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IU researchers, collaborators discover new therapeutic agents that may benefit leukemia patients

Oct. 2, 2013

INDIANAPOLIS -- An Indiana University cancer researcher and his colleagues have discovered new therapeutic targets and drugs that may someday benefit people with certain types of leukemia or blood cancer.

Reuben Kapur, Ph.D., the Frieda and Albrecht Kipp Professor of Pediatrics at the IU School of Medicine and a researcher at the Indiana University Melvin and Bren Simon Cancer Center, and colleagues discovered in pre-clinical and pharmacological models that cancer cells with a mutation in the KIT receptor -- an oncogenic/cancerous form of the receptor -- in mast cell leukemia and acute myeloid leukemia can be stopped.

Their findings were published online Sept. 16 in the Journal of Clinical Investigation and appeared in print Oct. 1.

According to Dr. Kapur, activating mutations of KIT receptors are almost always associated with a type of leukemia called mast cell leukemia. The mutations in the KIT receptor are found in about 90 percent of patients with this type of leukemia. In addition, activating mutations of KIT are also exclusively associated with a subtype of acute myeloid leukemia known as core binding factor leukemia. When KIT is associated with these two types of leukemia, the survival rate for patients is profoundly reduced in comparison to patients who do not have this mutation.

Dr. Kapur and colleagues investigated whether they could shut down the growth response that is induced by this mutation.

"We identified two new targets in leukemic cells bearing this mutation, which when targeted or inhibited, cause leukemia cells to die," Dr. Kapur said.

The researchers discovered that the two targets are Rac GTPase and Pak (p21-activated kinase). In return, they designed a novel Rac inhibitor -- EHop-016 -- that is considerably more potent than previously described inhibitors of Rac. They also demonstrated a novel role for Pak inhibition in leukemia using an existing Pak inhibitor.

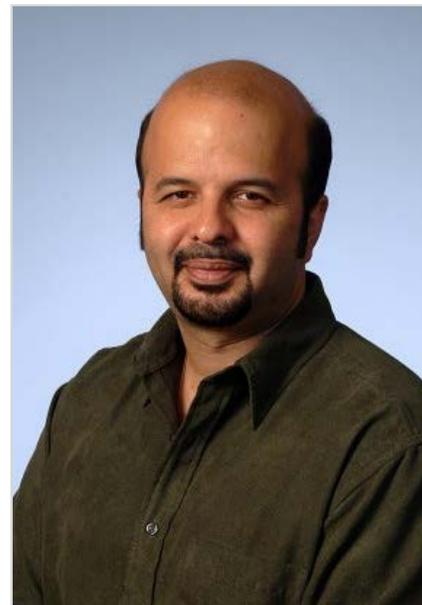
Both are being tested in pre-clinical models to further examine their growth inhibitory properties as well as long-term treatment-associated toxicity.

Dr. Kapur said treatments for leukemia have remained mostly unchanged in the past 30 years. Thus, researchers continue to search for better and more effective ways to treat this debilitating disease.

"We've been looking for new targets and new ways of treating leukemia and special types of leukemias," Dr. Kapur said. "Leukemia is an extremely complex disease. It's a combination of multiple alterations in the patient's DNA, which eventually results in leukemia. Therefore, it will be very difficult to cure leukemia with just one drug. It will have to be a combination of multiple drugs, if we're to cure this disease."

Dr. Kapur is also professor of biochemistry and molecular biology, of medical and molecular genetics, and of microbiology and immunology at the IU School of Medicine.

Principal authors of the study were Suranganie Dharmawardhane and Cornelis P. Vlaar of the Department of



Reuben Kapur, Ph.D.

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IUSCC news

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News briefs

Redesigned cancer center website launches

A redesigned IU Simon Cancer Center [website](http://www.cancer.iu.edu/) has launched. The redesigned site focuses on the cancer center's research and education missions. Whether you're at a desktop computer or using a mobile device, the site will respond to whatever you are using.



Members, you can find your bio here: <http://www.cancer.iu.edu/research-trials/directory.shtml>. Go to the alphabetical listing and click your name. If something needs updated, please send the update to iuccit@iupui.edu.

The redesigned site places an emphasis on the cancer center's researchers and their

accomplishments -- accomplishments that lead to better ways to prevent, diagnose and treat cancer. Information about membership, shared facilities, funding opportunities and more is located within the [research tab](#). It is an evolving project; changes and enhancements will happen on an ongoing basis.

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 Peachy Fund, which is publishing the 20th 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 Leshar at stephanierl@peacheyfund.org. Submissions are due Dec. 2. [Learn more about the cookbook](#). [Learn more about the Catherine Peachy Fund](#).

Indiana Clinical and Translational Sciences Institute receives \$30 million grant renewal

The Indiana Clinical and Translational Sciences Institute, a partnership among Indiana University, Purdue University and the University of Notre Dame, has received nearly \$30 million from the National Institutes of Health to continue its mission accelerating research discoveries across Indiana and beyond. [full story >](#)

Science profiles NCI director

Science magazine profiled Dr. Harold Varmus, director of the NCI, in its Oct. 25 issue. [Read "Varmus's Second Act."](#)

Cancer center members in the news

- **Bryan Schneider**, MD, has been named the Vera Bradley Investigator in Oncology.
- **Monet Bowling**, MD, is an author of a [study published online in the Journal of the American Medical Association](#) that shows a less-invasive procedure known as sentinel lymph node surgery successfully identified whether cancer remained in lymph nodes in 91 percent of patients with node-positive breast cancer who received chemotherapy before their surgery. In sentinel lymph node surgery, only a few lymph nodes, the ones most likely to contain cancer, are removed.
- Researchers from Purdue and IU are developing a system that uses tiny magnetic beads to quickly detect rare types of cancer cells circulating in a patient's blood, an advance that could help medical doctors diagnose cancer earlier than now possible and monitor how well a patient is responding to therapy. **Shadia Jalal**, MD, and **Daniela Matei**, MD, are working with their Purdue colleagues on this project. [full story >](#)
- At the Fourth International Thymic Malignancy Interest Group Annual Meeting, **Sunil Badve**, MBBS, MD, **Patrick Loehrer**, MD, and Yesim Gökmen-Polar, PhD, assistant research professor, presented study results that showed a genetic test now offers doctors an accurate and accessible method for making a precise diagnosis for differentiating thymomas from thymic carcinoma tumors. This information can help physicians choose the most effective and personalized treatment options for patients. This test, called DecisionDx-Thymoma, is available to physicians through Castle Biosciences Inc., which exclusively licensed the test from Indiana



Shadia Jalal, MD

University.

IU Simon Cancer Center

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