

Science Update

Novel Cell Signaling Pathway In Immune Response Discovered

Researchers at UCLA's Jonsson Comprehensive Cancer Center have discovered a novel anti-inflammatory cell signaling pathway that may serve as a vital Yin-Yang mechanism to maintain the delicate balance of immune response.

The discovery, published in the June 2007 issue of the peer-reviewed journal *Cell*, may lead to new ways to fight cancer and inflammatory diseases, said Ke Shuai, a professor of hematology/oncology, a researcher at UCLA's Jonsson Cancer Center and lead author of the study.

Shuai and his colleagues discovered the PIAS1 anti-inflammatory pathway, a pathway commonly used by a wide variety of stimulants that regulate immune system response and trigger inflammation. While inflammation is part of the body's natural defense system against infection, Shuai said, unbalanced inflammation can make people more vulnerable to diseases such as cancer. The PIAS1 pathway serves as the Yin to the inflammation triggering Yang, working to keep a healthy balance in the immune system.

Prostate Cancer Treatments Impact Quality of Life

A rigorous, long-term study of quality of life in patients who underwent one of the three most common treatments for prostate cancer found that each affected men's lives in different ways. The findings provide invaluable information for men with prostate cancer who are facing vital treatment decisions.

Researchers studied quality of life in men who either underwent radical prostatectomy, external beam radiation therapy, or implantation of radioactive seeds in their prostate gland. The three treatment options rank about equally in survival outcomes for most men, so specific impacts on quality of life become paramount in making treatment decisions, said Dr. Mark Litwin, the study's lead author and a researcher at UCLA's Jonsson Cancer Center.

Each of the three options did negatively affect quality of life, at least temporarily, with problems ranging from erectile dysfunction and minor incontinence to urinary and bowel irritation. The study tracked 580 men for five years. The results, published in the June 1, 2007, issue of the peer-reviewed journal *CANCER*, represent data from the first two years of the study. Those years, Litwin said, are when most of the negative impacts surface and resolve.

Potential New Target for Brain Cancer Therapy Discovered

An in-depth analysis of cell signaling networks in a deadly form of brain cancer led researchers from UCLA's Jonsson Cancer Center to identify a potential new target for therapy, a discovery that may lead to better ways to treat glioblastoma.

Previous work at UCLA provided proof-of-principle that molecularly targeted therapies can be effective in fighting glioblastoma, the most lethal of all cancers. Researchers then sought to find new targets for these leading-edge therapeutics, which attack the cancer cells and leave the healthy cells alone, said Dr. Paul Mischel, a professor of pathology and laboratory medicine, a researcher at UCLA's Jonsson Cancer Center and the lead investigator in the study.

Mischel and his team identified ASPM (abnormal spindle-like microcephaly) as a key gene in glioblastoma and demonstrated that it is over-expressed in cancer cells as opposed to normal cells. And, as such, it could be a target for inhibition. The study, published in the Nov. 14, 2006 issue of *Proceedings of the National Academy of Sciences*, also provided a blueprint for using genomic data to identify key networks and molecular targets for glioblastoma and other cancers.

Melanomas Send Chemical Signal to Promote Cancer Spread

Melanomas aid themselves in their quest to spread to other parts of the body by sending a chemical signal to the sentinel lymph node, the node most susceptible to the early spread of the cancer. The signal cripples the sentinel node's immune response, making it more vulnerable to the cancer, UCLA researchers discovered.

However, UCLA scientists were able to reverse the immune suppression by injecting patients with a compound that stimulates an immune response in the node. The discovery, outlined in the October 2006 issue of *Nature Reviews/Immunology*, provides valuable clues about how melanomas spread and may one day lead to new ways to treat this deadly form of skin cancer, which will strike more than 62,000 Americans this year. About 8,000 will die from the disease.

A new treatment would be a valuable tool for oncologists. Most melanoma patients undergo surgery, but few other treatments have proven effective against this aggressive cancer. Chemotherapy doesn't help much, nor do hormonal or vaccine treatments, said Dr. Alistair Cochran, a professor of pathology and laboratory medicine and surgery, a researcher at UCLA's Jonsson Cancer Center and lead author of the study.

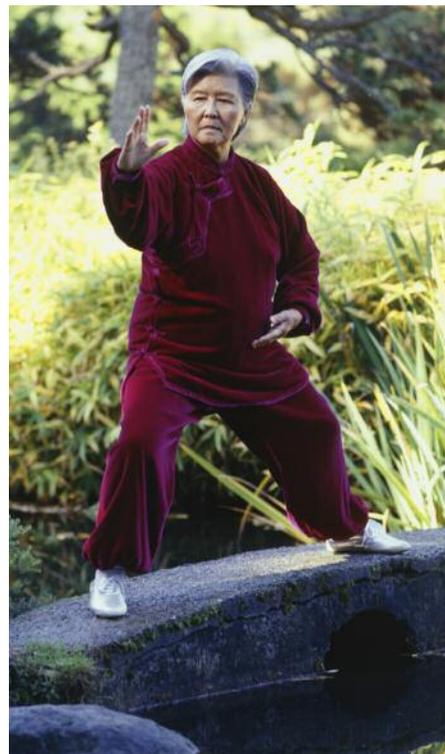
Drug That Battles Gleevec Resistance Extremely Effective

An experimental therapy that battles drug resistance in Chronic Myeloid Leukemia (CML) has proved "extremely effective" in fighting cancer, giving patients for whom all conventional therapies have failed another option, researchers at UCLA's Jonsson Cancer Center reported.

The drug, Sprycel, treats CML that has mutated and become resistant to the leukemia pill Gleevec, said UCLA researchers who conducted the study, published in the June 15, 2006 issue of the peer-reviewed *New England Journal of Medicine*.

The results are from a Phase I study of Sprycel. The early results were so favorable that several Phase II studies were launched last year and are almost completed. Because these trials have moved so quickly and because more positive results are anticipated, an advisory panel for the U.S. Food & Drug Administration recommended that the agency approve the drug, which could happen before the end of the month. Like Gleevec, Sprycel also is taken in pill form. (See related story on page 16)

Researchers characterized the Phase I study results as remarkable, saying the first human trial confirmed the pre-clinical laboratory work and scientific discovery done at UCLA's Jonsson Cancer Center, where the mechanisms and mutations behind Gleevec resistance were uncovered.



Biological Mechanism Behind Fatigue Uncovered

Breast cancer survivors who suffer from persistent, debilitating fatigue years after their diagnosis have something in common: their immune systems don't shut down following treatment, according to researchers at UCLA's Jonsson Cancer Center.

This constant immune system activation, which researchers discovered by measuring specific proteins in blood samples from survivors, may be causing the fatigue, UCLA researchers theorize. Their discovery may lead to behavioral interventions such as tai chi and yoga that will help alleviate persistent fatigue, which affects about a third of breast cancer survivors for years after they complete treatment.

The study is the first to look at the cellular basis for immune activation in fatigued breast cancer survivors, said Dr. Michael Irwin, a researcher at UCLA's Jonsson Cancer Center and the study's lead author. The research appeared in the May 1, 2006 issue of *Clinical Cancer Research*, the peer-reviewed journal of the American Association of Cancer Research. *

