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IU researchers earn \$3.2 million grant to develop, improve therapies for pancreatic cancer

March 11, 2013

INDIANAPOLIS -- Two Indiana University researchers have been awarded a multi-year, \$3.2 million grant to develop and improve therapies for pancreatic cancer, the fourth leading cause of cancer death in the United States.

Mark R. Kelley, Ph.D., Betty and Earl Herr Professor of Pediatric Oncology Research, and Melissa L. Fishel, Ph.D., assistant research professor of pediatrics, both at the [IU School of Medicine](#), were awarded a 5-year grant (CA167291) from the [National Cancer Institute](#) of the [National Institutes of Health](#). The two [Indiana University Melvin and Bren Simon Cancer Center](#) researchers will focus on investigating the signaling pathways and molecular mechanisms that contribute to pancreatic tumor progression and resistance to therapy.

Signaling pathway describes a group of molecules in a cell that work together to control one or more cell functions, such as cell division or cell death. After the first molecule in a pathway receives a signal, it activates another molecule. This process is repeated until the last molecule is activated and the cell function is carried out. Abnormal activation of signaling pathways can lead to cancer.

In their laboratory research, Drs. Kelley and Fishel plan to block a protein, redox factor 1 (Ref-1), which is crucial to regulating pancreatic tumor growth and metastasis. They will use a protein inhibitor that Dr. Kelley and colleagues developed that has shown promise in the lab in blocking Ref-1.

"We will study a particular protein, Ref-1, that we believe is involved in signaling between the tumor and the tumor's environment," Dr. Fishel said. "We hope to better understand how this protein signals and functions in the tumor microenvironment as well as in the tumor cells. We're hoping that if we can inhibit the function of Ref-1, we can blunt the tumor's ability to live."

Researchers have been learning that a tumor's microenvironment plays a significant role in the life and death of a tumor.

"We're realizing that it's not just the tumor that has to be treated," Dr. Kelley added. "You have to treat the tumor and the surrounding support structure, its microenvironment. Because pancreatic cancer is hard to treat, we think Ref-1 is a viable target both in the tumor and the microenvironment. If we can hit it in both places, it's a double win."

This latest pancreatic cancer project builds on Dr. Kelley's ongoing research into using inhibitors to prevent cancer cells from repairing the damage caused by anti-cancer therapies.

Drs. Kelley and Fishel will collaborate with other IU Simon Cancer Center researchers, which Dr. Kelley referred to as an example of "team science." The others include internationally recognized cancer researcher Murray Korc, M.D., the Myles Brand Professor of Cancer Research at the IU School of Medicine and director of the Indiana University-Purdue University Indianapolis Pancreatic Cancer Signature Center. The signature center, an IUPUI designation that represents a research strength and focus in an area that is not commonly studied, brings together nearly 50 basic scientists and clinicians who work to improve outcomes for pancreatic cancer patients.

The research team also includes Theresa Guise, M.D., Jerry and Peggy Throgmartin Professor of Oncology,

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Melissa Fishel (left) and Mark Kelley | PHOTO-BY IUSM OFFICE OF VISUAL MEDIA

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and Mircea Ivan, M.D., Ph.D., assistant professor of medicine, both at the IU School of Medicine. Dr. Guise is an expert on tumor microenvironment and metastatic disease, while Dr. Ivan is an expert in hypoxia, a condition in which there is a decrease in the oxygen supply. Pancreatic tumors are hypoxic, which makes them more aggressive and difficult to treat.

There is a need for new therapies for pancreatic cancer patients because current treatments typically only extend a person's life for six to 10 weeks. Only 6 percent of people with the disease survive more than five years after 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.

"Our hope and goal is to change the standard of care because it's not working," Dr. Fishel said. "Our hope is to bring a new therapy -- or a new one that would be used in conjunction with a current therapy -- to make inroads against this disease. Even if a new therapy doesn't kill the tumor, if it can penetrate the microenvironment to help other drugs get to the tumor, that would be beneficial."

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Researchers say NSAIDs can boost stem cells for transplants for cancer patients

March 13, 2013

Scientists say that non-steroidal anti-inflammatory drugs may be a boon to doctors gathering stem cells for transplants to treat patients with blood or bone marrow cancers, including non-Hodgkin's lymphoma and multiple myeloma.

The compounds, known as NSAIDs and which include aspirin, ibuprofen and other painkillers, increased the number of stem and progenitor cells harvested from the blood in animal testing and a small human study, according to work published online Wednesday in the journal *Nature* by a research team led by Indiana University School of Medicine scientists.

Stem cells and their immediate descendants, progenitor cells, are responsible for nearly all of the billions of blood and immune system cells produced in the body each day. Those key ancestor cells spend most of their lives in the bone marrow, where they are destroyed when physicians use high-dose chemotherapy to treat diseases such as multiple myeloma and non-Hodgkin's lymphoma. So before the bone marrow transplant begins, physicians collect stem and progenitor cells from the blood and then transplant them back to the patient following intensive chemotherapy, restoring the patient's ability to produce blood and immune system cells.

To increase the numbers of stem and progenitor cells collected, physicians treat patients with proteins called growth factors, which mobilize some stem and progenitor cells to leave the bone marrow and enter the circulating blood. However, up to 40 percent of patients fail to mobilize enough cells to get an optimum dose, potentially reducing transplant effectiveness. The drug Plerixafor is approved to help increase the cell mobilization; however its use can add about \$25,000 per patient.

"Researchers have been looking for new, more effective mobilizing agents, and NSAIDs could be those agents, and at a very low cost," said Louis M. Pelus, Ph.D., professor of microbiology and immunology at the IU School of Medicine and principal investigator for the study.

In animal studies, using an NSAID alone increased stem and progenitor cell counts in the circulating blood by four to six times, though the numbers of cells remained small. However, in combination with growth factors, the mobilization of cells was significantly greater than when the growth factors were used alone.

The mobilization effects of the NSAIDs were attributable to their role in blocking the production of Prostaglandin E, the same role that produces NSAIDs' benefits in reducing pain and inflammation.

"We showed that NSAIDs moved these cells out of the bone marrow on their own, and with a greater-than-additive, even synergistic effect, when used in combination with the growth factor that is normally used clinically to mobilize cells," said Dr. Pelus, an investigator with the Indiana University Melvin and Bren Simon Cancer Center.

Moreover, in the animal studies transplanted cells mobilized with NSAID assistance were more effective in repopulating the recipients' bone marrow than were those mobilized with growth factors alone.

In tests on seven healthy human volunteers, NSAIDs alone increased cell mobilization, but no tests using both growth factors and NSAIDs were conducted with the human volunteers.



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However, researchers have prepared grant proposals to conduct human clinical trials of the effectiveness of adding NSAIDs to the standard transplant protocols, Dr. Pelus said. The trials would likely use meloxicam, which is less likely to cause gastrointestinal discomfort and bleeding than other NSAIDs, he said.

In addition to Dr. Pelus, investigators contributing to the research were first author Jonathan Hoggatt of the IU School of Medicine and Harvard Medical School; Amber F. Hoggatt of the IU School of Medicine and the University of Illinois at Chicago; Khalid S. Mohammad, Pratibha Singh, Brahmananda R. Chitteti, Jennifer M. Speth, Peirong Hu, Bradley A. Poteat, Kayla N. Stilger, Sherif S. Farag, Magdalena Czader, Carlos H. Serezani, Theresa A. Guise and Edward F. Srour of the IU School of Medicine; Francesca Ferraro, Lev Silberstein, Frankie K. Wong and David T. Scadden of Harvard Medical School; and Ginger L. Milne and Richard M. Breyer of Vanderbilt University.

The research was supported by National Institutes of Health grants HL096305, CA143057, CA069 158, HL1 00402, DK37097, DK07519, HL07910 and HL087735, National Cancer Institute grant P30 CA082709 and a Center of Excellence in Hematology grant P01 DK090948.

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March 2013

Cancer researchers discover new type of retinoblastoma in babies

Not all forms of retinoblastoma, a pediatric cancer of the eye, may be inherited, a discovery that would spare children years of medical evaluations and offer the potential of drug therapy for an aggressive malignancy.

[Timothy Corson, PhD](#), a researcher at the [Eugene and Marilyn Glick Eye Institute](#) and the IU Simon Cancer Center, is a member of an international team that has discovered this childhood eye cancer is not always caused by a mutation of the “retinoblastoma gene.” That’s good news for some children who get this disease because it means they won’t have to undergo invasive exams over the course of their lifetime to determine whether the cancer has spread.

Dr. Corson, who researches pediatric ocular cancers, is one of 25 scientists who have worked on this for several years. Their paper, based on a study of more than 1,000 retinoblastoma patients, recently was published in *Lancet Oncology*.



Corson

“Traditionally, an aggressive retinoblastoma seen in a very young infant in the clinic would be suspected to be caused by an inheritable mutation, leading the patient to a childhood full of invasive clinical exams, and the fear of risk to their offspring,” Dr. Corson said.

This previously unnoticed class of tumors challenges the long-standing belief that all retinoblastoma are caused by a mutation of the tumor suppressor gene named after this cancer, RB1. Dr. Corson said this new group of retinal tumors has a normal RB1 gene and appears to be “driven” by extra copies of a cancer-causing gene called MYCN, a gene most commonly associated with another childhood cancer, neuroblastoma.

“Our study suggests that one in five patients with an early-onset tumor in a single eye may have MYCN retinoblastoma, and thus lack future risks. This kind of retinoblastoma can only be definitively diagnosed by molecular testing showing lack of mutations in the RB1 gene and amplification of the MYCN gene in the child’s tumor,” Dr. Corson said.

The MYCN retinoblastoma have fewer other mutations in their genome than classic retinoblastoma and have a distinctive cellular appearance to a pathologist, Dr. Corson said. Most importantly, they have features that render them immediately important clinically: They occur at a very young age and are extremely aggressive. In the future, they may be treatable with drugs that block the activity of MYCN.

“This is a landmark discovery in retinoblastoma genetics,” David Plager, MD, professor of ophthalmology at the Glick Eye Institute and director of the Pediatric and Adult Strabismus Service, said. “We are currently investigating a patient who fits the clinical description of MYCN retinoblastoma and, if confirmed, it will save the baby and his family the trouble and the expense of numerous future exams to monitor development of a tumor in the other eye.”

Dr. Corson, who immediately began consulting with Dr. Plager on the case, said the child's definitive diagnosis based on molecular testing could come within weeks.

About 300 new cases of retinoblastoma arise in the United States annually. Although survival rates are high with treatment, patients are often left with vision loss or blindness.

--Vicki Hermansen



March 2013

Call for abstracts: IUSCC's Cancer Research Day; abstracts due April 15

The IU Simon Cancer Center is currently accepting abstracts for posters to be presented at Cancer Research Day, which is Wednesday, May 22.

Abstracts should be submitted for one of the following research categories:

- Basic Science
- Behavioral
- Population Science/Epidemiology
- Translational/Clinical Research

Abstracts will be divided and compared by the following groups within each research category:

- clinical nurse
- graduate student
- medical student
- post-doctoral/medical fellow
- research technician
- faculty (not eligible for cash award)

Cash awards will be given for best poster(s) in each research category, by group. A panel of judges will be assigned to review abstracts and posters by research category and group. Individual laboratories may submit multiple abstracts; if space becomes limited, each laboratory will be asked to identify representative posters. Please submit abstracts to iusccrd@iupui.edu by April 15. Visit www.cancer.iu.edu/crd to download the abstract template.

Anil K. Sood, MD, professor and vice chair for translational research in the Departments of Gynecologic Oncology and Cancer Biology, co-director of the Center for RNAi and Non-Coding RNA, and director of the Blanton-Davis ovarian cancer research program at the University of Texas MD Anderson Cancer Center, presents the keynote address at 1:30 p.m. He will present "Targeting Tumor Angiogenesis using RNA Interference."

Cancer Research Day -- including the symposium, poster session, keynote address, and the awards ceremony -- all take place at the IUPUI Campus Center, 420 University Blvd., Room CE 450 (Multi-Purpose Room).

IU Simon Cancer Center Cancer Research Day is an annual event that aims to increase understanding and awareness of IU Simon Cancer Center research endeavors and encourage collaboration with other cancer research institutions in Indiana.



March 2013

News briefs

Databases aid mRNAs, miRNAs prognostic implications

PROGgene and PROGmiR are two databases for investigating prognostic implications of genes and miRNAs in cancers, developed by the Center for Computational Biology and Bioinformatics. PROGgene is gene expression based and PROGmiR is miRNA expression based survival analysis application. Researchers can use both these databases to study prognostic implications of mRNAs and miRNAs in multiple cancers. Datasources for both databases have been compiled from public resources such as Gene Expression Omnibus and the Cancer Genome Atlas (TCGA). With data on close to 20 cancers in repository, both tools offer the most comprehensive survival analysis available to date. PROGgene is available at compbio.iupui.edu/proggene and PROGmiR is available at compbio.iupui.edu/progmir. Questions? Contact Chirayu Goswami at cgoswami@iupui.edu. The databases have been made possible, in part, by a gift from the Vera Bradley Foundation for Breast Cancer.

New IT manager joins IUSCC

Jeff Johnson is the cancer center's new information technology development manager. He leads all IT projects pertaining to the mission-critical Clinical Trial Management System (OnCore) used across the cancer center and its shared facilities, partners and affiliates and is responsible for all IUSCC IT programs and databases. He can be reached at 278-2125; his office is located in the cancer pavilion (RT 370A).



Johnson

IUSCC accepting Wright Scholarship applications

The IU Simon Cancer Center is accepting applications for the William J. Wright 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 pursuing 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. [Download the application](#). The application deadline is April 15.

A Request for Proposals for the American Cancer Society Institutional Research Grant Competition

The IU Simon Cancer Center is pleased to announce the availability of funds for new pilot projects to assist new investigators who hold the rank of assistant professor, research assistant professor, or assistant scientist but without an active (i.e., NIH, NSF, ACS) national competitive research grant, regardless of the topic. These funds are from the American Cancer Society Institutional Research Grant (ACSIRG). This grant provides support for beginning investigators to enable them to initiate their independent research program. [Download the application](#).

Seeking speaker nominations for 2013-14

Cancer center members are encouraged to send nominations, along with CVs or biosketches, of potential speakers for the cancer center's Seminar Series by April 15, 2013. The cancer center's executive committee will select the nominees before the end of May based on national/international reputation, cancer center programmatic interests, and potential for collaboration. Please send your nominations to Chasity Spears (chasmill@iupui.edu). For additional details, please contact Harikrishna Nakshatri, IUSCC associate director for education, (hnaakshat@iupui.edu). The Seminar Series takes place on Thursdays from 3 p.m. to 4 p.m. in Walther Hall. The remaining series for this academic year can be found [here](#).

Upcoming events

●IU Simon Cancer Center basketball team participates in Coaches' Huddle April 13

The IU Simon Cancer Center has assembled a basketball team to participate in this year's American Cancer Society's Coaches' Huddle Basketball Tournament on Saturday, April 13 at Butler University. All games and activities will be held on the Butler University campus, utilizing Hinkle Fieldhouse and the Health & Recreation Complex (HRC). The first games begin at 8 a.m., with the championship game scheduled for approximately 5 p.m. (The start time for the cancer center's first game has not yet been determined.) Throughout the event, additional activities and entertainment will be offered in a family fun zone. Coaches vs. Cancer is a collaborative program between the ACS and the National Association of Basketball Coaches that empowers coaches of all sports, their teams and communities to join the fight against cancer. Since its inception in 1993, high school and college coaches across the country have raised more than \$60 million to help the ACS fund

groundbreaking cancer research, provide up-to-date cancer information, advocate for public health policies that benefit the community and provide free local programs that improve quality of life for cancer patients and their families and caregivers. For more information about the local event, contact Tara Miller at the ACS at Tara.Miller@cancer.org or 344-7807.



●IUSCC sponsors Relay for Life April 13-14

The IU Simon Cancer Center is a sponsor of this year's Relay for Life of IUPUI, an overnight community fund-raising walk. Cancer center member **Janaiah Kota**, PhD, is serving as captain of the Cure Cancer-IU Simon Cancer Center team. The team's goal is to raise \$2,000. If you would like to join Dr. Kota's team, please visit the [event Web site](#). This year's Relay for Life is 6 p.m. April 13 to 6 p.m. April 14 at the Taylor Courtyard, which is located west of the Kelley School of Business. This year's theme is "One World. One Hope." Activities are planned for the entire family. All are welcome to participate. For more information, visit the [event Web site](#).

●Indiana Cancer Consortium hosts "Navigating Cancer Care" April 25

Join the Indiana Cancer Consortium (ICC) during National Cancer Control Awareness Month as the ICC explores the past, present, and future of cancer care and law in Indiana. Guest of honor and keynote speaker Otis Brawley, MD, and others will make the case for evidence-based, scientifically justifiable cancer care from prevention through palliation. By the end of the event, attendees will learn to view cancer through

a scientific lens and lead more effectively by better navigating cancer guidelines, treatment, and the Affordable Care Act. This year's meeting, titled "Navigating Cancer Care: What We Know, What We Don't Know, and What We Believe," is 9 a.m. to 4 p.m. April 25 in Indianapolis. There is no cost to attend. [Registration is now open.](#)

●HPV vaccine presentation slated for May 6

John Schiller, PhD, head of the Neoplastic Disease Section, Laboratory of Cellular Oncology, Center for Cancer Research at the NCI, presents "HPV Vaccines: Past, Present and Future" at 4 p.m. Monday, May 6 in Walther Hall, room 203. Dr. Schiller played a central research that led to the development of current HPV vaccines and is continuing work on developing second-generation HPV vaccines. His presentation is sponsored by the IUPUI Center for HPV Research.

Reminders

●Missed a Combined Seminar Series?

Have you missed a Combined Seminar Series? You can now watch it online. An archival listing of past Seminar Series events is [here](#). Also, you can find the current lineup of speakers [here](#).

●24 Hours of Booty returns

24 Hours of Booty is back for a second year in Indianapolis. The Booty Loop will be held at Butler University June 28-29. The event will host more than 400 riders who will raise more than \$200,000 for cancer research and survivorship. The IU Simon Cancer Center has been chosen as the local beneficiary for this event. For more information or to register, check out www.24hoursofbooty.org or contact Theresa Vernon at tm5@iu.edu. You can register as an individual, form your own team, or join the cancer center's team, Pedaling Cures. All cycling levels welcome.



●Wanted: Assistant for Summer Research Program

An assistant is needed for the IU Simon Cancer Center's Summer Research Program. The assistant acts as a liaison with high school and undergraduate students, program faculty mentors, IUPUI Center for Research and Learning and the Summer Research Program Committee. Flexible hours from March to May; full-time hours from June to July. If you know of excellent candidates, please refer them to the [full description](#).

●IUSCC's Cancer Center Support Grant due in fall 2013

In September 2013, the IU Simon Cancer Center's National Cancer Institute Cancer Center Support Grant (CCSG) will be due. Consequently, the cancer center's executive committee and research program leaders are currently undertaking a critical review of the program and its membership, as well as finalizing program themes, goals and aims. All members are encouraged to assist their program leaders as they begin working on their respective narratives. The program leaders will need assistance from their members on compiling research highlights for those narratives. Program leaders are also planning retreats and participation among members is important. The CCSG is an important source of funding for the cancer center's shared facilities. This support, along with IU Simon Cancer Center funding, assures that cancer center members have access to the highest quality technology for their research.



●Membership changes

Membership criteria into the IU Simon Cancer Center has changed to include full-time faculty of any Indiana university who contribute on some level to the cancer center's mission of research, education, patient care and community outreach. Full membership criteria is [here](#).

●**Researchers: Share your news**

Is your research about to be published in a journal? Are you about to present your research at a professional meeting? Have you received national funding for your research? Share your news with [Michael Schug](#), IUSCC communications manager.

●**Funding opportunities**

For the latest funding opportunities, visit <http://www.cancer.iu.edu/research/funding/>.

Cancer center members in the news

- **Kent Robertson**, MD, who conducted a [groundbreaking new study](#) that could change the outlook for those with neurofibromatosis, talked with Sound Medicine about his research. [Listen to Sound Medicine](#).
- **Hari Nakshatri**, BVSc, PhD, will receive an outstanding achievement award from the Society of American Asian Scientists in Cancer Research (SAASCR) during its annual meeting April 7 in Washington, D.C.
- **Max Schmidt**, MD, PhD, MBA, was a finalist in the advancements in health care category in this year's *Indianapolis Business Journal's* Health Care Heroes awards program.
- Three IU Simon Cancer Center members are among 18 faculty members from the IU School of Medicine who are recipients of 2012-13 [IU Collaborative Research Grants](#). The grants support research aimed at advancing a research field and impacting the lives of residents in Indiana, the United States and the world. The program also aims to increase IU's competitiveness for external funding involving innovative and transformative research. Award winning proposals fit at least one of the following subject areas: biological and health sciences, physical sciences and computer sciences, and social and behavioral sciences. The maximum amount is \$75,000, except for "exceptional cases" which have received a greater amount. The three recipients are: **Nadia Carlesso**, MD, PhD, and colleagues for "Role of the Epigenetic Regulator Cfp1 In Hematopoietic Stem Cell (HSC) Response To Stress," **Melissa Kacena**, PhD, and colleagues for "Thrombopoietic Agents in Bone Regeneration: Development of a Mini-Pig Bone Healing Model," and **Amber Mosley**, PhD, and colleagues for "Identifying Post-translational Modifications in Protein Complex Assembly through STAP."



Carlesso

New grants

David Gilley, PhD

"Targeting Telomere Dysfunction for Early Breast Cancer Detection"
Avon Foundation

Mark Kaplan, PhD

"Plasticity of IL-9-secreting T Cells"
NIH-NIAID

Irina Petrache, MD

"Mechanism and Role of Smoking-Generated Endothelial Microparticles"
American Heart Midwest

Anna Maria Storniolo, MD

"The Susan G. Komen for the Cure

Patrick Loehrer, MD

“To Develop Sustainable Research
Capacity for Cancer and Tobacco Control
in Kenya Across the Lifespan”
West Virginia University

Samy Meroueh, PhD

“Docking uPAR for Selective Targeting of
Cancer Metastasis”
American Cancer Society

Lida Mina, MD

“A Phase I Double Blinded Prospective
Study of Metformin vs. Placebo in
Overweight or Obese Women at Elevated
Risk”
IU Health

Tissue Bank at the IU Simon Cancer
Center Kenya Project”
Komen Cancer Foundation

John Turchi, PhD

“Development of Novel Agents
Targeting Genome Stability and
Maintenance for Treating Ovarian
Cancer”
NERx Biosciences