Indiana University Melvin and Bren Simon Cancer Center Scientific Report \bigcirc

Executive Committee

MISSION

The mission of the Indiana University Melvin and Bren Simon Cancer Center is to decrease the mortality and suffering from cancer by conducting outstanding translational research, providing excellence in education, and by delivering high quality patient-centered care.

VISION

To eradicate cancer as a health care burden to our global society.

GOALS

Foster excellence in transdisciplinary research

- Translate research into the clinic to provide the highest quality multidisciplinary patient care Provide nationally recognized
- interdepartmental graduate and post-graduate education and training programs
- Expand the statewide comprehensive cancer control program





Patrick Loehrer Sr., MD Director

Harikrishna Nakshatri.

Associate Director

BVSc, PhD

of Education



Mark Kelley, PhD Associate Director of Basic Science Research



Victoria Champion, PhD. RN Associate Director of Population Science Research



Sherif Farag, MBBS, PhD Associate Director of Clinical Research



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Michael Darling, MHA Associate Director of Administration

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From the director

What a remarkable year 2014 turned out to be for all of us at the IU Simon Cancer Center. The year began with our intensive all-day site visit by 24 reviewers from the National Cancer Institute and NCI-designated cancer centers. They came to campus in February to evaluate our five research programs. It was their job to make sure those programs met the NCI's rigorous criteria.

Our co-leaders ably presented overviews of their respective programs and fielded questions from the reviewers. Our preparation, which started more than a year before the site visit, paid off, with our co-leaders doing an outstanding job. At the end of the day, relief set in; but anxiousness followed because many months would pass before we would know how well we did.

By fall, we learned that our NCI designation was renewed and our research programs were strongly reviewed. We were also awarded a five-year, \$7.8 million support grant—an increase of 20 percent from the previous award in 2008. That increase is especially significant in these tough times for research funding. Overall, our total funding from the NCI for all of our grants was up 20 percent, too.

What does the NCI designation mean? It means the cancer center's five research programs meet the NCI's rigorous criteria for world-class, state-of-the-art programs in multidisciplinary cancer research. The NCI designation places the IU Simon Cancer Center in an elite group of only 68 cancer centers across the country that focus on the rapid translation of research discoveries to directly benefit people with cancer.

What does the designation mean for Hoosiers and others? It means that the scientific discoveries made by researchers at the IU Simon Cancer Center benefit patients close to home. It means that the physicians treating patients in the clinics interact with the scientists investigating cancer in the laboratories. In all, more than 200 physicians and researchers are collaborating to develop breakthrough cancer treatments. That teamwork leads to advances against the disease.

That team science approach focused directly on patients doesn't happen anywhere else in Indiana. The IU Simon Cancer Center is the only NCI-designated cancer center in Indiana that provides patient care. That means that people from all 92 Indiana counties have sought out our expertise. Patients from different parts of the nation and from around the world have traveled here for care.

For four decades, men from around the world have sought the expertise of Lawrence Einhorn, MD, the physician scientist who established the cure for testicular cancer 40 years ago. We marked that milestone in the fall of 2014. You can read much more about that on pages 12-13.

And 2014 marked the 10th consecutive year in which Rafat Abonour, MD, once again took to his bike, cycling over three days to raise both awareness and funds for multiple myeloma. Turn to pages 14-15 to read more about that and other news highlights.

Throughout the year, our researchers continued to better understand the molecular changes that cause cancer, and they worked on developing targeted therapies to prevent and treat cancer. In the next few pages, we share five stories from our research programs, giving you a sampling of just some of the work IU Simon Cancer Center investigators accomplished in 2014. As we look to another year, we'll continue to be ever diligent, dedicated and profoundly aware that much remains to be done to further make an impact against this devastating disease.

Thank you for taking a moment to learn more about the IU Simon Cancer Center.

Patrick J. Loehrer, Sr., MD H.H. Gregg Professor of Oncology Director, *IU Simon Cancer Center* Associate Dean for Cancer Research *Indiana University School of Medicine*

Photo: Tim Yates, Office of Visual Media/IU School of Medicine

SCIENTIFIC DISCOVERIES MADE BY IU SIMON CANCER CENTER RESEARCHERS BENEFIT PATIENTS.

Breast Cancer research program

Kathy Miller, MD Professor of Medicine Ballve Lantero Scholar in Oncology IU School of Medicine

Harikrishna Nakshatri, BVSc, PhD Marian J. Morrison Professor in Breast Cancer Research Professor of Surgery Professor of Biochemistry and Molecular Biology IU School of Medicine

MEMBERS

Sunil Badve, MBBS, MD Monet Bowling, MD Crislyn D'Souza-Schorey, PhD Siyuan Zhang, MD, PhD Jill Fehrenbacher, PhD David Flockhart, MD, PhD David Gilley, PhD Linda Han, MD Chunyan He, ScD Brittney-Shea Herbert, PhD Mircea Ivan, MD, PhD Philip Johnson, PhD Lang Li, PhD Laurie Littlepage, PhD Yunlong Liu, PhD Samy Meroueh, PhD Lida Mina, MD Kenneth Nephew, PhD Jenifer Prosperi, PhD Milan Radovich, PhD Zachary Schafer, PhD Bryan Schneider, MD Todd Skaar, PhD Keith Stantz, PhD Anna Maria Storniolo, MD Hiromi Tanaka, PhD Claire Walczak, PhD

Clark Wells, PhD Hiroki Yokota, PhD

PROGRAM GOALS

The Breast Cancer research program is a highly interactive program in which members combine basic, clinical and translational research skills to understand the biology underlying breast cancer and apply that understanding to improve prevention, diagnosis and treatment. The program's vision is advanced by focused work in three themes:

Theme 1: Cell signaling pathway alterations

AIM 1: Deregulated cell-cell communication AIM 2: Cancer stem cell phenotype

AIM 3: Hormonal signaling and resistance

Theme 2: Genomic/epigenomic deregulation

AIM 1: Gene regulation AIM 2: Telomerase dysfunction and inhibition AIM 3: Characterization of the normal breast AIM 4: MicroRNA (miRNA) networks

Theme 3: Therapeutic individualization

AIM 1: Biomarkers of recurrence and metastasis AIM 2: Biomarkers of response and toxicity AIM 3: Pathways driven clinical trials AIM 4: Impact of treatment and disease on function



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Improving breast cancer therapy one step at a time

A hallmark of solid tumors is chromosome instability resulting from genetic material being haphazardly distributed between two daughter cells during mitosis, that important part of the cell cycle when a mother cell divides into two daughter cells identical to each other and their parent. In studying the workhorse for mitosis, a complex subcellular assembly of microtubules and more than 1,000 other proteins called the mitotic spindle, IU cell biologist and IU Simon Cancer Center researcher **Claire Walczak**, **PhD**, is looking for ways to keep those two daughter cells faithful to their mother.

Her work has been focusing on the activity of specialized, self-assembling microtubules in the mitotic spindle and how overexpression or inhibition of certain enzymes that localize to these microtubules cause an unequal distribution of genetic information, or aneuploidy, which is a tell-tale sign of a solid tumor. During mitosis, microtubules undergo rapid changes in both their assembly and disassembly properties, and these dynamics are coupled to the movement of the chromosomes on the spindle. Blocking the dynamics of these microtubules impairs movement of the chromosomes and blocks mitotic progression.

Paclitaxel (Taxol), for example, is a breast cancer treatment drug known as a mitotic inhibitor, which stabilizes microtubules and interferes with their breakdown; yet many tumors become resistant to the drug.

Dr. Walczak hopes to use basic biology—understanding the dynamics of mitosis and microtubule assembly, an integral process of the cell cycle—as a translational tool for uncovering new and better mitotic inhibitors that are clinically relevant and beneficial to breast cancer patients. One enzyme Dr. Walczak and team are looking at is Aurora B kinase, which helps control proper attachment of the chromosomes to the mitotic spindle. Known to be oncogenic—"cancer-causing"—Aurora B kinase and other Aurora enzymes have become prime targets for drug development as they are central to mitosis.

Specifically, Dr. Walczak's group is interested in Aurora B's relationship to the regulator protein MCAK, which has a role in depolymerizing microtubules and in attachment of chromosomes to the spindle, which are pivotal parts of mitosis.

"The accurate regulation of MCAK is important for ensuring faithful segregation of chromosomes in mitosis and for safeguarding chromosome stability," Dr. Walczak said. "We also know that Aurora B inhibits MCAK activity by reducing its affinity for microtubules."

Understanding how conformational changes occur can provide a mechanism for regulating MCAK activity, particularly depolymerization, or unraveling, she added. The lab's latest work has shown that MCAK depolymerization activity is inhibited by Aurora B-dependent phosphorylation—the process by which a phosphate is added to a protein, which in turn can alter the function and activity of protein enzymes by turning them on and off.

"We want to understand how Aurora B inhibits MCAK at the molecular level because if we can understand that, we might be able to make drugs like Taxol better at killing cancer cells," she said. "We are truly hoping that we can be the ones to develop some MCAK inhibitors that are beneficial to patients."

By Steve Chaplin

WE MIGHT BE ABLE TO MAKE DRUGS LIKE TAXOL BETTER AT KILLING CANCER CELLS.

Cancer Prevention and Control research program



David Haggstrom, MD, MAS

Associate Professor of Medicine, IU School of Medicine Research Scientist, *Regenstrief Institute* Founding Director, IUPUI Center for Cancer Population Analytics and Patient-Centered Informatics

Jiali Han, PhD

Rachel Cecile Efroymson Professor in Cancer Research *IU School of Medicine* Professor and Chair of Epidemiology *IU School of Public Health*

Victoria Champion, PhD, RN Distinguished Professor Mary Margaret Walther Professor o

Mary Margaret Walther Professor of Nursing Edward W. and Sarah Stam Cullipher Chair IU School of Nursing

In late 2014, Dr. Haggstrom succeeded Dr. Champion as co-leader.

MEMBERS

Asok Antony, MD Darron Brown, MD Debra Burns, PhD Janet Carpenter, PhD, RN Betsy Fife, PhD J. Fortenberry, MD Joan Haase, PhD, RN Susan Hickman, PhD Karen Hudmon, DrPH Thomas Imperiale, MD Pascal Jean-Pierre, PhD Shelley Johns, PsyD Kurt Kroenke, MD Chiung-iu Liu. PhD Juhua Luo, PhD Brenna McDonald, PsyD Beth Meyerson, PhD Patrick Monahan, PhD Catherine Mosher, PhD Hongmei Nan, MD, PhD

Julie Otte, PhD, RN Kevin Rand, PhD Susan Rawl, PhD Jamie Renbarger, MD Douglas Rex, MD Sheri Robb, PhD Andrew Saykin, PsyD Peter Schwartz, MD, PhD Marcia Shew, MD Jodi Skiles, MD, MS Yiqing Song, MD, ScD Nathan Stupiansky, PhD Michael Vasko, PhD Terry Vik. MD Diane Von Ah, PhD, RN Bree Weaver, MD Fletcher White, MS, PhD Jianjun Zhang, MD, PhD Gregory Zimet, PhD

PROGRAM GOALS

The members of the Cancer Prevention and Control research program are engaged in innovative and collaborative research with the potential to decrease cancer morbidity and mortality. They are also involved in prevention and early detection of debilitating symptoms caused by cancer treatment while tailoring cancer treatment to individuals. The program's themes focus on three crucial challenges across the cancer continuum: preventing the occurrence of cancer; increasing effectiveness and adherence to cancer screening; and identifying mechanisms of treatment-related neurotoxicities (neuropathy and cognitive dysfunction) while improving symptom burden from cancer therapies.

Theme 1: Prevention (HPV and Lung Cancer)

AIM 1: Understand the transmission of HPV (e.g., modes of HPV transmission and vaccines) and reduce the incidence of HPV-related cancers through improving rates of vaccination and safe sexual practices.

AIM 2: Decrease the prevalence of tobacco use through smoking cessation, prevention of tobacco uptake, and reducing relapse through translation of evidence based tobacco reduction interventions to the community.

Theme 2: Early Detection

AIM 1: Develop and implement risk-based and cost-effective methods of delivering CRC screening.

AIM 2: Test translation and cost-effectiveness of tailored interventions to increase cervical, breast and CRC screening.

Theme 3: Survivorship

AIM 1: Evaluate mechanisms, treatment and prevention of chemotherapy-induced neurotoxicity (chemotherapy-induced peripheral neuropathy [CIPN] and cognitive dysfunction).

AIM 2: Detect and test interventions to alleviate symptom burden in cancer patients and their families.

Bold denotes members accepted in 2014

IU Simon Cancer Center researchers tackling effects of neurotoxicity on cancer patients

Basic and clinical scientists led by members of the cancer center's Cancer Prevention and Control (CPC) and Experimental and Developmental Therapeutics (EDT) research programs have come together to confront the debilitating and sometimes lifelong neurotoxic effects of chemotherapy on cancer survivors.

As more people survive or live longer with cancer, the consequences of the neurotoxicity that's part and parcel of chemotherapy have come under greater scrutiny. Side effects of cancer therapy can include loss of cognitive function, sometimes known as "chemo brain" or "chemo fog," and/or chemotherapy-induced peripheral neuropathy (CIPN)—a range of disorders that affect the nervous system. Patients affected by CIPN often report sensory difficulties such as persistent tingling in their extremities, loss of reflexes, pain and enhanced sensitivity to non-painful stimuli such as touch or cold.

"It's a major problem," said CPC's **Michael Vasko**, **PhD**, who formed a Neurotoxicity Working Group along with EDT's **Jamie Renbarger**, **MD**, and **Mark Kelley**, **PhD**. "Roughly 40 percent of patients who are on various chemotherapies can develop these neuropathies." The roots of the working group can be traced to a collaboration between Drs. Vasko and Kelley that focused on the study of chemotherapy-induced changes in neurons and DNA repair. The group is taking an innovative approach to solving the problems associated with neurotoxicity by delving into the basic science behind them, as opposed to taking a strictly clinical approach.

"Until you understand the basic science mechanism, there's no way you can come up with drugs to treat it," Dr. Kelley said. "In our work, we focus on the role of DNA repair pathways that appear to be involved with peripheral neuropathy, whereas other investigators focus on different mechanisms." Several members of the working group, including Dr. Vasko and **Jill Fehrenbacher**, **PhD**, specialize in sensory neurobiology. "We realized there were multiple laboratories around campus doing similar things relating to chemo pain and sensory function," Dr. Vasko said. "We decided we needed to get these various researchers together."

Collectively, the members of the working group have expertise in a wide range of areas, including pediatrics, genetics, imaging science, neurology, biochemistry and molecular biology. "We are probably one of the few groups in the country with such a cadre of folks with this kind of expertise," Dr. Kelley said. However, members continue to work on individual projects that will contribute to the overall body of research that will help achieve the group's broader goals. For example, Drs. Kelley and Vasko recently published in PLOS ONE an article that examined the role of APE1, a DNA repair protein that appears to play a role in repairing oxidative DNA damage brought on by anticancer drugs cisplatin, oxaliplatin and carboplatin. The study was funded by a five-year grant from the National Cancer Institute to study DNA repair and cancer treatment in sensory neurons.

Dr. Kelley calls the working group "a poster child for team science. A lot of good discoveries are made when you break out of your siloes. We've been able to recruit a number of scientifically diverse individuals and bring their expertise to bear; that's why we're so excited about it."

The group's work overlaps the cancer center's Cancer Prevention and Control, Experimental and Developmental Therapeutics, and Breast Cancer research programs and is geared toward examining chemotherapy-induced peripheral neuropathy in both adults and children. Finding help for the latter is of utmost importance, Dr. Kelley said, and links the group's work with behavioral and population science in terms of long-term symptom management and translational medicine.

"People can live a long time with chemo-induced peripheral neuropathy," Dr. Kelley said. "Just as we have gotten more successful with pediatric oncology, where there is an 85 percent survival rate in some pediatric cancers, the treatments are still very intense. That's why what we are doing is so important. We need to turn our attention to quality of life going forward."

By Brian Hartz

Drs. Kelley (left) and Vasko. Photo: Tim Yates, Office of Visual Media/IU School of Medicine

WE ARE PROBABLY ONE OF THE FEW GROUPS IN THE COUNTRY WITH SUCH A CADRE OF FOLKS WITH THIS KIND OF EXPERTISE.

Experimental and Developmental Therapeutics research program

ROGRAM LEADERS

Daniela Matei, MD Professor of Medicine Professor of Obstetrics and Gynecology *IU School of Medicine*

Zhong-Yin Zhang, PhD Chair, Department of Biochemistry and Molecular Biology Robert A. Harris Professor IU School of Medicine

MEMBERS

Lata Balakrishnan, PhD Timothy Corson, PhD Joseph Dynlacht, PhD Lawrence Einhorn, MD Leslie Fecher, MD Michael Ferguson, MD Thomas Gardner, MD Millie Georgiadis, PhD Nasser Hanna, MD Thomas Hurley, PhD Shadia Jalal, MD Hiremagalur Jayaram, PhD Steven Johnson, PhD Chinghai Kao, PhD Mark Kelley, PhD Michael Koch, MD Janaiah Kota, PhD Suk-Hee Lee, PhD Hyun-Suk Lim, PhD Patrick Loehrer, MD Lindsev Mavo, PhD Marc Mendonca, PhD Samy Meroueh, PhD Amber Mosley, PhD Grzegorz Nalepa, MD, PhD Bert O'Neil. MD Jamie Renbarger, MD

Safi Shahda, MD Chie-Schin Shih, MD John Turchi, PhD Jingwu Xie, PhD Xiao-Ming Yin, MD, PhD Jian-Ting Zhang, PhD Adam Zlotnick, PhD

PROGRAM GOALS

The multidisciplinary Experimental and Developmental Therapeutics program promotes and facilitates development of new cancer therapies from bench to bedside. Through basic science and clinical research, the program's physicians and scientists from 12 departments within Indiana University School of Medicine and Indiana University - Purdue University Indianapolis endeavor to discover and develop novel anti-cancer therapeutics.

Theme 1: Target identification and validation

AIM 1: To target DNA repair pathways.

AIM 2: To target protein-protein interaction.

AIM 3: To target signaling molecules and enzymess.

Theme 2: Discovery and development of novel anti-cancer agents

AIM 1: Develop protein tyrosine phosphatases based novel anti-cancer agents.

AIM 2: Design novel strategies to prevent chemotherapy induced neuronal damage.

AIM 3: Pursue epigenetic interventions in cancer.

Theme 3: Mechanisms of drug action and clinical trials

AIM 1: Biomarkers and molecular pharmacology.

AIM 2: Clinical trials (Phase I, II, III) for solid tumors in adults and children.

Bold denotes members accepted in 2014

P 6/7

IU team collaborates, finds an ovarian cancer target

Each week, Daniella Matei, MD, sees and treats women with ovarian cancer, the deadliest of all gynecologic cancers. Far too many of her patients have advanced disease as there is no current effective means of early detection.

But Dr. Matei, a physician scientist, has been designing and conducting clinical trials for the past 12 years. She hopes that someday ovarian cancer can be found in its very early stages. She stays focused—both in the lab and at the bedside—because her patients motivate her and give her a reason to get up in the mornings, she said.

Over the past several years, she and her Indiana University colleagues have been interested in learning about the ways in which ovarian cancer cells form, dislodge from the primary tumor and form spheres. Those spheres serve as a vehicle for disseminating the cancer cells.

They started looking at the specific genes that are up-regulated when cancer cells grow in spheres. One of the genes that they initially explored was ALDH1A1. Dr. Matei learned that **Thomas Hurley**, **PhD**—who has expertise with that family of enzymes—was also doing work with ALDH1A1. They soon collaborated and determined which genes were turned on or off during tumor growth.

"We found that a gene called ALDH1A1 was up-regulated during tumor formation and that blocking the function of this gene either genetically or by drug-induced inhibition we could block tumor growth," Dr. Hurley explained.

Both said they were pleasantly surprised by this finding. Dr. Hurley used a process known as structure base drug discovery that led to the finding. "We have the ability to look at the 3D structure of these enzymes via a technique called structure base drug discovery," Dr. Hurley said. "We basically use X-rays to find where the atoms are in the protein, which allows us allows us to look at how and where the drug binds. You end up with pictures that show where the drug binds. That leads us to next ask 'What can we do to optimize the drug?"

Their work was published in Oncogene and was supported with funding from the National Institutes of Health (R01-018123) and the U.S. Department of Veterans Affairs.

"The significant finding was that ALDH1A1 is a key determinant of ovarian cancer tumor formation," Dr. Hurley said. "This was the first demonstration that a drug that specifically targets the function of this gene could inhibit tumor growth. There had been a number of correlative studies that associated increased ALDH1A1 with tumor characteristics and poor prognosis, but no studies had been performed that selectively blocked the function of ALDH1A1 by the use of a drug-like compound."

Dr. Hurley pointed out that much work still needs to be done in order to develop a new ALDH1A1 inhibitor into a drug for patients.

Dr. Matei said that prior to the approval in late 2014 of bevacizumab as a treatment for ovarian cancer, no other drug had been approved in the past decade. "Our discovery adds to the potential to one day providing newer treatments for this deadly disease," she said.

By Michael Schug

Drs. Matei (left) and Hurley. Photo: Tim Yates, Office of Visual Media/IU School of Medicine

THIS WAS THE FIRST DEMONSTRATION THAT A DRUG THAT SPECIFICALLY TARGETS THE FUNCTION OF THIS GENE COULD INHIBIT TUMOR GROWTH.

Hematopoiesis, Hematologic Malignancies, and Immunology (HMI) research program

ROGRAM LEADERS

Hal E. Broxmeyer, PhD **Distinguished Professor** Mary Margaret Walther Professor Emeritus Professor of Microbiology/Immunology

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G. David Roodman, MD, PhD Director, Division of Hematology/Oncology Professor of Medicine IU School of Medicine

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Jianyun Liu, PhD Yan Liu PhD Keith March, MD, PhD Christie Orschell, PhD Sophie Paczesny, MD, PhD Louis Pelus, PhD Irina Petrache, MD Michael Robertson, MD Carlos Serenzani, PhD Rebecca Silbermann, MD David Skalnik, PhD Edward Srour, PhD Jie Sun, PhD Attaya Suvannasankha, MD Jeffrey Travers, MD, PhD Mingjiang Xu, M.D, PhD Feng-Chun Yang, MD, PhD Mervin Yoder, MD Baohua Zhou, PhD

PROGRAM GOALS

The goal of the Hematopoiesis, Hematologic Malignancies, and Immunology research program is to advance the treatment of hematologic malignancies and disorders of hematopoiesis. The main efforts are (1) to understand normal hematopoietic cell regulation, abnormalities associated with leukemia, lymphoma and myeloma, (2) to determine how to most efficaciously treat those conditions, and (3) to contribute to improvements in hematopoietic cell transplantation, especially with cord-blood, a clinical area initiated and enhanced by HMI members. The programmatic goal is to develop novel therapeutic approaches for treating patients with malignancies.

Theme 1: Hematopoiesis

AIM 1: Enhance engraftment of HSCs for clinical cord blood, bone marrow and mobilized peripheral blood transplantation.

AIM 2: Enhance mobilization of HSCs/HPCs for collection for clinical use.

AIM 3: Characterize cell and molecular biology of selfrenewal, proliferation, survival, differentiation and migration of HSC/HPC in the context of cytokine and microenvironmental interactions.

Theme 2: Malignant Hematology

AIM 1: Determine changes in cancer and bone cell interactions that enhance tumor growth, bone destruction and angiogenesis, to identify therapeutic targets for treatment of hematologic malignancies.

AIM 2: Identify genes linked by intracellular signaling pathways that decrease tumor suppressor expression and exploit as targets for treating hematologic malignancies.

AIM 3: Determine efficacy of novel approaches for treatment of hematologic malignancies.

Theme 3: Immunology

AIM 1: Enhance anti-tumor immunity to treat hematologic malignancies.

AIM 2: Characterize immune cells and modulate graftversus-host disease and after HCT.



Scientists identify biomarker to predict immune response risk after stem cell transplants

Researchers from Indiana University, the University of Michigan, the Fred Hutchinson Cancer Research Center and the Dana-Farber Cancer Institute have identified and validated a biomarker accessible in blood tests that could be used to predict which stem cell transplant patients are at highest risk for a potentially fatal immune response called graft-versus-host disease.

Although transplant specialists have been able to reduce its impact, graft-versus-host disease remains a leading cause of death among patients who receive a stem cell transplant from another person, known as an allogeneic transplant. Such transplants are used to treat blood and bone marrow cancers such as leukemia and multiple myeloma, often as a last resort. Graft-versus-host disease occurs when immune cells from the transplant see the patient's body as foreign and attack it.

Approximately 20,000 allogeneic stem cell transplants were performed worldwide in 2012. Thirty to 40 percent of stem cell transplant recipients whose donor is related will experience graft-versus-host disease. The percentage could rise to 60 to 80 percent if the patient and donor are not related.

The researchers found that patients with a high level of a protein named ST2 were more than twice as likely to have graft-versus-host disease that resisted standard treatment with steroids; and nearly four times as likely to die within six months of the transplant. Their findings were reported in the New England Journal of Medicine.

"What we found particularly significant was that this marker was a better predictor than the clinical severity of the disease when it was diagnosed," said Sophie Paczesny, MD, PhD, senior author of the study.

Thus, patients with low ST2 levels were more likely to respond to treatment regardless of how serious their graft-versus-host disease was graded, while patients with high ST2 levels were less likely to respond to treatment, whether their disease was graded less serious or more serious.

"This blood test, which is currently available to clinicians, will make informed treatment possible as the clinicians will now be able to adjust therapy to the degree of risk rather than treating every patient the same way," Dr. Paczesny said.

In subsequent research, Paczesny's team has shown that this biomarker is drug targetable and blocking its action alleviates graft-versus-host disease in a relevant experimental model. The drug, which is currently available for other diseases, could be used for graft-versus-host disease in the near future.

While the disease most commonly appears about 30 days after the transplant, higher ST2 levels in blood samples taken as early as 14 days after transplant—far before the clinical signs of graft-versus-host disease are apparent—were associated with an increased risk of death from the toxicity of the transplant.

Therefore, the authors noted, early identification of patients who likely won't respond to standard treatments is important and would allow physicians to consider additional therapies and early intervention. On the other hand, patients with low risk will not need to have additional medicine further suppressing their immune system. But, they cautioned, additional large prospective studies are needed to better define the levels of risk predicted by the ST2 marker.

The research was funded by grants (RC1HL101102, R01CA168814, P01-CA039542 and T32-HL007622) from the National Institutes of Health.

By Eric Schoch

Dr. Paczesny. Photo: Tim Yates, Office of Visual Media/IU School of Medicine

GRAFT-VERSUS-HOST DISEASE OCCURS WHEN IMMUNE CELLS FROM THE TRANSPLANT SEE THE PATIENT'S BODY AS FOREIGN AND ATTACK IT.

Tumor Microenvironment and Metastases research program



Theresa Guise, MD Jerry and Peggy Throgmartin Professor of Oncology Professor of Medicine IU School of Medicine

Murray Korc, MD Myles Brand Professor of Cancer Research Professor of Medicine Professor of Biochemistry and Molecular Biology *IU School of Medicine* Director *Center for Pancreatic Cancer Research*

MEMBERS

Elliot Androphy, MD Andrea Bonetto, PhD D. Wade Clapp, MD Karen Cowden Dahl, PhD Hong Du, PhD Melissa Fishel, PhD James Fletcher, MD John Foley, PhD Reginald Hill, PhD Peter Hollenhorst, PhD Heather Hundley, PhD David Ingram, MD Travis Jerde, PhD Melissa Kacena, PhD Chien-Chi Lin, PhD Anirban Mitra, PhD Khalid Mohammad, MD, PhD Samisubbu Naidu, PhD Kenneth Nephew, PhD Heather O'Hagan, PhD Beth Pflug, PhD Karen Pollok, PhD Lawrence Quilliam, PhD Kent Robertson, MD, PhD Ravi Sahu, PhD Dan Spandau, PhD M. Sharon Stack, PhD

David Waning, PhD Ronald Wek, PhD Kenneth White, PhD Jingwu Xie, PhD Yan Xu, PhD Cong Yan, PhD Feng-Chun Yang, MD, PhD Toshiyuki Yoneda, DDS, PhD Teresa Zimmers, PhD

PROGRAM GOALS

The overall goals of the Tumor Microenvironment and Metastasis research program are to: 1) advance a basic understanding of the role of cancer cell stromal interactions in cancer initiation, progression and metastasis; 2) evaluate the functions of the metastatic niche; and 3) translate discoveries of the pathobiology of solid tumors, tumor microenvironment and metastatic niche into new cancer targets and novel therapies that prevent metastases.

Theme 1: Cancer cell-stroma interactions

AIM 1: Determine the role of the stroma in neuroplexiform tumors associated with neurofibromatosis.

AIM 2: Determine how cell-specific transforming growth factor-beta TGF- β signaling affects solid tumor growth and metastasis.

AIM 3: Determine the role of cancer cell-stroma interactions in HPV (human papillomavirus) carcinogenesis.

AIM 4: Characterize tumor-stroma interactions and the role of stromal inflammation, hypoxia and microRNAs in solid tumor development and progression.

AIM 5: Determine the mechanisms of tumor growth (primary and metastatic) in the brain.

Theme 2: The metastatic niche

AIM 1: Determine the role of the bone microenvironment in tumor growth.

AIM 2: Determine the mechanisms of pancreatic ductal adenocarcinoma (PDAC) metastasis in relation to p53 and Hedgehog signaling.

AIM 3: Determine mechanisms of ovarian cancer metastasis.

Investigators explore ways to block cancer-related muscle wasting

Although new to the IU Simon Cancer Center and the IU School of Medicine, **Teresa Zimmers**, **PhD**, has been studying the muscle-wasting disease cachexia for about 15 years. "I was doing my graduate work when someone else in the lab discovered a molecule, myostatin, which has a remarkable property: When you inhibit it, muscles grow," Dr. Zimmers said. "So, it blocks muscle growth. My role was to show what happens when there's too much myostatin. When we did that, we saw that the mice appeared to waste away, much like what happens in patients with cancer or AIDS."

Since then, Dr. Zimmers has discovered several other new molecular pathways responsible for weight loss and muscle and fat wasting in cancer and other diseases.

Until recently, Dr. Zimmers said, cachexia has been given short shrift by medical researchers despite some recent high-profile examples of its debilitating and appearance-altering effects. Think back to how gaunt and frail Steve Jobs and Patrick Swayze appeared before they died.

"There was a bias for a long time among cancer researchers that cachexia is a feature of death, not necessarily a cause of death," Dr. Zimmers said. "To get support for our efforts, we have to prove to oncologists that it is not inevitable and that addressing muscle loss will improve patient outcomes."

She said educating the medical community about cachexia has been difficult because the disease had struggled for attention. Dr. Zimmers said it's underfunded and underrepresented in medical-science literature, with only about 3,500 papers published, compared to more than 100,000 for prostate cancer, for example. However, rising commitment from the National Cancer Institute is increasing research nationally.

Cachexia is not found exclusively in cancer patients; it can also affect people suffering from AIDS, multiple sclerosis, tuberculosis, congestive heart failure and other ailments. Among cancer patients, it occurs most frequently among those with pancreatic cancer or upper gastrointestinal cancers. "It's estimated that a third of patients with cancer actually die from muscle wasting," Dr. Zimmers said. "But there is hope. In mice, we can block cancer-related muscle wasting and prolong life without reducing the tumor, suggesting we might be able to do the same for patients."

Dr. Zimmers said that finding a way to fight cachexia can drastically improve patients' chances for survival.

"Patients who have cachexia don't respond well to chemotherapy and surgery," she said. "We think that if you can improve muscle and fat mass in patients, you can keep them functioning well longer and improve their receptiveness to treatment."

Likewise, curing a patient's underlying disease will rid them of cachexia. "The problem is that there are very few cancers that we can definitively cure," Dr. Zimmers said.

Dr. Zimmers' research has focused primarily on pre-clinical studies. One of the reasons she came to IU was the opportunity to join experts here in pursuing translational research in cancer cachexia.

"We've started some correlative studies, and we are beginning to understand how our mouse studies are related to what patients are experiencing," she said. "The goal is to identify mechanisms we can go after using targeted therapies."

Dr. Zimmers also has been the driving force behind the formation of a Cachexia Working Group. Made up of fellow IU researchers, the group has expanded to become the Midwest Cancer Cachexia Consortium, as researchers from Ohio State University add their time, efforts and unique expertise to the cause.

"Moving forward, we have banded together to study this devastating condition and to find cures," she said.

By Brian Hartz

Dr. Zimmers (center) and her lab. Photo: Tim Yates, Office of Visual Media/IU School of Medicine

DR. ZIMMERS IS THE FORCE BEHIND THE CACHEXIA WORKING GROUP, EXPANDING IT TO BECOME THE MIDWEST CANCER CACHEXIA CONSORTIUM.



MARKING A MILESTONE: Dr. Einhorn revolutionized cancer care

ohn Cleland was a 23-year-old newlywed college student when doctors diagnosed him with testicular cancer in November 1973. Despite surgery and a round of chemo, his cancer came roaring back, and treatment did nothing but make him sicker.

At one point, he weighed a ghostly 106 pounds, and the sores in his mouth were so painful that he sometimes spit his saliva into a cup rather than swallow it.

Some 95 percent of young men who were diagnosed with the disease in the 1970s would die from it, and it looked like Cleland would suffer the same fate. But on Sept. 27, 1974, Cleland's young Indiana University oncologist, Lawrence Einhorn, MD, offered one last option.



John Cleland, Dr. Einhorn (right). Photo: Liz Kaye, IU Communications

"I'd had a chest X-ray in the morning and he sat me down and showed me the chest films," Cleland says, recalling the details as if it were yesterday. "Even someone who'd never looked at chest films before would probably know that this guy was in serious trouble. The chest X-rays almost looked like Swiss cheese. He told me at that time that there wasn't much more that he could do for me. As I sat there thinking, my head spinning and my heart pounding out of my chest, he finally said, 'Well, there is one other thing we could try. You could be one of the very first people to ever try a new chemotherapy.""

Unable to tell his parents and wife he was giving up, Cleland agreed, and Dr. Einhorn added the experimental agent Cisplatin

to the chemotherapy drugs bleomycin and vinblastine. A miracle ensued. The cancer seemingly melted away, and it did not return. For the first time in history, a solid, metastatic tumor had been cured. Cleland and hundreds of thousands of other men around the world are alive today as a result.

AN UNLIKELY HERO

In 1973, Dr. Einhorn was the first oncologist on faculty at the IU School of Medicine. He was just shy of his 31st birthday.

Testis cancer might not typically be a disease on which a doctor would stake his career. Though the leading cancer killer of young men at the time, it is nonetheless rare. The average physician might only see patients with the disease in dribs and drabs.

The Indiana University School of Medicine was different.

Young men with the disease were flocking to University Hospital from around the United States because John Donohue, MD, offered radical, heroic surgery that other urologic surgeons wouldn't even consider. He even managed to save 20 percent of patients whose disease had spread to the abdomen. But many of the patients he operated on still developed a recurrence.

"Then, in walked a young Larry Einhorn, who, as John would describe him, was a young man wearing a paisley shirt and plaid pants who would become a most unlikely hero," says Patrick Loehrer, Sr., MD, director of the IU Simon Cancer Center. "Larry told this preeminent researcher in the surgical treatment of testicular cancer,

'I've got an idea for testis cancer. Would you allow me to work with some of your patients?'

And that began one of medicine's most impactful partnerships that would change this disease forever."

His idea involved the experimental drug Cisplatin. The drug contains the metal platinum and helps prompt the death of otherwise immortal cancer cells.

When Dr. Einhorn set his sights on it, Cisplatin had been tested on a wide range of cancers as part of an early phase trial. It proved terribly toxic, and the results weren't spectacular. It might have been permanently shelved, but Dr. Einhorn noticed that the drug was killing cancer cells in a very small subset of patients with testis cancer.



I THINK YOU'RE GONNA MAKE IT

With all this in mind, Dr. Einhorn offered John Cleland this brand new therapy. Cleland didn't know that only one other person with advanced testis cancer had tried this particular combination of drugs; he died. "We had no idea whether this was going to help for a couple days, a couple weeks, a couple months, let alone cure the disease," Dr. Einhorn says. Cleland had already endured four previous kinds of chemotherapy, each seemingly more brutal than the last. The new regimen was equally wretched. He would undergo five days of treatment, take three weeks off, and then do it all over again. On the first day of each course, the average patient would throw up 12 times.

On Oct. 20, 1974—less than a month into the treatment—it didn't seem that it was working. In fact, Cleland felt downright awful. His fever spiked above 104, and his wife and some friends drove him from his Lafayette home to the emergency room at IU. Doctors ordered a chest X-ray. The next day, as he lay in a hospital bed, the door to his room ajar, he saw Dr. Einhorn and his nurse, Becky Furnas Bond, exit the elevator. "I knew just from their body language and body motions that somebody had some good news or something was happening that was pretty happy," he says.

"They just kept coming toward my room and coming toward my room, and finally they walked in and Dr. Einhorn said, 'John, I think you're gonna make it."

His chest X-rays were clear. "When he told me, it was like I was floating in the air. I know I was touching the mattress, but it sure never felt like it," says Cleland, who went on to have three children with his wife Judy and to work as a high school teacher for 31 years. "It felt like I was 6 inches off the mattress. Probably the best feeling I've ever had in my life. Sheer bliss."

Of course, the response of a single patient doesn't qualify as a cure. The cancer could have come back, and others might not have responded the same way. Dr. Einhorn and his team continued, almost always with the same improbable results. Dr. Einhorn had cured testis cancer. But that wasn't good enough for him. In the decades that followed, he continued to refine the treatment to spare patients some of the most terrible side effects. He also substantially reduced the length of the treatment, from two years in 1974 to a mere nine to 12 weeks today. Cisplatin, once destined for the pharmacologic graveyard, is now used in the initial treatment for 11 types of cancer. Meanwhile, Dr. Einhorn remains the international expert on testicular cancer, and patients seek him out from around the globe.

THE BEST JOB IN MEDICINE

Despite 40 years of celebrity in his field, friends and family note that Larry, as he's known, remains the same modest, thoughtful person he was before he developed the cure. Even though he has received offers from some of the most prestigious medical schools in the country, he has never given much thought to leaving, in part because he loves Indianapolis, but also because he truly believes there is nowhere better than the IU School of Medicine for him to have an impact.

He's quick to give credit to his IU colleagues on the testicular cancer treatment team, saying urologist Richard Foster, thoracic surgeon Kenneth Kesler and pathologist Thomas Ulbright are some of the best in the world at what they do. "It's very unusual to have such a cadre of people who specialize in a disease like that," he says.

He remains focused on helping patients, whether through research or the expert care he provides. He still logs 12-hour days at the office, and he regularly takes phone calls at home from patients or other physicians seeking his guidance. "I've been very lucky that I'm healthy," he says. "You never know what's going to happen from day to day. I think oncologists recognize that more than others. I love the work I do. I really enjoy teaching, mentoring faculty and taking care of patients. For me, I have the best job in oncology, if not the best job in medicine."

By Karen Spataro

DR. EINHORN'S GRATEFUL PATIENTS AND FRIENDS CONTRIBUTE TO A NEW SURVIVORSHIP PROGRAM. SEE PAGE 14.

2014 News highlights

IU PHYSICIAN SCIENTIST CELEBRATES 10 YEARS OF MILES FOR MYELOMA WITH 300-MILE, 3-DAY BIKE RIDE

For the 10th consecutive year, Rafat Abonour, MD, settled onto his bicycle's saddle in October to raise awareness and funds for multiple myeloma, an incurable cancer of plasma cells. He cycled for three days, traveling more than 300 miles from Indianapolis to southwest Indiana and back to Indy.

While he's covered more than 1,700 miles as part of his annual Miles for Myeloma fundraising event, the most important strides he's made haven't been on the roads. Fueled by \$2.75 million donated by patients, families and other Miles for Myeloma supporters, Dr. Abonour and his colleagues in the multiple myeloma program at the IU Simon Cancer Center have helped win approval of new drugs, developed methods to alleviate debilitating symptoms of the disease and illuminated how myeloma hijacks the body's normal systems. Their work, combined with the efforts of researchers elsewhere, is paying off: Survival rates for myeloma have doubled in the past decade. But more must be done. The average patient still lives only about seven years after symptoms develop.

Dr. Abonour and his fellow myeloma experts at the IU Simon Cancer Center are exploring how the marrow microenvironment and myeloma patients' abnormal immune systems contribute to tumor growth, bone destruction and chemotherapy resistance. The cause or causes of multiple myeloma are unknown, but people who contract the disorder are typically over age 65. Other risk factors include being male, African American and related to someone already affected by myeloma. The disease is akin to leukemia and lymphoma in that it originates in a person's bone marrow and then can spread throughout the body, weakening bones and potentially damaging vital organs and compromising the immune system. Dr. Abonour said myeloma's complexity and tendency to attack multiple body sites make it particularly tricky.

"What's perplexing is that it's not really one disease," he said. "What we are trying to figure out is how to have a definition of the different subtypes. Some are easier to treat and sometimes can be cured. And our goal is to identify those patients and treat them differently.

"When I started working on multiple myeloma, we had one or two drugs with which to treat it; now we have six and should have a couple more by the end of the year. So I'm not as pessimistic as I used to be. This is a cancer that is rare, but we can find a cure," he added.

By Karen Spataro

DR. EINHORN'S GRATEFUL PATIENTS, FRIENDS CONTRIBUTE TO A NEW SURVIVORSHIP PROGRAM

Family, friends, colleagues and men grateful for their lives gathered in September to honor Lawrence Einhorn, MD, IU Distinguished Professor, Livestrong Foundation Professor of Oncology at IU School of Medicine and a researcher at the IU Simon Cancer Center. The event recognized the 40th anniversary of the cure for testicular cancer and celebrated Dr. Einhorn for developing the treatment.

It was in September 1974 when Dr. Einhorn tested the platinumbased drug Cisplatin with two additional drugs that were effective in killing testis cancer cells. The combination became the cure for this once deadly disease.

"When Dr. Einhorn began his work four decades ago, there was no term 'cancer survivor,'" Patrick J. Loehrer, MD, director of the IU Simon Cancer Center, said. "Thanks to Dr. Einhorn's research and leadership, 95 percent of the most common cancer in young men is curable. Today, the IU Simon Cancer Center is uniquely positioned to develop a program of significant magnitude for all survivors."

Dr. Einhorn and his colleagues are developing a survivorship program that will utilize gene sequencing technology. Dr. Einhorn's personalized medicine approach will allow a treatment team to evaluate the risks for adverse side effects before therapy and map a treatment plan that reduces toxicity and anticipates and manages unavoidable complications throughout each patient's lifetime.

More than \$3 million from grateful patients and friends has been raised to launch the program. This includes a leadership gift of \$2.5 million from A. Farhad Moshiri of Monaco. His gift creates the Lawrence H. Einhorn Chair in Cancer Research to be held by a survivorship program director and additional support for the director's research.

In addition, the children of Sidney and Lois Eskenazi also have pledged \$300,000 to honor Dr. Einhorn and celebrate their parents' 60th wedding anniversary. The gift from Sandy, Dori (Meyers), and David Eskenazi and their spouses establishes the Sidney and Lois Eskenazi Fellowship in Hematology/Oncology at the Indiana University School of Medicine.

"IU is home to unique expertise in personalized medicine that focuses on genetic risks for side effects, and blending genetics data for both tumor and patient will be the 'platinum' standard of future treatment and lifelong health management for survivors," Dr. Loehrer added.



Dr. Abonour crosses the finish li Photo: David Jaynes

IU SIMON CANCER CENTER EARNS PRESTIGIOUS NCI DESIGNATION AGAIN

The Indiana University Melvin and Bren Simon Cancer Center was recognized again as a premier cancer center by the National Cancer Institute following an in-depth peer review. The NCI renewed the center's Cancer Center Support Grant and the prestigious designation in September following a multistep competitive process. Overall, the NCI rated the cancer center's research activities as "excellent" and awarded it a five-year, \$7.8 million support grant—an increase of 20 percent from the previous award in 2008.

The NCI designation places the IU Simon Cancer Center in an elite group of 68 cancer centers across the country that focus on the rapid translation of research discoveries to directly benefit people with cancer. It is the only NCI-designated cancer center in Indiana that provides patient care. Since its founding, IU Simon Cancer Center researchers have made protocol-defining discoveries that have changed the way doctors treat testicular cancer, breast cancer, gastrointestinal cancer, genitourinary cancer, leukemia, multiple myeloma, thymoma and thymic carcinomas and thoracic cancer.

Cancer Center History

- **1992** The National Cancer Institute awarded a planning grant to the IU School of Medicine for a cancer center, establishing the Indiana University Cancer Center under the direction of Stephen Williams, MD
- 1999 IU Cancer Center earned its first NCI designation
- 2004 Designation renewed
- 2006 The cancer center is renamed the Indiana University Melvin and Bren Simon Cancer Center
- 2008 Designation renewed
- **2009** Patrick Loehrer Sr., MD, is named the cancer center's second director following the death of Dr. Williams
- 2014 Designation renewed

GLOBAL REACH: NEW CHRONIC DISEASE BUILDING GOING UP IN KENYA

Construction continues on a 120,000-square-foot building in Eldoret, Kenya (*see photo below*). The IU Simon Cancer Center partnered with AMPATH—Academic Model Providing Access to Healthcare—to create a sustainable oncology health care system in western Kenya. The new building, scheduled to open in spring 2015, will provide outpatient clinics for those with chronic non-communicable diseases such as cancer, diabetes, cardiovascular disease and mental illness. AMPATH is a partnership between Moi University School of Medicine, Moi Teaching and Referral Hospital in Eldoret and a consortium of 11 North American academic health centers led by IU.

In related news, an international team of oncology research specialists led by IU was awarded a \$3.3 million grant from the National Cancer Institute to study HPV and cervical cancer in Kenyan women with HIV/AIDS. The grant will enable the researchers to create a sustainable approach to education, clinical care and research, with the goal of providing early detection screenings for human papillomavirus and cervical cancer. The five-year grant was awarded to the AMPATH-Oncology Institute in Eldoret. **Darron Brown, MD**, and **Patrick Loehrer, MD**, are among the lead researchers.

Shared facilities

ANGIO BIOCORE

Angelo Cardoso, MD, PhD | Director Emily Sims | Manager

317.274.4385 | cancer.iu.edu/angiobiocore

The Angio BioCore is a state-of-the-art facility that has been established through the IU Simon Cancer Center to conduct validated and highly reproducible *in vitro* and *in vivo* angiogenesis, endothelial, hematopoietic and multi-parametric flow cytometry assays and their role in normal and patient-related hematologic and cardiovascular disorders.

BEHAVIORAL AND CANCER CONTROL RECRUITMENT CORE

Stephanie Wofford, MSM | Manager

317.278.0608 | cancer.iu.edu/behavioral

The mission of the Behavioral and Cancer Control Recruitment Core is to serve the needs of all cancer center investigators whose research is not related to therapeutic clinical trials but involves human subjects, including cancer patients. This developing core of the IU Simon Cancer Center was established to optimize behavioral and cancer control research recruitment. Its purpose is to coordinate, support accrual and supervise recruitment of all approved behavioral and cancer control studies. The core provides supervised recruitment throughout the IUSCC, other sites and regional social networks. In addition, it provides recruiter training, communication with clinical care groups, recruitment material preparation and ongoing recruitment strategy assessment.

BIOSTATISTICS & DATA MANAGEMENT

Susan Perkins, PhD | Director 317.274.2626 | cancer.iu.edu/biostats

The Biostatistics and Data Management Core of IU Simon Cancer Center has statistical, data management, administrative and educational responsibilities. The core participates in every level of research, from study planning and monitoring to data analysis and dissemination of results.

CHEMICAL GENOMICS

Zhong-Yin Zhang, PhD | Director 317.274.8025 | cancer.iu.edu/chemgen

The mission of the Chemical Genomic Core is to provide IU investigators with cost-effective access to high throughput screening of structurally-diverse, drug-like small molecules in biological assays provided by the investigators. This enables investigators to discover small molecule tools for basic research, therapeutic development and diagnostic applications. The core incorporates instrumentation, compound libraries, computer database and a staff experienced in assay development, high throughput screening and laboratory robotics. It is a service and collaborative research resource where facility staff works closely with each investigator through all stages of the screening process, providing an opportunity for IU students and fellows to gain experience and training in high throughput screening at the facility.

CLINICAL PHARMACOLOGY ANALYTICAL CORE

Jamie Renbarger, MD | Scientific Director

David Jones, PhD | Director

317.630.8726 | cancer.iu.edu/cpac

The Clinical Pharmacology Analytical Core provides services to IU Simon Cancer Center members as well as the Indiana University School of Medicine faculty to assist in the:

quantification of drugs and/or metabolites
protein binding of drugs
pharmacokinetic analysis of data

CLINICAL TRIALS OFFICE

Shadia Jalal, MD | Medical Director, Adult CTO James Croop, MD, PhD | Director, Pediatric CTO Kerry Bridges, MBA, RN, CCRC | Administrator, Adult CTO Linda Battiato, MSN, RN, OCN | Associate Administrator, CTO Melissa Lee, BS, CCRA | Clinical Research Manager, Pediatric CTO 317.274.2552 | cancer.iu.edu/cto

The Clinical Trials Office is a shared resource for IU Simon Cancer Center members. Services enable the efficient conduct of adult and pediatric trials and include Protocol Review and Monitoring, training and supervision of staff and maintenance of research databases.

FLOW CYTOMETRY RESOURCE FACILITY

Edward Srour, PhD | Director

317.274.3589 | cancer.iu.edu/flow

The Flow Cytometry Resource Facility (FCRF) provides flow cytometric analysis and cell sorting services to IU Simon Cancer Center investigators. FCRF provides consultation, technical advice and collaboration, thus, promoting the application of cutting-edge flow cytometric technology to varied scientific needs of cancer center scientists.

IN VIVO THERAPEUTICS CORE

Karen Pollok, PhD | Director

317.274.8891 | cancer.iu.edu/ivt

The mission of the *In Vivo* Therapeutics (IVT) Core is to provide IUSCC investigators with cost-effective and comprehensive services to facilitate the development and testing of novel pharmacological and cellular therapies.

THERAPEUTIC VALIDATION

Nagendra K. Prasad, BVSc, PhD | Director 317.278.6608 | cancer.iu.edu/therapeutic

The Therapeutic Validation Core (TVC) assists clinical investigators in the development and execution of correlative biological assays needed to validate mechanism(s) of action of candidate drugs/therapies and to develop and test new hypotheses. It also provides technical and intellectual support in the development, implementation and validation of predictive and pharmacodynamic biomarkers for novel, molecularly-targeted anti-cancer agents.

TISSUE PROCUREMENT AND DISTRIBUTION

Mary Cox | Operations Manager Oscar Cummings | Director George Sandusky, DVM, PhD | Associate Director Attaya Suvannasankha, MD | Associate Director 317.274.4320 | cancer.iu.edu/tissue

Tissue Procurement and Distribution provides samples for the discovery of new drug targets and biomarkers, the development of cancer cell lines and DNA and RNA research. It serves as a resource for the centralized banking of tissue, blood, bone marrow and buccal swab specimens procured from patients.

TRANSGENIC AND KNOCK-OUT MOUSE

Loren Field, PhD | Director 317.630.7776 | cancer.iu.edu/mouse

The Transgenic and Knock-Out Mouse Core provides services for the production of genetically modified mice. The facility also provides cryopreservation services and advice concerning animal breeding maintenance of the resulting mouse colonies.

This report is also available at cancer.iu.edu/news.

SEGMENENER STREET



535 Barnhill Drive | Indianapolis, IN 46202 | cancer.iu.edu