Researchers focus on potential tool for predicting survival, staging prostate cancer in Cancer Cell

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INDIANAPOLIS -- Researchers with the Indiana University School of Medicine have identified a molecule that promotes metastasis of advanced prostate cancer to the bone, an incurable condition that significantly decreases quality of life. The research, published online in the journal Cancer Cell, may offer new targets for diagnosing and treating this common disease.

The researchers homed in on a protein that is essential in multiple cell functions such as cell growth and proliferation and, in some cases, natural cell death. The protein, TGF-beta, also has been found to promote bone metastasis in patients with breast cancer and melanoma.

Prostate cancer is the second most common cancer among men, according to the American Cancer Society. More than 2 million men in the United States are prostate cancer survivors. ACS estimates that 220,800 new cases of prostate cancer are diagnosed annually in all age groups and that 27,540 men succumb to the disease each year. When diagnosed in the early stages, prostate cancer is often successfully treated. However, in advanced stages, metastasis to the bone is common. The tumors in the bone are incurable, cause increased pain and bone fractures, and potentially hasten death.

Bone disease experts Theresa A. Guise, M.D., senior author of "The TGF-beta Signaling Regulator PMEPA1 Suppresses Prostate Cancer Metastases to Bone," and lead author Pierrick GJ. Fournier, Ph.D., showed in earlier research that TGF-beta is active in the proliferation of metastatic disease. By inhibiting the action of TGF-beta, the researchers reasoned that bone metastases could be reduced in advanced disease.

By analyzing the genes present in patients with advanced disease, the researchers focused on the protein PMEPA1, which is abundant in primary prostate cancer cells but less common in advanced disease, including metastatic bone tumors.

To investigate the clinical significance of PMEPA1, the researchers compared its presence in normal tissue to primary tumors, finding that the gene was active in prostate, breast and lung cancer tumors. The opposite was true of TGF-beta, which led the researchers to determine that the presence of TGF-beta regulates the activity of PMEPA1.

"Comparing data on patients with prostate or breast cancer, we found those with low amounts of PMEPA1 developed metastases faster and had shorter survival," Dr. Guise said. "By inhibiting TGF-beta, we believe we could reduce the spread of prostate cancer to the bone and increase survival."

Drs. Guise and Fournier think that with additional analysis, the presence of PMEPA1 may serve in the future as a diagnostic tool to predict the likelihood of prostate cancer metastases and serve as an indicator of survival, similar to the Gleason score and PSA counts currently used by physicians to stage prostate cancer and determine options for treatment.

Theresa Guise, M.D.

Print Quality Photo

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Print Quality Photo

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"This finding could make a difference in how prostate cancer is treated in the future," Dr. Fournier said. "The unknown qualities of cancer frequently lead to aggressive treatments that are unnecessary. If we can determine a laboratory test that can serve as an indicator of the likelihood of progression or the severity of the disease, we could make better decisions about treatments and improve the quality of life for many patients."

Dr. Fournier is a principal investigator at the Center for Scientific Research and Higher Education at Ensenada (CICESE), Baja California, México, and formerly an assistant research professor at the IU School of Medicine. Dr. Guise is the Jerry W. and Peggy S. Throgmartin Professor of Oncology and professor of medicine at the IU School of Medicine.

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IUSCC news

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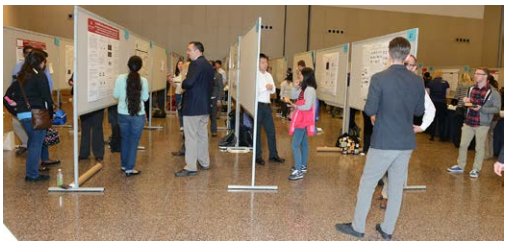
News briefs

Record number of researchers participate in IU Simon Cancer Center's Cancer Research Day

A record number of people presented their research May 21 during the IU Simon Cancer Center's Cancer Research Day. One hundred and forty-two graduate and medical students, clinical nurses, postdoctoral and medical fellows, and research technicians conducting cancer research at Indiana University-Purdue University Indianapolis, Indiana University Bloomington, Purdue University and the Harper Cancer Research Institute -- a collaboration between the IU School of Medicine and the University of Notre Dame -- submitted abstracts from four categories. The winners are posted online at www.cancer.iu.edu/crd.



Cancer center members serving as summer mentors

The research labs are filled again this summer with high school and college students as they gain hands-on experiences with IU Simon Cancer Center researchers. Fourteen students are participating in the Summer Research Program (SRP), which aims to increase the number of high school and undergraduate students from underrepresented populations pursuing biomedical and behavioral science careers by providing positive and meaningful firsthand exposure to these fields. The following cancer center members are serving as mentors: **Elliott Androphy**, MD; **Jill Fehrenbacher**, PhD; **Theresa Guise**, MD; **Heiko Konig**, MD, PhD; PhD; **Lang Li**, PhD; **Chien-Chi Lin**, PhD; **Lindsey Mayo**, PhD; **Marc Mendonca**, PhD; **Khalid Mohammad**, MD, PhD; **Hari Nakshatri**, BVsc, PhD; **Susan Rawl**, PhD; **Fletcher White**, PhD; **Clark Wells**, PhD; and **Greg Zimet**, PhD; Also, seven students from Indianapolis Public Schools are participating in the Future Scientist Program, which helps educate and foster interest in scientific studies. The following cancer center members are serving as mentors: **Elliot Androphy**, MD; **Tao Lu**, PhD; **Khalid Mohammad**, MD, PhD; **Hongmei Nan**, MD, PhD; **David Roodman**, MD; **Uma Sankar**, PhD; and **Theresa Zimmers**, PhD.

ICTSI annual meeting, Watanabe Prize Lecture set for September

The seventh annual meeting of the Indiana Clinical and Translational Sciences Institute and awarding of the second Watanabe Prize in Translational Research will be Friday, Sept. 11 at Hine Hall on the IUPUI campus.

This year's winner of the Watanabe Prize and the meeting's keynote speaker will be Carl H. June, MD, Richard W. Vague Professor in Immunotherapy and director of the Center for Cellular Immunotherapies in the Perelman School of Medicine at the University of Pennsylvania.

The Watanabe Prize in Translational Research presented by the Indiana CTSI and the IU School of Medicine recognizes a member of the scientific or medical community who has achieved outstanding accomplishments in translational research. As the recipient, Dr. June will spend several days in Indiana to share his knowledge with audiences at the IU School of Medicine and partner institutions. The Indiana CTSI annual meeting will also highlight two outstanding young investigators named Watanabe Translational Scholars. They will present a brief overview of their research during the event and will be mentored by Dr. June over the next two years.

For more information, contact Indiana CTSI at info@indianactsi.org.

IU Simon Cancer Center awards nearly $86,000 for 5 shared resource pilot projects

The IU Simon Cancer Center recently funded five shared resource pilot projects, totaling $85,971. Since the fall of 2013, the cancer center has awarded three rounds of such funding to 29 projects, totaling $505,000.

The current five projects, PIs, and the IUSCC cores used are:

- "Repositioning Proton Pump Inhibitors for Pancreatic Cancer Treatment," **Jian Ting Zhang**, PhD, In Vivo Therapeutics
- "Enhancing Anti-angiogenic Clinical Drugs Using E3330: Combination Studies," **Mark Kelley**, PhD, Angio BioCore
- "In Vivo Targeting of Histone Deacetylase 6 (HDAC6) for Glioblastoma Multiforme (GBM) Treatment," **Ahmad Safa**, PhD, In Vivo Therapeutics, CPAC, and Tissue Procurement and Distribution cores
- "Understanding and Targeting TP53 Mutations in Acute Myeloid Leukemia," **Yan Liu**, PhD, Bioinformatics
- "Generation of Fbxo3 Murine Model Utilizing Crispr/Cas Technology," **Wade Clapp,** MD, Transgenic and Knock-Out Mouse Core

The IU Simon Cancer Center shared resource pilot funding program is intended for research projects that can take advantage of assistance from any of the IUSCC shared resources/cores for obtaining preliminary data for a new or new extension of an existing project.

A primary goal of the IU Simon Cancer is to stimulate multidisciplinary and translational research. The aim of each of the IUSCC shared resources is to provide state-of-the-art shared facilities that support the research of cancer center members. Thus, this pilot funding mechanism leverages the use of these shared resources to aid in obtaining preliminary data for multi-disciplinary, translational research projects that will ultimately lead to extramural funding.

Based on the interest and popularity of this particular pilot funding mechanism, it is anticipated that another call will be issued in the fall or early

spring for proposals utilizing IUSCC shared resources.

Questions? Contact Mark R. Kelley (mkelley@iu.edu) or Crystal Munson (crybanks@iupui.edu).

Wright Scholarship recipients announced

Talar Kharadjian and Christopher Haskins have been named recipients of William J. Wright Scholarships from the IU Simon Cancer Center. Each is a $7,000 scholarship.

The Wright Scholarship is awarded to third-and fourth-year medical students, physicians in cancer-related post-doctoral training programs, and/or medical doctors who are employed by the IU School of Medicine pursing cancer-related fellowship training, all of whom demonstrate the commitment and potential for conducting cancer research, and all of whom demonstrate outstanding character and well-defined professional goals.

The expectation for this award is that the student will devote at least two months of their school year to a project that will further the care of patients with cancer, including a formal basic, translational or clinical science research project, quality improvement project, health outcome research, or cancer awareness program.

Students with research grants that are already supporting their education are not eligible.

This award is supported by the IU Simon Cancer Center William J. Wright Scholarship Fund.

Cancer center members in the news

Rex

- **Douglas Rex**, MD, wrote "PillCam 2 adequate for patients who cannot undergo conventional colonoscopy," which appeared in Healio Gastroenterology.

- **Kandace Ludwig**, MD, has been named medical director of the breast care program at IU Health's North Central Region (IU Health North, Saxony, and Tipton hospitals) breast care program. In her new role, she will practice at both IU Health North and Saxony hospitals.

- **Oscar W. Cummings**, MD, has been named the Lawrence M. Roth Professor of Pathology. He will retain his current title of professor of pathology and laboratory medicine. The appointment was effective May 1.

- The following have been recognized with a Trustee Teaching Award by the IU Board of Trustees for their sustained and consistent teaching excellence: **J. Dennis Fortenberry**, MD, MS; **Linda Han**, MD; **Naveen Manchanda**, MD; and **Jie Sun**, PhD. **Michael House**, MD, and **Kenneth Kesler**, MD, earned a Basic and Clinical Science Teaching Award.

- The following are lead authors who will present abstracts at the annual ASCO meeting in Chicago, which is May 29-June 2:

    - **Daniela Matei**, MD, will present a poster, "Epigenome and Genome Alterations in Platinum Resistant Ovarian Cancer."

Jalal

- **Shadia Jalal**, MD, will present an oral abstract, "Results from a Randomized Study of Carboplatin and Etoposide (CE) with or without Palifosfamide (Pa) in Extensive Stage Small Cell Lung Cancer (ES-SCLC): The MATISSE study."

- **Kathy Miller**, MD, will present two posters: "Cisplatin with or without Rucaparib after Preoperative Chemotherapy in Patients with Triple Negative Breast Cancer: Final Efficacy Results of Hoosier Oncology Group BRE09-146" and "HERMIONE: A Phase 2, Randomized, Open Label Trial Comparing MM-302 Plus Trastuzumab with Chemotherapy of Physician's Choice Plus Trastuzumab, in Anthracycline Naive HER2-positive, Locally Advanced/Metastatic Breast Cancer Patients Previously Treated with Pertuzumab and Ado-trastuzumab Emtansine (T-DM1)." She will also present two sessions: "Novel Agents in Triple-Negative Breast Cancer" and "Novel Antibody-Drug Conjugates and Rational Combination."

- Also, **Lawrence Einhorn**, MD, and **Nasser Hanna**, MD, each will present a session. Dr. Einhorn will present "Salvage Approaches in Refractory Germ Cell Tumors," while Dr. Hanna will present "Current Standards and Clinical Trials in Systemic Therapy for Stage III Lung Cancer: What is New?"

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