IUSCC news

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News briefs

IU cancer researcher awarded nearly $2.6 million to increase colorectal cancer screening

An Indiana University cancer researcher has been awarded nearly $2.6 million to compare interventions to increase colorectal cancer screening among underserved patients with limited resources.


Rawl

Susan Rawl, PhD, professor of adult health at the IU School of Nursing and a researcher at the Indiana University Melvin and Bren Simon Cancer Center, received the award from the Patient-Centered OutcomesResearch Institute (PCORI).

Dr. Rawl and colleagues will compare two interventions -- a mailed tailored DVD alone to a mailed tailored DVD plus a telephone-based patient navigator -- to usual care to increase colorectal screening rates.

The researchers will target 750 patients between the ages of 50 and 75 who were referred and scheduled to have a colonoscopy, but they either cancelled or did not attend the scheduled appointment. The DVD and the DVD plus the patient navigator are designed to educate people about the importance and benefits of screening as well as provide assistance to overcome each individual's barriers.

According to Dr. Rawl, patient navigation and computer programs that are personalized to the unique needs of each user have been shown to be effective approaches to increasing colorectal cancer and other cancer screening, but no studies have combined them to examine their effectiveness.

"We will examine whether these interventions improve knowledge about colon cancer and screening and change health beliefs about screening," Dr. Rawl said. "Ultimately, the goal is to test whether these interventions are effective approaches to getting people screened."

People do not go to their appointments for a variety of reasons, including a lack of awareness of the need for screening and the benefits of screening, fear of pain, fear of finding cancer, unpleasantness of bowel preparation, cost, transportation issues, and an unwillingness to undergo invasive testing while not experiencing any symptoms.

Colorectal cancer is the third most common cause of cancer deaths in the country. About one-half of the deaths could be prevented if appropriate colon cancer screening was widely implemented.

Screening varies from annual stool testing with fecal occult blood tests or fecal immunochemical tests, sigmoidoscopy every five years, or colonoscopy every 10 years. The effectiveness of any screening depends on the rate of adherence. In 2014, only 41 percent of the people referred for colonoscopy completed the test in a local health system.

"Through this study, we seek to learn how to best educate and motivate people to get a colorectal cancer screening test because it can be a life saver," Dr. Rawl said. "This study -- when completed -- has the potential to change how health care providers and health care systems educate, counsel and prepare patients for screening. Our results may lead them to implement one or both of these interventions in a variety of health systems as a way to increase this much-needed screening."

"This project was selected for PCORI funding not only for its scientific merit and commitment to engaging patients and other stakeholders, but also for its potential to fill an important gap in our health knowledge and give people information to help them weigh the effectiveness of their care options," said PCORI Executive Director Joe Selby, MD, MPH. "We look forward to following the study's progress and working with Indiana University to share the results."

Dr. Rawl's study was selected for PCORI funding through a highly competitive review process in which patients, clinicians and other stakeholders joined clinical scientists to evaluate the proposals. Applications were assessed for scientific merit, how well they will engage patients and other stakeholders, and their methodological rigor among other criteria.

Dr. Rawl, director of the nursing school's National Institute of Nursing Research-funded T32 training program in behavioral nursing research, and director of the PhD in Nursing Science program, is co-leader of the IU Simon Cancer Center's Cancer Prevention and Control research program. The 50 scientists in the program work to decrease cancer morbidity and mortality, and are involved in the prevention and early detection of debilitating symptoms caused by cancer treatment while tailoring cancer treatment to individuals.

Her research interest is focused on behavioral oncology, with a special emphasis on interventions to promote cancer screening and reduce cancer risk. Her studies, funded by the National Cancer Institute and the National Institute for Nursing Research, have tested computer-based, tailored health promotion interventions to motivate colorectal cancer screening.

She is the immediate past chair of the board of directors of the American Cancer Society, Lakeshore Division and president of the Midwest Nursing Research Society.

PCORI is an independent, nonprofit organization authorized by Congress in 2010. Its mission is to fund research that will provide patients, their caregivers and clinicians with the evidence-based information needed to make better-informed health care decisions. For more information about PCORI's funding, visit www.pcori.org.

IU School of Medicine researchers dive deep into DNA to predict adverse drug reactions

Oct. 25, 2016

INDIANAPOLIS – Two Indiana University School of Medicine scientists are exploring uncharted genetic pathways in search of tools to predict whether patients will react well or poorly to drugs, in research supported by a new $1.69 million, three-year grant from the National Cancer Institute.

Yunlong Liu, PhD, associate professor of medical and molecular genetics and of biostatistics, and Todd Skaar, PhD, associate professor of medicine, are focusing on differences in people's reactions to chemotherapy drugs paclitaxel and clofarabine, but say they expect their techniques will be applicable to assessing other drugs' toxicities as well.

Drs. Liu and Skaar were among five research teams to receive grants in a program overseen by the National Human Genome Research Institute, all of which were designed to evaluate genetic variants that have been discovered in less-traveled sections of the genome. Most researchers have focused on the sections of the DNA that are directly involved in the process of producing proteins, Liu said. But those sections of DNA – the gene coding regions – make up only about 2 percent of human DNA, he said.

Other scientists receiving the recent NHGRI grants will focus on portions of the DNA that work as regulatory mechanisms, such as controlling when the coding regions turn on and off.

"Our interests are more in the mechanics of splicing," said Dr. Skaar.

Splicing refers to a process – in the gene-coding regions – of removing sections of DNA that aren't needed for protein expression. Those unneeded sections are called introns. The sections of DNA needed are called exons. After the cell's molecular machinery connects together the appropriate exons, the protein construction process continues.

But how to tell exons from introns? With little DNA "signs." Between the exons and introns are short sections of DNA code that identify adjacent sections as one or the other, much like road signs that tell drivers what's ahead. Much as road signs that are missing or askew can result in lost drivers, variations in the DNA signs can result in proteins that malfunction, or don't function.

Skaar and Liu are collaborating with Michael Eadon, assistant professor of medicine at IU School of Medicine, and with Eileen Dolan, PhD, professor of medicine at the University of Chicago, who developed a list of genetic variants potentially related to drug toxicity by performing an analysis of a group of immune system cell lines in the laboratory.

Individually testing each of the 100,000 candidates in cells would be an impossible task, so Liu will use biostatistical techniques and computer machine learning to predict which of the candidates are most likely to affect drug toxicity.

Skaar's lab will then test the resulting 1,000 or so candidate variations to determine their activities in cells,

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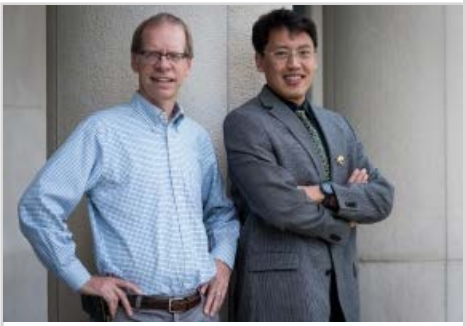

Todd Skaar, PhD, (L) and Yunlong Liu, PhD

Print Quality Photo

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using techniques his lab has developed to dramatically speed up the process.

The final candidate markers will be tested in Dr. Dolan's cell lines in Chicago, a process that should lead to clinical tests in humans to validate whether or not they can be used to accurately predict patients' responses to the chemotherapy drugs.

"Later, we expect that this process will be available to be used in literally every other genomic study that is out there," said Dr. Liu.

IU research reveals link between molecular mechanisms in prostate cancer and Ewing's sarcoma

Discovery of gene link could mean children suffering from rare cancerous tumor may respond to future prostate cancer treatments

Oct. 25, 2016
FOR IMMEDIATE RELEASE

BLOOMINGTON, Ind. -- Medical researchers at Indiana University Bloomington have found evidence for a link between prostate cancer, which affects millions of men age 50 and older, and Ewing's sarcoma, a rare form of cancer that affects children and young adults.

The results of the study, reported today in the journal Cell Reports, suggest that the molecular mechanism that triggers the rare disease Ewing's sarcoma could act as a potential new direction for the treatment of more than half of patients with prostate cancer.

A form of bone and soft tissue cancer that affects about one in 1 million children and young adults age 10 to 19, Ewing's sarcoma is terminal in 44 percent of teens age 15 to 19 and 30 percent of children. Over 100,000 men are diagnosed with prostate cancer each year in the U.S, with more than 99 percent of cases occurring after age 50.

"This research shows that the molecular mechanism involved in the development of most prostate cancers is very similar to the molecular mechanism known to cause Ewing's sarcoma," said Peter Hollenhorst, an associate professor in the Medical Sciences Program at IU Bloomington, a part of the IU School of Medicine. "It also suggests that this mechanism might be used to explore a common treatment for both diseases, one of which is not often pursued by drug companies due to its rarity."

Hollenhorst is also a member of the Indiana University Melvin and Bren Simon Cancer Center in Indianapolis.

Other authors on the paper include Vivekananda Kedage, a graduate student in the IU Bloomington College of Arts and Sciences' Department of Molecular and Cellular Biochemistry, and Travis J. Jerde, an associate professor in the Department of Pharmacology and Toxicology at the IU School of Medicine in Indianapolis. Kedage is the first author on the study.

There are 28 genes in the human body known as ETS genes, four of which are known to produce proteins that cause prostate cancer. These four cancer-causing genes, or "oncogenes," are called ETV1, ETV4, ETV5 and ERG, the last of which has been implicated in over 50 percent of all prostate cancers. The other three combined play a role in about 7 percent of prostate cancers.

Ewing's sarcoma results from errors in the chromosome repair process that causes the merger of two separate gene segments into a mutant hybrid gene, also known as a chimeric or fusion gene. One of these genes is called EWS, the other is a gene that produces ETS proteins.

Hollenhorst's study is the first to show that the proteins produced by the EWS gene interact with all four ETS proteins known to trigger prostate cancer. Moreover, the EWS protein only interacts with proteins from these four harmful ETS genes, not the other 24 ETS genes not found to play a role in prostate cancer.

"A molecular mechanism that sets these four genes apart from the ones that don't trigger cancer has never been identified until now," Hollenhorst said. "This is significant because it suggests that any compound that disrupts EWS-ETS interaction would specifically inhibit the function of the four oncogenes and not the others, which play important roles in the healthy function of the body."

The team also found the ETS genes implicated in prostate cancer interact with the un-mutated form of the EWS gene. In Ewing's sarcoma, the small blue tumors that characterize the disease do not occur unless mutation occurs.

IU scientists used a combination of laboratory experiments and mouse models to observe the interaction of EWS and ETS proteins in prostate cells. The majority of the experiments involved observing the behavior of ETS oncogenes in prostate cancer cell cultures to reveal interaction with EWS proteins.

In experiments at the IU School of Medicine, they also introduced the ERG gene into normal human prostate cells in mice, which triggered the formation of tumors. The scientists then introduced an artificial mutation in the ERG gene to disrupt interaction with the proteins produced by the EWS gene. In these mice, the tumors failed to form.

"Together, the results indicated that the interaction between ERG and EWS is important for tumor formation," Hollenhorst said. "We chose to focus our greatest efforts on the ERG protein since it is responsible for over 50 percent of all prostate cancers, and therefore the potential to benefit the greatest number of people."

Based upon the strength of the work reported in the study, Hollenhorst and colleagues at IU Bloomington and the IU School of Medicine have received a grant from the IU Simon Cancer Center to search for molecules that could potentially disrupt ETS-EWS interaction. Their work will be conducted in collaboration with a facility at Purdue University that specializes in screening for these molecules.

Additional authors on the paper are Nagarathinam Selvaraj, postdoctoral researcher, and Justin A. Budka, graduate student, in the Medical Sciences Program at IU Bloomington; and Joshua P. Plotnik and Taylor R. Nicholas, graduate students in the IU Bloomington College of Arts and Sciences' Department of Biology. Jerde is also a member of the IU Simon Cancer Center.

This research was supported in part by the American Cancer Society.

IUSCC sponsors Relay for Life

The IU Simon Cancer Center proudly sponsored the Relay for Life of IUPUI on Oct. 21. More than 35 teams raised more than $18,000 for the American Cancer Society event. During the campus event, the American Cancer Society recognized grant recipients **Lei Li**, PhD, and **Catherine Sears**, MD.

VP Biden delivers Cancer Moonshot Report

On Oct. 18, the White House released the report of the Cancer Moonshot Task Force. The report consists of a detailed set of findings and recommendations to accelerate our understanding of cancer and its prevention, early detection, and treatment. Read report.

Victoria Champion, PhD, RN, receives the President's Medal for Excellence for her commitment to research in behavioral oncology, which has improved the quality of life for countless cancer survivors. The award was presented by IU President Michael McRobbie during the celebration of the new IU School of Nursing Champion Center for Cancer Control Research on Oct. 27. With 13 faculty members pursuing groundbreaking research in oncology, IU School of Nursing has the largest number of oncology research-intensive faculty in the country, making the creation of this new center a strategic component for building the school's research portfolio well into the 21st century. ***Liz Kaye photo***

Cancer center members in the news

- **Douglas Rex**, MD, presented findings from a study at the American College of Gastroenterology annual scientific meeting in Las Vegas in mid-October. His study found that remimazolam was a safe and effective agent for conscious sedation during outpatient colonoscopy. Also, Dr. Rex presented findings from a clinical trial that tested bowel-cleansing food bars in such flavors as lemon cooler and white chocolate and drinks in mixed berry and orange that may someday be used as part of colonoscopy preparation. CNN turned to Dr. Rex for his expertise.
- **Hal Broxmeyer**, PhD, and colleagues wrote "Glucose-independent Acetate Metabolism Promotes Melanoma Cell Survival and Tumor Growth," which was published in the Journal of Biological Chemistry.
- **Mark Kelley**, PhD, is a panelist on "The Next Giant Leap: Making the Cancer Moonshot a Reality" on Nov. 16 in Boston. Dr. Kelley joins panelists from Harvard, the NCI, Northwestern, Cleveland Clinic, and others who will discuss the challenges ahead and ways to foster support and collaboration. Also, Dr. Kelley is among a dozen "critical" players in the development of the state's life sciences initiative, according to a white paper on the $62 billion industry. Read " Powering Indiana's Life Sciences Community: Profiles of Money, Molecules and Management."
- **Jian-Ting Zhang**, PhD, and colleagues wrote "FASN Regulates Cellular Response to Genotoxic Treatments by Increasing PARP-1 Expression and DNA Repair Activity Via NF-kB and SP1." The findings of this study have revealed a potential molecular pathway for

how fatty acid synthase (FASN) overexpression causes drug and radiation resistance and contributes to poor clinical prognosis of cancer diseases. The study was published in the "Proceedings of the National Academy of Sciences in the United States of America."

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