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## IU cancer researchers: Retinoblastoma dysfunction promotes pancreatic cancer cell growth

Dec. 16, 2013

INDIANAPOLIS -- Indiana University cancer researchers have discovered that a protein that normally suppresses tumors actually promotes the growth and spread of pancreatic cancer.

Murray Korc, M.D., the Myles Brand Professor of Cancer Research at the [Indiana University School of Medicine](#) and a researcher at the [Indiana University Melvin and Bren Simon Cancer Center](#), and colleagues have shown that the retinoblastoma protein, a tumor suppressor, often malfunctions in pancreatic cancer. That dysfunction enables an inhibitory protein to promote pancreatic cancer growth.

The research was published online today in the [Journal of Clinical Investigation](#).

As a result of the dysfunctional retinoblastoma protein, pancreatic cancer cells lose their ability to be inhibited by transforming growth factor-beta, or TGF- $\beta$ , which is a key negative regulator of cell proliferation, according to Dr. Korc. Instead, the cells become stimulated by TGF- $\beta$  due to activation of abnormal downstream signals known as non-canonical pathways.

The researchers also showed that TGF- $\beta$  induces the expression of a growth-stimulating molecule called Wnt7b, which is not usually found in a normal adult pancreas. This combination allows TGF- $\beta$  to directly enhance pancreatic cancer cell proliferation and survival.

Dr. Korc explained the combination of TGF- $\beta$  and Wnt7b actions: "You have a cancer in which the accelerator is stuck to the floor and the brake is broken. But because of the malfunctioning retinoblastoma protein, the combined actions of TGF- $\beta$  and Wnt7b convert the broken brake into a second accelerator."

Because the abnormal pathways activated by TGF- $\beta$  and Wnt7b can be disrupted with drugs, Dr. Korc suggested that the findings open up a new avenue for exploring novel therapeutic combinations in pancreatic cancer.

However, Dr. Korc cautioned that more work remains to be done to determine how to best restore the regulatory functions of the retinoblastoma protein and prevent the harmful actions of TGF- $\beta$ .

"We have to figure out how to target these important pathways and to prevent bypass pathways from being activated," he said.

Co-authors of the study were A. Jesse Gore, Samantha L. Deitz, Lakshmi Reddy Palam and Kelly E. Craven from the Department of Medicine at the IU School of Medicine.

The study was made possible, in part, by grant R37-CA-075059 awarded by the National Cancer Institute of the National Institutes of Health.

For the past two decades, Dr. Korc's work has focused on aberrant growth-factor signaling in pancreatic cancer. More recently, he began studying genetic mouse models of pancreatic cancer, with the goal of designing novel therapeutic strategies.

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Murray Korc, M.D.

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He is internationally recognized for his seminal contributions to the understanding of the roles of the epidermal growth factor receptor and TGF- $\beta$  in pancreatic cancer. His research team discovered that TGF- $\beta$  molecules are expressed at high levels in the cancer cells in human pancreatic tumors and that targeting TGF- $\beta$  can suppress its ability to exert so-called paracrine effects in the pancreatic tumor microenvironment.

Only 6 percent of patients survive the disease five years following diagnosis. According to the National Cancer Institute, there will be an estimated 45,220 new cases of pancreatic cancer and 38,460 deaths from the disease in 2013.

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# IUSCC news

November 2013

## News briefs

### Navigators help researchers at IUPUI, IU-B, Notre Dame, Purdue

Researchers, did you know there are navigators to help you more easily connect with translational science resources across the state? Tammy Sajdyk, PhD, a neuroscientist and clinical and translational sciences research officer at the Indiana Clinical and Translational Sciences Institute, is the new IUPUI campus navigator. There are additional navigators at IU Bloomington, Purdue University and the University of Notre Dame. [full story >](#)

### New faculty hold roles at IUSCC

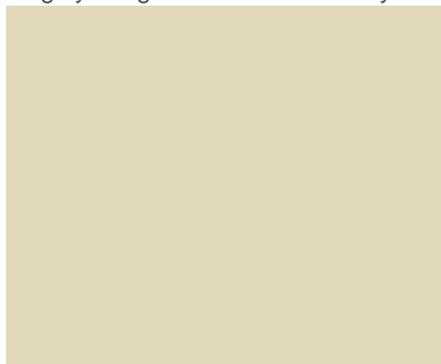
Two new faculty members at IU will hold positions at the IU Simon Cancer Center. Bert H. O'Neil, MD, has been named the inaugural Joseph W. and Jackie J. Cusick Professor of Oncology and professor of medicine at the IU School of Medicine. He also will be the phase I director at the IU Simon Cancer Center and a full member of the [Experimental and Development Therapeutics research program](#). Jiali Han, PhD, has been named professor and chair of the Department of Epidemiology at the [Fairbanks School of Public Health](#) and the Rachel Cecile Efrogmson Professor of Cancer Research at the IU Simon Cancer Center. Dr. Han will also serve as co-leader of the cancer center's [Cancer Prevention and Control research program](#).

### Dr. Abonour earns Cornerstone Award

**Rafat Abonour**, MD, was one of five people recently honored by IU and the IU Foundation at this year's Partners in Philanthropy event. Dr. Abonour received a Cornerstone Award, which recognizes those individuals whose partnership and volunteer involvement have been instrumental in the success of a single IU philanthropic initiative for a campus, program, or school.

A highly sought-after consultant by oncologists worldwide, Dr. Abonour has dedicated his professional life to groundbreaking research and first-rate patient care. Dr. Abonour is director of the cancer center's Adult Clinical Research Office, associate dean of clinical research, and associate professor of medicine, pathology and laboratory medicine at the IU School of Medicine. His research is focused on autologous stem cell transplantation and hematologic malignancies.

Dr. Abonour established the first clinic devoted





to multiple myeloma patients in Indiana, championing a new mode of treatment that is now being used by other groups around the world and serving as a source of inspiration for further research. In addition, with the help of

a committee of his patients and their family members, he initiated the Miles for Myeloma fundraising event, personally running and bicycling to several Indiana cities. When discussing Miles for Myeloma, Dr. Abonour said to a room full of his patients, "Since all of you travel so many miles to come to me all the time, why don't I try coming to you?"

Starting in 2005, he and his fellow cyclists have covered more than 1,600 miles on Hoosier roadways and have raised more than \$2.3 million from more than 9,500 donors to support the challenge of curing this rare and currently incurable blood cancer.

View a [video biography](#) of Dr. Abonour.

### Recipes sought for cookbook that benefits breast cancer program at IU

Do you like to cook? Do you have a favorite original recipe that you'd like to share with others? If so, you can submit your recipe for consideration to the Catherine Peachey Fund, which is publishing the 20<sup>th</sup> anniversary edition of its "Just Peachey" cookbook. Sales of the cookbook will raise money to fund breast cancer research and programs at Indiana University. The first edition sold 57,000 copies. If you want to submit a recipe for consideration, please contact Stephanie Rufenbarger Leshner at [stephanierl@peacheyfund.org](mailto:stephanierl@peacheyfund.org). Submissions are due Dec. 2. [Learn more about the cookbook.](#) [Learn more about the Catherine Peachey Fund.](#)



The Vera Bradley Foundation for Breast Cancer recently presented more than \$2 million to the IU Simon Cancer Center, wrapping up its current \$10 million pledge. Since 1998, the foundation has contributed \$20 million to the cancer center's [breast cancer research program](#).

### AMPATH program marks 23 years



IU President Michael McRobbie (left) and Joe Mamlin, AMPATH field director, celebrate at the recent 2013 Kenya Gala. The gala's theme, "Building Friendships, Brightening Futures," represented the relationships and growth the AMPATH program has seen over the past 23 years. The AMPATH program (Academic Model Providing Access to Healthcare) began as a partnership between IU School of Medicine and Moi University School of Medicine and Moi Teaching and Referral Hospital. The AMPATH Consortium currently includes nine additional North American academic institutions. The oncology program was created in 2002.

### Cancer center members in the news

- **Hari Nakshatri**, BVSc, PhD, has been elected to the board of directors on the Cancer Biology Training Consortium. CABTRAC was established to facilitate the exchange of ideas between individuals and institutions dedicated to the mission of training the next generation of cancer researchers. The consortium works closely with more than 50 institutions as well as the National Cancer Institute's Cancer Training Branch. Also, Nakshatri was a co-author of "[PROGene: Gene Expression Based Survival Analysis Web Application for Multiple Cancers](#)," published in the *Journal of Clinical Bioinformatics*. The authors summarized that a Web application they created is a tool that scientists can use to identify potential prognostic mRNA biomarkers to follow up with further research.
- **Sherif Farag**, MBBS, PhD, has been named the inaugural Lawrence H. Einhorn Professor of Oncology at the IU School of Medicine.
- The American Association for Cancer Research, the Cancer Therapy & Research Center at The University of Texas Health Sciences Center at San Antonio, and Baylor College of Medicine will be hosting the [2013 CTRC-AACR San Antonio Breast Cancer Symposium](#) Dec. 10-14. The symposium provides news on state-of-the-art breast cancer research, including experimental biology, etiology, prevention, diagnosis, and therapy of breast cancer and premalignant breast disease. The following cancer center members are participating: **Linda Han**, MD; **Mark Henderson**, MD; **Kathy Miller**, MD; **Hari Nakshatri**, BVSc, PhD; **Jenifer Proserpi**, PhD; **Milan Radovich**, PhD; **Bryan Schneider**, MD; and **Anna Maria Storniolo**, MD.
- Patients who seek treatment from physicians who more frequently perform a



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high-risk endoscopic procedure are less likely to be admitted to the hospital or require a repeat procedure, according to a study done by first author **Gregory Cote**, MD, MS. The article, "[Lower Provider Volume Is Associated with Higher Failure Rates for Endoscopic Retrograde Cholangiopancreatography](#)," was published in the journal *Medical Care*.

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