IU scientists to lead $12 million national initiative for new treatments for inherited cancers

Aug. 31, 2015

INDIANAPOLIS -- The Indiana University School of Medicine has been selected to lead a five-year, $12 million national research project to develop new treatments for diseases of a genetic mutation that leads to disfiguring and life-threatening tumors and other developmental disorders, mainly in children.

The grant, one of the highly competitive and coveted projects funded by the National Cancer Institute's Specialized Programs of Research Excellence initiative, is the first such SPORE grant to focus on pediatric cancers.

"This grant enables us to engage in research from the basic science lab to clinical trials to discover new treatments for a broad range of devastating cancers and related disorders, drawing on a team of some of the finest researchers in this field across the country," said D. Wade Clapp, M.D., chairman of the Department of Pediatrics at the IU School of Medicine and a member of both the IU Melvin and Bren Simon Cancer Center and the Herman B Wells Center for Pediatric Research.

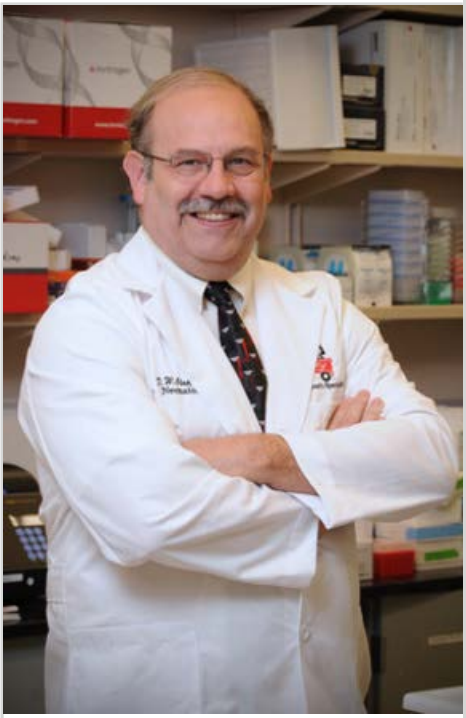
Dr. Clapp, who will serve as the corresponding principal investigator for the new project, said the funding will enable researchers to determine the complete genetic sequence of the research participants, providing unique opportunities to design precise treatments for patients, to adopt new research techniques and better understand how tumors develop resistance to drugs.

The disease at the heart of the project is neurofibromatosis type 1, which affects 1 in 3000 children and is the most common inherited syndrome causing a predisposition to cancer. Neurofibromatosis is more prevalent than cystic fibrosis, Duchenne muscular dystrophy and Huntington's disease combined, according to the Children's Tumor Foundation.

The mutation in the NF1 gene leads to a variety of symptoms, from mild to severe. Patients can develop café au lait spots and disfiguring tumors on or just under the skin. Internally, tumors can develop along nerve tissue and cause problems if they begin to press against vital organs or the windpipe. Some patients suffer from chronic pain.

In addition, recent research has found NF1 mutations in a variety of other types of cancers. NF1 mutations also affect an important molecular signaling protein called Ras, which, Dr. Clapp noted, is involved with more than a third of all cancers. In the process of developing better treatments for those with NF1 disorders, the research should also point the way toward new therapies for many other cancers, he said.

Dr. Clapp and colleagues at IU have been leaders in neurofibromatosis research, having first reported in 2008 that the drug Gleevec appeared to be the first effective treatment for neurofibromatosis type 1 tumors. Subsequent research substantiated that finding, but also determined that in some patients genetic factors and tumor resistance hampered Gleevec's effectiveness.



D. Wade Clapp, M.D.

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The National Cancer Institute's Specialized Programs of Research Excellence, generally known as SPORE, are highly competitive grants awarded to projects that assemble research activities ranging from a better understanding of basic human biology all the way to clinical trials that lead to new treatments.

In addition to researchers from IU, the neurofibromatosis SPORE group -- with the acronym DHART SPORE -- will include collaborators from the University of California at San Francisco, the National Cancer Institute, the University of Texas Southwestern, Johns Hopkins University, the University of Alabama-Birmingham and the University of North Carolina.

New risk score for colorectal cancer could guide screening test selection

Sept. 4, 2015

INDIANAPOLIS – Researchers at the Regenstrief Institute and the Indiana University School of Medicine have developed a new risk assessment scoring system that could help physicians judge which patients can forgo invasive colonoscopy testing for cancer screening and which should receive the test.

According to published literature and guideline organizations, 85 percent of the population is classified as “average risk” for colorectal cancer, which accounts for 55,000 deaths per year. Yet colorectal cancer screening tests, while cost-effective, are underused and can be used inefficiently because of the current inability to more precisely tailor screening methods according to risk.

"The main question was,'can the risk factors most frequently associated with the risks for colorectal cancer and advanced, precancerous polyps be used in combination to stratify risk for advanced neoplasia in average-risk persons'?", said study lead author Thomas F. Imperiale, M.D., Regenstrief Institute investigator and professor of medicine at the IU School of Medicine.

The results of the study, "Derivation and Validation of a Scoring System to Stratify Risk for Advance Colorectal Neoplasia in Asymptomatic Adults," was published in the Sept. 1, 2015, issue of Annals of Internal Medicine.

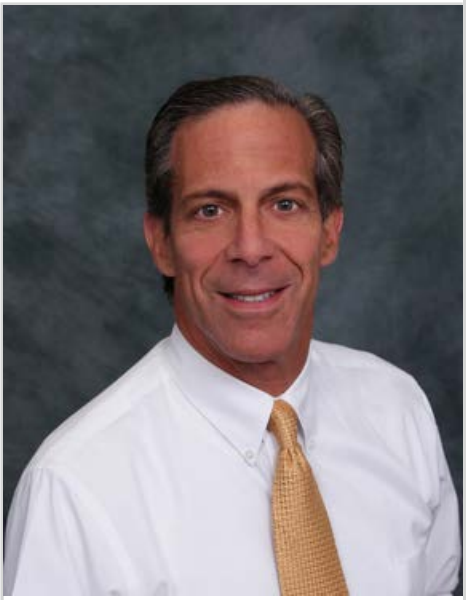
The study was conducted with average-risk patients (i.e., no high-risk familial cancer syndromes) aged 50 to 80 years who were undergoing initial screening colonoscopy in several Midwestern endoscopy units and practices. Points for the risk assessment score were assigned based on risk factors for both colorectal cancer and advanced precancerous polyps: age, gender, family history of colorectal cancer, smoking history, and waist circumference. Participants were then separated by score into very low, low, intermediate and high risk categories. The researchers found that there indeed were fewer advanced neoplasms in the low and very low risk groups, suggesting that less invasive tests such as sigmoidoscopies or occult blood tests might be appropriate for those patients. However, those in the higher risk groups might need a colonoscopy.

"Our hope is that knowing the risk of advanced neoplasia may make colorectal screening more patient-centered with respect to choosing a screening test," Dr. Imperiale said.

The biggest challenges, he said, "Is getting to the point where providers are comfortable using the scoring system, reassuring patients at very low and low risk that non-colonoscopy based strategies may be as effective, and convincing high risk patients who do not want colonoscopy, to have one."

Additional authors of this study were Patrick O. Monahan, Ph.D., and Timothy E. Stump, of the Regenstrief Institute, Elizabeth A. Glowinski, R.N., of the University of Indianapolis, and David F. Ransohoff, M.D., of the University of North Carolina School of Medicine.

An editorial accompanied this study in the journal. This work was supported by National Cancer Institute grant R01CA104459, the Walther Cancer Institute, the Indiana University Simon Cancer Center, and a Project Development Team within the Indiana CTSI NIH/NCRR grant UL1TR001108.



Thomas F. Imperiale, M.D.

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September 2015

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The Komen Tissue Bank at the IU Simon Cancer Center and IU researchers **Theresa Guise**, MD, and **Chunyan He**, ScD, are recipients of new Komen research grants.
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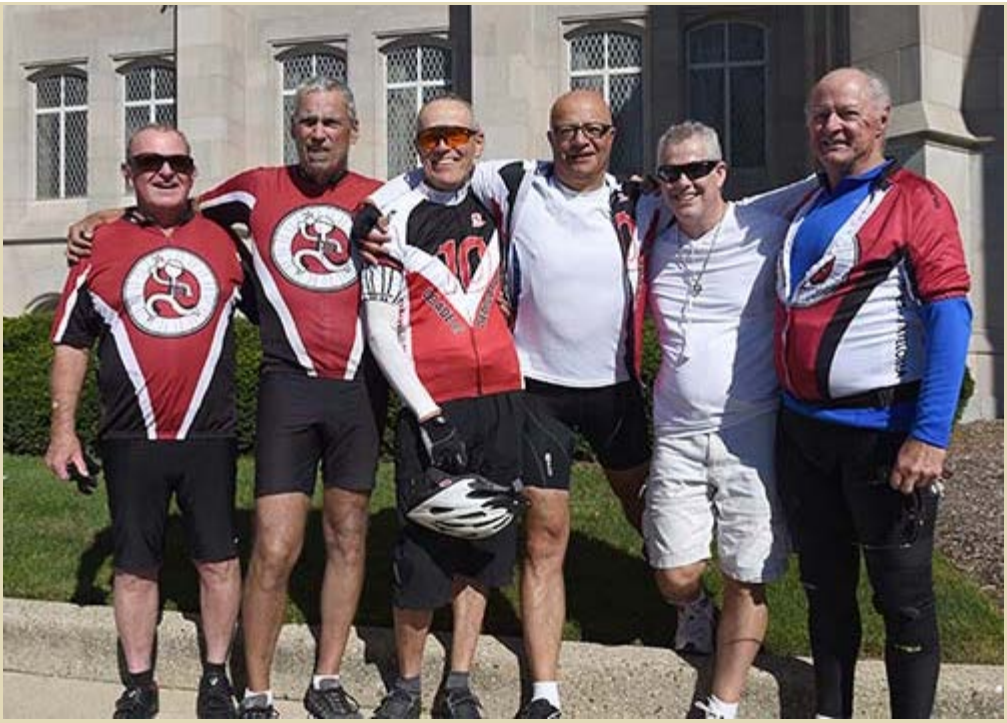
IUSM researchers bring in record amount of grants in fiscal year 2015

Bucking a national trend of tight resources for biomedical research, Indiana University School of Medicine scientists brought a record $302.3 million in research grants and awards to the school in fiscal year 2015, a 17 percent increase over 2014.
full story>

Save the date: IUSCC hosts Walther retreat Oct. 17

The IU Simon Cancer Center hosts the Walther retreat from 8 a.m. to 1:30 p.m. Saturday Oct. 17. Breakfast and registration begin at 7:30 a.m. The meeting's focus is to discuss translational bioinformatics/lipid metabolism and obesity in cancer as well as building collaborative research efforts between IU, Purdue, and Notre Dame in these areas. All cancer center members are encouraged to attend. Please RSVP to Kristen Scott at kscott4@iupui.edu. The retreat will be at the Ritz Charles, 12156 N. Meridian St., Carmel.



Rafat Abonour, MD, (fourth from left) and his fellow cyclists catch their breath after this year's Miles for Myeloma cycling event. Beginning under the Gateway Arch in St. Louis on Sept. 10, the 11th annual ride concluded in Indy on Sept. 12 with a finish-line celebration. To date, nearly $3 million has been raised for multiple myeloma research at IU.

Patrick Loehrer, MD, (second from left) and colleagues gather for their first face-to-face TCGA Thymoma Data Analysis meeting. The IU Simon Cancer Center hosted the meeting in downtown Indianapolis Sept. 17 and 18. The meeting brought together researchers from IU, the National Cancer Institute, the Genome Institute, UNC Lineberger Cancer Center, University Medical Centre Mannheim, Hospital de Cancer de Barretos, and the Broad Institute of Harvard among others.

Cancer center members in the news

- **Richard Foster**, MD, **Lawrence Einhorn**, MD, **Clint Carey**, MD, MPH, and colleagues wrote "Outcomes of postchemotherapy retroperitoneal lymph node dissection following high-dose chemotherapy with stem cell transplantation," which was published in Cancer.

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