IU researchers identify key mechanism and potential target to prevent leukemia

Nov. 13, 2014

INDIANAPOLIS -- Researchers have identified two proteins that appear crucial to the development -- and patient relapse -- of acute myeloid leukemia. They have also shown they can block the development of leukemia by targeting those proteins.

The studies, in animal models, could lead to new effective treatments for leukemias that are resistant to chemotherapy, said Reuben Kapur, Ph.D., Freida and Albrecht Kipp Professor of Pediatrics at the Indiana University School of Medicine.

The research was reported today in the journal Cell Reports.

"The issue in the field for a long time has been that many patients relapse even though chemotherapy and other currently available drugs get rid of mature blast cells quite readily," Dr. Kapur said, referring to the cancerous cells that overrun the blood system in leukemia.

"The problem is that the majority of patients relapse because they have remaining residual leukemic stem cells in the bone marrow that are resistant to currently available therapies, including chemotherapy," he said.

Mutations in two cellular structures known as receptors have previously been identified as cancer-causing. Patients with those mutations generally have a poor prognosis, but scientists have been uncertain what mechanism led to leukemia in the stem cells with those mutations.

In the Cell Reports paper, Dr. Kapur, first author Anindya Chatterjee, Ph.D., and their colleagues describe the mechanism that leads to the development of acute myeloid leukemia, identifying two proteins known as FAK and PAK1 as key to the process.

In experiments with mice, the researchers showed that eliminating, or "knocking out," the genes that produce FAK and PAK1 prevented the development of leukemia in mice, even though their bone marrow stem cells contained the cancer-causing receptor mutations. Eliminating the FAK and PAK1 proteins did not prevent the mice from otherwise producing and maintaining a normal blood system, the researchers said.

In additional experiments in mice and human cell tissue samples, the researchers identified several drug compounds that target FAK and PAK1 -- now available for experimental use but not approved for use in humans -- that were just as effective in blocking development of leukemia as knocking out the FAK and PAK1 genes.

The next step is to continue testing and refining those experimental drug compounds to verify their effectiveness for potential testing in human trials, Dr. Kapur said.

Dr. Kapur is director of the program in hematologic malignancies and stem cell biology at the Herman B Wells Center for Pediatric Research and an investigator at the Indiana University Melvin and Bren Simon Cancer Center.

Other researchers contributing to the work were Joydeep Ghosh, Baskar Ramdas, Raghuveer Singh Mali, Holly Martin, Michihiro Kobayashi, Sasidhar Vemula, Victor H. Canela, Emily R. Waskow, H. Scott Boswell, Yan Liu and Rebecca J. Chan of the IU School of Medicine; Valeria Visconte and Ramon V. Tiu of the Cleveland Clinic; Catherine C. Smith and Neil Shah of the University of California, San Francisco; and Kevin D. Bunting of the Emory University School of Medicine.

Reuben Kapur, Ph.D.

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IU Simon Cancer Center members among Indy Monthly's "Top Docs"

IU Simon Cancer Center members are among more than 350 IU School of Medicine physicians in more than 60 specialties and sub-specialties recognized as “Top Docs” in Indianapolis Monthly’s November issue. (See news release.)

The list was compiled by Castle Connolly Medical Ltd., a health care research and information company, which selected this year's honorees by asking physicians to recommend someone they would see themselves or suggest to a company member. Participants in the survey included about 700 licensed medical professionals in the Indianapolis area representing 60 specialist and hundreds of areas of expertise.

The following members of the IU Simon Cancer Center were recognized in the “Top Docs” issue:

Colon and Rectal Surgery: Bruce W. Robb

Endocrinology, Diabetes and Metabolism: Theresa Guise

Gastroenterology: Naga Chalasani, Douglas K. Rex and Stuart Sherman

Gynecologic Oncology: Frederick B. Stehman

Hematology: Rafat Abonour, Jose Azar, Larry D. Cripe, Sherif S. Farag, and G. David Roodman

Medical Oncology: Lawrence H. Einhorn, Patrick J. Loehrer, Kathy D. Miller, Michael J. Robertson and Anna Maria Storniolo

Neurological Surgery: Aaron Cohen-Gadol and Scott A. Shapiro

Neurology: Edward J. Dropcho

Orthopaedic Surgery: Lawrence Daniel Wurtz

Otolaryngology: Michael G. Moore

Pathology: Sunil Badve and Thomas M. Ulbright

Pediatric Hematology-Oncology: Sandeep Batra, James M. Croop, Robert J. Fallon, Kamnesh R. Pradhan, Jamie Renbarger and Terry A. Vik

Plastic Surgery: William A. Wooden

Radiation Oncology: Kevin P. McMullen

Surgery: Gary L. Dunnington, Linda K. Han, Thomas J. Howard, Mary A. Maluccio, and Douglas J. Schwartzentruber

Thoracic & Cardiac Surgery: Thomas J. Birdas, and Kenneth A. Kesler

Urology: Richard Bihrle, Richard S. Foster, Michael O. Koch, and Chandru P. Sundaram

Vascular and Interventional Radiology: David M. Agarwal and Matthew S. Johnson

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IUSCC news

November 2014

News briefs

Breast cancer researcher to lead radiation oncology at IU School of Medicine

Richard C. Zellars, MD, from the Johns Hopkins University School of Medicine has been named professor and chair of radiation oncology at the Indiana University School of Medicine, pending approval by the IU trustees. He will begin his new duties in January.
full story>


Zellars

Cincinnati Cancer Institute hosts survivorship program in March 2015

The University of Cincinnati Cancer Institute's Cancer Survivorship Program is hosting "Transforming Cancer Survivorship Through Research and Best Practice," from 8 a.m. to 4 p.m., Friday, March 27, at the Kingsgate Marriott Conference Center, 151 Goodman Drive, Cincinnati.

The event is planned to educate and meet the needs of physicians, nurses, psychologists, residents, medical students, social workers, counselors, dieticians and other oncology health professionals on the best practices and latest research for cancer survivorship. Julia Rowland, PhD, director of the National Cancer Institute Office of Cancer Survivorship, will be the keynote speaker.

For the full agenda, abstract requirements or to register, visit www.uchealth.com/events/transformingsurvivorship. Questions? Contact Shanah Cole at (513) 558-9908.

A group of students from Crawfordsville High School recently visited campus. While here, each delivered presentations on different cancers and received input from faculty on pathways leading

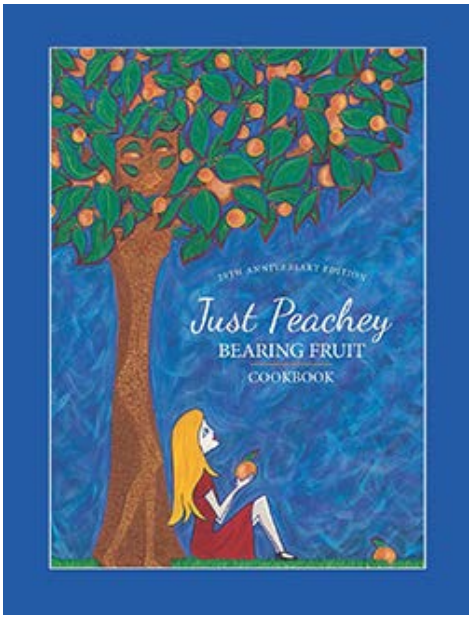
to cancer.

Free resource for caregivers

As more patients are being cared for at home, family caregivers are coming under increasing stress. A free resource, Help for Cancer Caregivers.org, provides information to assist caregivers with practical matters like talking to healthcare providers, managing medication, dealing with challenges like employment, transportation, home safety, and emergency preparedness. Most importantly, *HelpForCancerCaregivers.org* helps caregivers care for themselves. Members of the IU Simon Cancer Center and the IU School of Informatics and Computing collaborated to build the resource. Johnson & Johnson, Michigan State University's College of Nursing, WellPoint Inc., and others were also involved.

Cookbook makes for great holiday gifts, supports breast cancer research

Consider giving family and friends *Just Peachey: Bearing Fruit,* a cookbook and breast health reference, as holiday gifts. Developed by the Catherine Peachey Fund, the book is the 20th anniversary edition of *Just Peachey: Cooking Up a Cure*, which sold 57,000 copies and established the Catherine Peachey Fund as a funding resource for breast cancer researchers in Indiana.



The fund is a 100-percent volunteer organization with less than 5 percent overhead. All of the revenue from sales of the cookbook will be granted to research and programs at IU. To date, the Catherine Peachey Fund has granted $2,447,143 to Indiana University.

Just Peachey: Bearing Fruit includes more than 500 recipes from celebrities, chefs, cancer survivors, physicians, researchers, and friends and family. The pink pages at the front of the book were overseen by Anna Maria Storniolo, MD, medical editor.

The cookbook is available at amazon.com and Bright Ideas (on the north side of Broadripple) for $24.99. Or you can purchase from Liz Parsons, Vivian Murphy, or at the Komen Tissue Bank at the IU Simon Cancer Center.

Cancer center members in the news

- **Emma Rossi**, MD, and **Daniela Matei**, MD, are among the presenters at the Society of Gynecologic Oncology's annual meeting in Chicago in March 2015. Dr. Rossi is also an invited faculty speaker. All five (three residents and two fellows) submissions from IU were accepted.

- **Larry Cripe**, MD, has been named editor-in-chief for the National Cancer Institute Physician Data Query (PDQ) Supportive and Palliative Care editorial board, effective March 2015. The board is responsible for developing and maintaining evidence-based PDQ cancer information summaries for health professionals and the public.

- **Shelley Johns**, PsyD, presented a podium presentation, Impact of Mindfulness Training on Avoidant Coping and Advance Care Planning, at the inaugural meeting of the American Society of Clinical Oncology's Palliative Care in Oncology Symposium. **Susan Hickman**, PhD, presented a poster, Decision Making for Older Adults with Advanced Cancer: Patient and Family Member Perspectives.

- **Hal Broxmeyer**, PhD, received an honorary degree from the Peking Union Medical College. He unexpectedly received it after delivering a plenary talk in a meeting on hematopoietic stem cells in Tianjian, China.

- **Nasser Hanna**, MD, and **Lawrence Einhorn**, MD, wrote "Testicular Cancer -- Discoveries and Updates," which was published Nov. 20 in the New England Journal of Medicine.

New members

Andrea Bonetto, PhD
Department of Surgery
Associate member, Tumor Microenvironment and Metastasis

Juhua Luo, PhD
School of Public Health-Bloomington
Associate member, Cancer Prevention and Control

Jianyun Liu, PhD
Department of Microbiology and Immunology
Associate member, Hematopoiesis, Hematologic Malignancies, and Immunology

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