



December 2009

New understanding of how to prevent destruction of a tumor suppressor: discovery may lead to new treatments for late-stage cancers

Researchers from the IU School of Medicine and colleagues at the University of Texas Southwestern and Case Western University have determined how the protein Mdm2, which is elevated in late-stage cancers, disables genes that suppress the growth of tumors.

The finding may lead to the development of new drugs for late-stage breast cancer and other difficult to treat malignancies.

The investigators, led by **Lindsey Mayo**, PhD, have identified a critical pathway that stimulates the production of Mdm2 causing an increase in the level of protein that bind to p53, the most common tumor suppressor, as well as other tumor suppressors, and extinguishes tumor suppression activity. The study appears in the January 2010 issue of the *Journal of Clinical Investigation*.

Dr. Mayo says that keeping Mdm2 inactive and preventing the destruction of the tumor suppressor that Mdm2 targets is critical to preventing cancer from spreading within the body.

To explain the role of Mdm2 and how the newly identified pathways function, Dr. Mayo uses the analogy of a fluorescent ceiling fixture in which Mdm2 is the fluorescent bulb. "Initially, it was only known that the light was on, not how it was turned on. We discovered the wall switch and wires that connect to the light fixture to turn on the fluorescent light."

"This work provides new evidence about an important mechanism that tumor cells use to promote metastasis," Dr. Mayo added. "While it has long been known that the loss of tumor suppressor activity triggers cancer, knowledge of how these cancer inhibitors are turned on and off has eluded researchers. Understanding the signaling pathways that elevate Mdm2 is critical to preventing cancer from spreading within the body and key to attacking many late-stage cancers."

While it is too early to speculate on which chemical compounds may yield successful drugs, Dr. Mayo says this new insight into Mdm2 and its pathways provides a useful roadmap to stimulate development of new compounds which

could bind to Mdm2 to inhibit the protein and stop its attacks on tumor suppressors.



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Annual report to the nation finds continued declines in overall cancer rates

Rates of new diagnoses and rates of death from all cancers combined declined significantly in the most recent time period for men and women overall and for most racial and ethnic populations in the United States, according to a report from leading health and cancer organizations.

The drops are driven largely by declines in rates of new cases and rates of death for the three most common cancers in men (lung, prostate, and colorectal cancers) and for two of the three leading cancers in women (breast and colorectal cancer). New diagnoses for all types of cancer combined in the United States decreased, on average, almost 1 percent per year from 1999 to 2006. Cancer deaths decreased 1.6 percent per year from 2001 to 2006.

These findings are from a report authored by researchers from the National Cancer Institute (NCI), part of the National Institutes of Health, the Centers for Disease Control and Prevention (CDC), the American Cancer Society (ACS), and the North American Association of Central Cancer Registries (NAACCR). The report was published online Dec. 7, 2009, in the journal *Cancer*.

Overall cancer rates continue to be higher for men than for women, but men experienced the greatest declines in incidence and mortality rates.

For colorectal cancer, the third most frequently diagnosed cancer in both men and women, and the second leading cause of cancer deaths in the United States, overall rates are declining, but increasing incidence in men and women under 50 years of age is of concern, the report said.

In the Special Feature section, the authors used modeling projections of colorectal cancer rates to find that, with accelerated cancer control efforts to get more Americans to adopt more favorable health behaviors (such as quitting smoking) and higher use of screening (such as colonoscopy), as well as optimal treatment outcomes for colorectal cancer (such as more effective chemotherapy), there could be an overall colorectal cancer mortality reduction of 50 percent by 2020.

Other highlights from the report show that in men incidence rates have declined for cancers of the prostate, lung, oral cavity, stomach, brain, colon and rectum, but continue to rise

for kidney/renal, liver, and esophageal cancer, as well as for leukemia, myeloma and melanoma. In women, incidence rates decreased for breast, colorectal, uterine, ovarian, cervical and oral cavity cancers, but increased for lung, thyroid, pancreatic, bladder, and kidney cancers, as well as for non-Hodgkin lymphoma, melanoma and leukemia.

[Read the full report.](#)



December 2009

News briefs

IU Simon Cancer Center, Good Samaritan Hospital announce affiliation agreement

The IU Simon Cancer Center, Clarian Health, and Good Samaritan Hospital announced in early December an affiliation agreement.

The agreement gives the Vincennes, Ind.-based hospital access to the resources and services of the IU Simon Cancer, an IU School of Medicine and Clarian Health partnership.

The affiliation, which was announced during a news conference at the Good Samaritan Hospital Cancer Pavilion Dec. 1, includes clinical, research, and educational components.



A New Day of Hope

- The clinical component ensures access to the IU Simon Cancer Center's highly specialized physicians, its reports and results to Good Samaritan's referring physicians and their patients, and makes IU Simon Cancer Center physicians available for second opinions.
- The research component makes it possible for Good Samaritan patients to enroll in clinical trials at the cancer center and through the Hoosier Oncology Group, a working association of IU medical center physicians and 400 oncologists statewide.
- The educational component will allow the Good Samaritan staff to participate in grand rounds and conferences, special education venues, lectures by IU faculty, and training for non-physician staff.

"We look forward to collaborating with the physicians and staff at Good Samaritan Hospital Cancer Pavilion," Fuad Hammoudeh, administrator of IU Simon Cancer Center / Clarian Health cancer programs, said. "The affiliation agreement is good news for cancer patients and their families in the Vincennes area. We are committed to supporting and enhancing the excellent cancer services

already available at Good Samaritan Hospital."

The IU Simon Cancer Center and Memorial Hospital and Health Care Center in Jasper, Ind., formed an affiliation agreement in February 2007.

Society for Translational Oncology offers discount

The Society for Translational Oncology (STO) is pleased to offer IU Simon Cancer Center faculty and staff a [complimentary 30-day online subscription](#) to its official journal, *The Oncologist*. This offer provides access to 10 CME courses from its extensive collection, compliments of STO. Please contact Sharon.Lee@TheOncologist.com for any questions about registering for the free trial and Tracey.Cave@STO-online.org for STO information.

Bat for the Cure

In a continuing effort to save lives and improve awareness about prostate cancer, Ed Randall's Bat for the Cure charity sponsored free, simple PSA screenings during the Baseball Winter Meetings at the Indiana Convention Center on Dec. 9 in partnership with the IU Simon Cancer Center and Clarian Health.

New phone numbers at IU Hospital

Indiana University Hospital is changing to a new phone system in January. The conversion will provide users with leading-edge communication technology while significantly reducing Clarian's phone system costs. The prefixes for Clarian-owned phones at IU Hospital will change from 274/278 to 944/948. The cutover dates for the new phone system at IU Hospital are: Patient phones: Jan. 13; facility/staff phones: Jan. 15. All requests for phone services at IU Hospital, including moves, additions or changes, should be directed to the IS Service Desk at 962-2828.

Summer Research Program applications available

Do you know of high school and college students interested in exploring a career in cancer research? If so, encourage them to apply for this summer's IU Simon Cancer Center Summer Research Program. The cancer center's annual program places students with a mentor physician or researcher for nine weeks (June 1-July 31). The students will work with faculty who are doing research in the most progressive areas of cancer research. Students interested in the Summer Research Program can find additional information and an online application at www.cancer.iu.edu/srp. Applications are due March 1, 2010.

Students wanted for NCI summer program

The Summer Cancer Research Fellowship program provides a unique opportunity for eligible current sophomore or junior undergraduate students to engage in innovative integrative biology approaches to cancer research through the National Cancer Institute's (NCI) Integrative Cancer Biology Program (ICBP). The ICBP, composed of nine multi-disciplinary centers across the United States, focuses on the analysis of

cancer using systems biology approaches.

Selected student participants are paired with a faculty-mentor from a participating ICBP Center based on the student's indicated research interests. Through mentored research projects, faculty lectures, seminars, discussions and other activities, the student gains both an understanding and appreciation of major questions currently under investigation and the novel research approaches being used within the ICBP Centers. If you know of interested students, direct them to http://icbp.nci.nih.gov/summer_program/ for further information. The application deadline is Jan. 25.

Cancer center members in the news

- **Linda Malkas**, PhD, has been invited to serve on the editorial board of *Cancer Research*, effective Jan. 1. In addition to advising the editor-in-chief on the direction of the journal, editorial board members are asked to review manuscripts for scientific content, clarity of presentation, and acceptability for publication. Also, Dr. Malkas recently appeared on the *Indianapolis Star's* "Biz Buzz." [Watch.](#)



Malkas

- New research, led by **Henry Pitt**, MD, published in the December issue of the *Journal of the American College of Surgeons* finds that the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) is a powerful tool for assessing outcomes of uncommon, high-risk surgical procedures, including pancreatic necrosectomy. "Within 12 months, ACS NSQIP accumulated extensive data on 161 patients that had undergone pancreatic necrosectomy, a number that would take most hospitals decades to accumulate," Dr. Pitt said. "This study demonstrates that ACS NSQIP is a powerful data repository that provides hospitals with a practical tool to assess how well they are doing with uncommon, high-risk operations." Others involved in the study were: **Thomas Howard**, MD, **Attila Nakeeb**, MD, **Max Schmidt**, MD, PhD, MBA, **Keith Lillemoe**, MD, and **Nicholas Zyromski**, MD.
- Lapatinib plus trastuzumab are significantly better than lapatinib alone in extending the lives of breast cancer patients whose tumors are HER2-positive, according to Kimberly Blackwell, MD, of Duke University Medical Center. Blackwell presented the findings at the CTRC-AACR San Antonio Breast Cancer Symposium. **George Sledge**, MD, and others were also involved in the study.

New grants

Kent Robertson, MD, PhD

"Pilot Study of Gleevec/Imatinib Mesylate (STI-571, NSC716051) in Neurofibromatosis (NF1) Patients with Plexiform Neurofibromas"

U.S. Department of Defense

Andrew Saykin, PsyD

"Amyloid Imaging, VMCI, and Analysis for ADNI"

Northern California Institute for Research & Education