human

genetics at the University of Utah School of Medicine, and HCI investigator Stephen Lessnick, MD, PhD, assistant professor in the Department of Pediatrics and adjunct assistant professor in the Department of Oncological Sciences, created synovial sarcoma in mice and demonstrated its resemblance to the human tumor.

Capecchi’s pioneering technology, for which he won the Nobel Prize in Physiology or Medicine for 2007, enabled the specific gene that causes synovial sarcoma in the human to be introduced into the mouse genome and turned on in various muscle cells. They found that when this gene was turned on in myoblasts (muscle precursor cells), the cells became cancerous 100 percent of the time. The cancers that developed were very similar to synovial sarcoma tumors found in humans. There were also indications that another unidentified factor in nearby joint cartilage was involved in the development of synovial sarcoma.

Capecchi says he plans to study whether the altered gene must continue working for the tumor to keep growing and spreading. If that hypothesis is true, the gene itself would be a target for possible new drugs to treat synovial sarcoma. However, the study also identified other genes that are overactive in synovial sarcoma tumors, and they may also be potential targets for anticancer medicines.



Mario Capecchi, PhD, won the 2007 Nobel Prize in Physiology or Medicine for his pioneering work in gene targeting technology.

New Indicator for Breast Cancer Metastasis
Research by Alana Welm, PhD, assistant professor in the Department of Oncological Sciences and HCI investigator, used a mouse model of breast cancer to demonstrate that a gene called MSP promotes tumor growth and metastasis, the spread of cancer from its primary site to other parts of the body. She developed this model during her postdoctoral training with 1989 Nobel Prize winner J. Michael Bishop at the University of California, San Francisco.

When the MSP gene is turned on in mouse breast tumors, it increases metastasis. An MSP test for human tumors would help identify people whose breast cancer is more likely to spread through the body. MSP also offers a potential target for new breast cancer treatments. When an MSP-specific treatment is developed, testing for MSP in breast tumor tissue may identify appropriate candidates to receive that treatment. These results were reported in the *Proceedings of the National Academy of Science* in May 2007.

MSP is turned on in about 10 percent of human breast tumors, so the test and treatment could impact approximately 18,000 breast cancer patients in the United States annually.

In autumn 2007, Welm won the highly prestigious and competitive Era of Hope Scholar Award for Breast Cancer Research. She has also received a grant from the Breast Cancer Research Foundation and the American Association for Cancer Research to develop an MSP test for human breast cancer tissue in collaboration with Philip Bernard, MD, assistant professor in the Department of Pathology and HCI investigator. The second aim of the research is to test possible new MSP-specific therapies in mice.



Alana Welm, PhD, uses mouse models to study breast cancer.

“Our mouse model has shown that it is quite representative of the human disease,” says Welm. “The tumors grow and metastasize to the same locations as in humans. Mouse models really do inform us about the clinical aspects of the disease. Without these mice, we would not have followed the MSP pathway to this potential new treatment.”

On the web: See a list of HCI researchers’ publications in 2007:
huntsmancancer.org/annualreport2007



A clinical trial initiated at Huntsman Cancer Institute (HCI) could result in a new way to predict the most effective cancer drugs for patients with non-small cell lung cancer (NSCLC) and identify a patient’s response early in treatment. This information could improve survival rates and decrease treatment costs; patients would receive the most effective drugs for their cancer.

The trial will use noninvasive imaging techniques and blood tests to develop biomarkers (biochemical features that measure the progress of disease and response to treatment) that can predict which patients with NSCLC are most likely to benefit from a combination of bevacizumab (Avastin) and erlotinib (Tarceva).

“This is the first time these drugs have been tested as a first-line treatment for NSCLC, although they already have FDA approval for use along with chemotherapy,” says Wallace Akerley, MD, HCI’s senior director of clinical research and an initiator of the trial, along with John Hoffman, MD, director of HCI’s Molecular Imaging Program. Andrea Bild, PhD, assistant professor in the Department of Pharmacology and Toxicology and a member of HCI’s Cancer Center Support Grant’s Molecular Imaging, Diagnostics, and Therapeutics (MIDT) program, is also a co-investigator. The study’s imaging and biomarker portion is funded by the University of Utah’s Synergy program, which supports innovative projects bringing university research groups together.

Eventually, cancer patients throughout Utah can take part in the clinical trial via the Huntsman-Intermountain Cancer Care Program, a research alliance between HCI and Intermountain Healthcare.