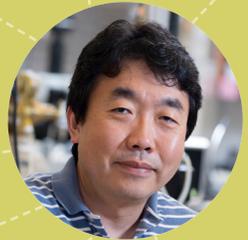


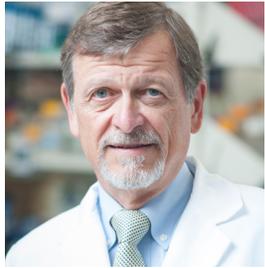
CANCER STORIES



ANNUAL REPORT, 2014-15



WELCOME



I'd like to tell you a story. It's my cancer story.

Unfortunately, you may very well have your own cancer story: Battling and surviving this horrible disease yourself. Or caring for a loved one, friend, neighbor or colleague. Or sadly, burying your wife, mother, grandfather, son or daughter.

Mine starts in Georgia where I grew up, loving the outdoors, the satisfactory crunch of dried leaves under my shoes, the warmth of the sun on my face, the chirping of birds, the hush of a frosty early morning hike. Binoculars in one hand and a field guide in the other, I studied birds, trees, flowers and bugs. It was inevitable, I thought, that I would become a field biologist or forestry researcher, nurturing my love of both nature and science.

At 20 years of age, I was in college in Texas and well on my way toward this goal when I met and fell in love with Jackie. We married and started our life together, following our plan for me to finish school, start my career and raise our family. After graduating with a degree in biology, I matriculated in graduate school and began the pursuit of a graduate degree in field biology.

And then my destiny changed almost overnight. Within a six-month span of time, my 53-year-old father, Wallace Jay Ratliff, and my father-in-law, William "Jack" Harmonson, both lost their lives to cancer. I was devastated. Our dads had left us too soon. They would never again walk in the woods on a sunny fall day or see the stars twinkling on a clear summer night. They would never again kiss their wives or tell their children that they loved them.

As a son and son-in-law, I grieved these losses deeply. And as a biology student, I wondered how tiny rogue cells inside human beings could cause so much pain and misery. I had to do something. I had to fight it.

So I changed my career direction, switching my studies from field biology to human biology. Cancer research became my life's work. Moving inside the laboratory, where I could view these tiny cells with powerful, sometimes colossal machines, I began seeking ways to lessen the pain, reduce the hurt, diagnose the disease sooner. Prolong life.

Since then, I have been privileged to work on several breakthroughs in cancer treatment and prevention. At Washington University in St. Louis, I was on the team that developed the prostate specific antigen test — the PSA, which, combined with a digital rectal exam, is the most widely used test for detecting prostate cancer. I also was part of research that led to a new treatment for bladder cancer.

In 2007, I was named the Robert Wallace Miller Director of the Purdue University Center for Cancer Research, where, for the last eight years, I have led one of only 68 cancer centers in the country designated by the National Cancer Institute. In this remarkable place, nearly 100 elite scientists from disciplines as varied as biology and mechanical engineering collaborate with each other and with experts around the world on cancer discovery.

On the following pages are more cancer stories from my fellow researchers, both how they're battling cancer in their own families and in the lab.

Each year, more cancer stories have happier endings as we make new promising discoveries. Thank you for your continued support.

Dr. Timothy L. Ratliff
Robert Wallace Miller Director
Purdue University Center for Cancer Research



Tim Ratliff and his family at The Challenge 5K Run/Walk.

ABOUT US

The Purdue University Center for Cancer Research focuses on basic discovery, the foundation for innovative cancer solutions. Leveraging Purdue's strengths in engineering, veterinary medicine, nutrition science, analytical chemistry, medicinal chemistry, pharmacy, structural biology and biological sciences, the center brings together nearly 100 researchers from across the university, along with collaborators around the world, to share ideas, insights and findings.

Research programs include cell identity and signaling, chemical and structural biology, drug delivery and molecular sensing, and medicinal chemistry. Five discovery groups focus on bladder, brain, breast and prostate cancer, and the relationship between cancer and obesity.

NCI RENEWAL

The National Cancer Institute (NCI) first designated the Purdue University Center for Cancer Research as a basic science cancer center in 1978, and Purdue has maintained that status continuously since then. **In spring 2015, the NCI renewed the Purdue University Center for Cancer Research's designation**, awarding the center \$8 million in funding over the next five years.

NCI·CC

A Cancer Center Designated by the National Cancer Institute

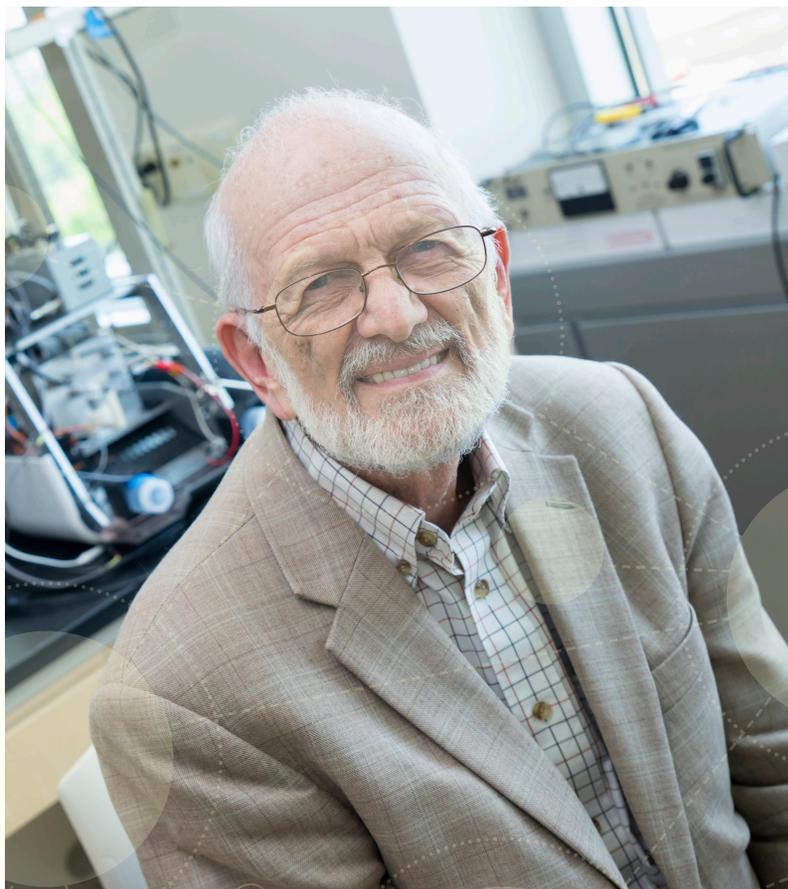
"Notably, the center has clear examples of having translated a number of its discoveries," the review stated. **"The center is poised to move to a new level of national impact in drug discovery and development."**

The NCI-designated cancer centers program recognizes centers around the country that meet rigorous criteria for world-class, state-of-the-art programs in multidisciplinary cancer research. These centers put significant resources into developing research programs, faculty and facilities that will lead to better approaches to prevention, diagnosis and treatment of cancer.

Out of thousands of cancer facilities in the nation, only 68 are designated by the National Cancer Institute. Of those, 20 are cancer centers, 41 are comprehensive cancer centers and 7 are basic science cancer centers.



GRAHAM COOKS



“In the brain, a few millimeters of tissue can mean the difference between normal and impaired function. Molecular information can help a surgeon precisely and comprehensively remove the cancer.”

STRIVING TO SAVE LIVES IN THE OPERATING ROOM

Since discovering its scientific wonders as a graduate student in South Africa 50 years ago, R. Graham Cooks has dedicated himself to bringing mass spectrometry to the masses. Now the same technology that he’s perfected to identify pesticides on grocery store vegetables and to detect explosives in luggage could soon be saving lives in the operating room.

In 2014, Cooks and his collaborators at Harvard University announced that a Purdue-designed mass spectrometer to help brain surgeons test and more precisely remove cancerous tissue was successfully used during surgery. Earlier this year, he began collaborating with Dr. Aaron Cohen-Gadol, a surgeon, and Dr. Eyas Hattab, a pathologist, both at Indiana University School of Medicine, in order to establish a database for evaluating different states and grades of brain tumors.

“We’re hoping to get this as a standard of care with mass spectrometry being used during neurosurgery,” says Cooks, the Henry Bohn Hass Distinguished Professor of Chemistry and a newly elected member of the National Academy of Sciences.

Typically during brain surgery, a surgeon must remove tissue and then send samples to a pathology lab for review, a time-consuming and challenging process. “Brain tumor tissue looks very similar to healthy brain tissue, and it is very difficult to determine where the tumor ends and the normal tissue begins,” Cooks says.

“In the brain, a few millimeters of tissue can mean the difference between normal and impaired function. Molecular information should help a surgeon to precisely and comprehensively remove the cancer.”

The new tool sprays a microscopic stream of charged solvent onto the tissue surface to gather information about its molecular makeup, producing a color-coded image that reveals the location, nature and concentration of tumor cells. Within seconds, surgeons can detect residual cancerous tissue that otherwise may have been left behind.

Cooks’ work is especially promising for gliomas — aggressive, fast-growing brain tumors that usually return because surgeons simply can’t locate and remove all the cancerous cells. “These usually have dreadful outcomes, and the fact that there is so often recurrence can be traced back to the fact that margins are really, really difficult,” he says. “I think it’s fair to say that there’s a lot of enthusiasm for using molecular pathology tools in the operating room.”

BUMSOO HAN

FIGHTING CANCER ON A MICROCHIP

For all we know of cancer today, some cancer treatment is still a trial-and-error process, with clinicians trying different types of chemotherapy drugs separately or in cocktails, hoping that one will work.

For patients battling serious side effects, that's a gut-wrenching situation. For those with aggressive tumors who don't have much time to get the drug right, that's a potentially life-or-death matter.

Bumsoo Han wants to help change that, and the engineer is using his expertise in heat and mass transfer and fluid mechanics to do so.

Collaborating with other cancer researchers in biological sciences and chemistry, Han is recreating tumor microenvironments in vitro, using a tumor-microenvironment-on-chip (T-MOC) device.

The new system allows researchers to study the complex environment surrounding tumors and the barriers that prevent targeted delivery of medications, says Han, an associate professor of mechanical engineering.

"When people are testing new drugs for cancer, they typically use a petri dish or a small animal model," says Han, an associate professor of mechanical engineering with a courtesy appointment in biomedical engineering. "But the petri dish is not really indicative of what happens to human beings when they are given anti-cancer therapies. It's the same thing with animal models. There are a lot of differences between animals and humans."

The T-MOC system, however, has the potential to mimic cancer in humans. Measuring about 1.8 inches square, it contains microfluidic channels where tumor and endothelial cells (the thin layer of simple cells lining the interior surface of blood and lymphatic vessels) are cultured. The chip also incorporates an extracellular matrix — a spongy, scaffold-like material made of collagen found between cells in living tissue.

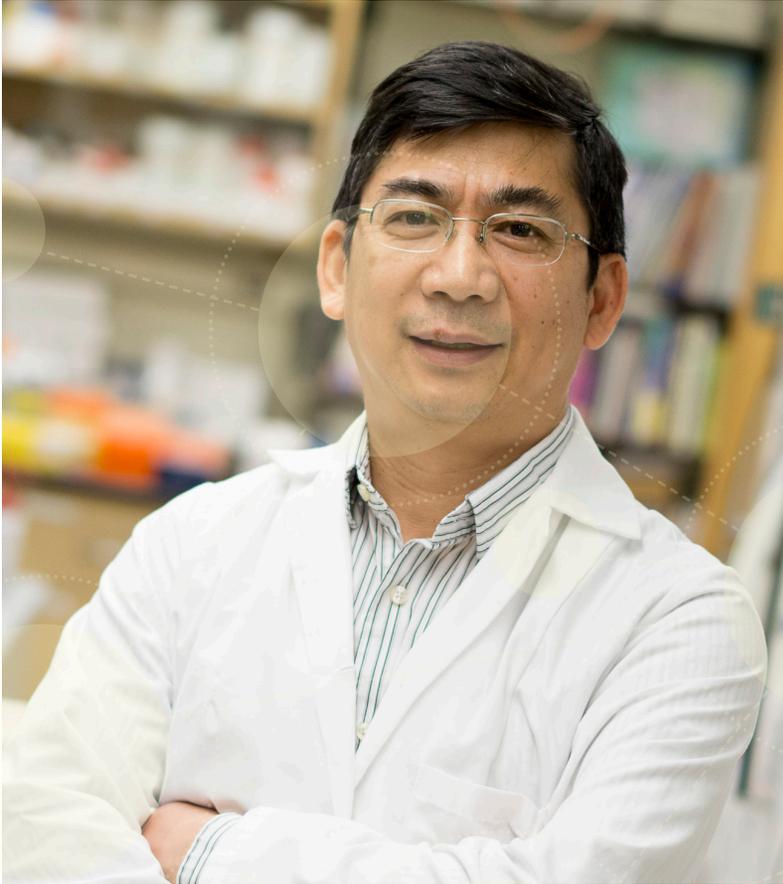
Already, Han and his collaborators have tested the technology using human breast cancer and endothelial cells and have studied how nanoparticles move within the microenvironment. Now, they're focusing on anticancer drugs.

Eventually, the T-MOC system might be used to grow tumor cells from individual patients to gauge the effectiveness of specific drugs. "There are 20 to 30 different types of chemotherapeutic drugs for breast cancer, and it is very difficult for doctors to choose effective ones," Han says. "I hope our platform will be able to screen down those choices to improve the treatment outcome as well as patients' quality of life."



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CHANG-DENG HU



“For primary prostate cancer treatment, you could start radiation therapy plus a drug that can prevent neuroendocrine differentiation from happening. That is the best case scenario.”

PREVENTING PROSTATE CANCER FROM RECURRING

Prostate cancer is frequently curable when it's not aggressive and is contained within the prostate. But that fact is little comfort to the approximately 25 percent of patients who are diagnosed with high-risk prostate cancer, who have a high tendency of the cancer recurring (30-50 percent).

Cheng Deng Hu wants to improve the odds among those 25 percent, and he hopes to do that by finding new ways to battle radioresistance, in which a tumor recurs after radiation treatment. Specifically, he is looking at the neuroendocrine (NE) cells and NE-like cells that are present in prostate cancer.

“In normal people, we have less than 1% of neuroendocrine cells,” says Hu, a professor of medicinal chemistry and molecular pharmacology. “However, in prostate cancer patients, we see an increase in the number of neuroendocrine-like cells.” These NE-like cells, which are believed to develop from prostate cancer cells, are associated both with the spread of prostate tumors and a poor prognosis.

Previous research has shown that some prostate cancer cells undergo transdifferentiation, turning into NE-like cells as a result of androgen deprivation therapy and chemotherapy. In laboratory studies, Hu observed the same phenomenon when prostate cancer cells were exposed to radiation, and so he teamed up with clinicians at Indiana University School of Medicine to study a small group of patients undergoing radiation therapy.

In four out of nine patients, the team noted a significant increase in certain NE markers, demonstrating that radiation therapy can induce these cellular changes.

“This finding is really interesting and significant,” says the professor, who's making plans for a larger-scale clinical study at Mayo Clinic to replicate their findings. He's also collaborating with researchers at Purdue and beyond to develop new drugs to prevent radiation-induced neuroendocrine differentiation.

“Also, we hope in the future we would be able to treat recurrent tumors differently,” he explains. “If, after radiation therapy, the patient comes back two years later and has a recurrence, the cells would likely have undergone genetic and epigenetic changes and would need different treatment. Or, for primary prostate cancer treatment, you could start radiation therapy plus a drug that can prevent neuroendocrine differentiation from happening. That is the best case scenario.”

ANDREA KASINSKI

GIVING HOPE TO PEOPLE WITH LUNG CANCER

In her laboratory in the new Bindley Bioscience Center's Multidisciplinary Cancer Research Facility, a sunlit environment where graduate assistants bustle between fluorescent imaging systems and injectable plate readers, Andrea Kasinski is laser-focused on two goals.

Her first goal: to better understand how cancer therapeutics work. "A lot of times we take a small-molecule drug and try it, but we don't know why it works," says Kasinski, the William and Patty Miller Assistant Professor of Biological Sciences. "I want to know what we are hitting and what the potential side effects are."

Her second goal: to give people hope. "It's always important to ground myself in the idea that our work can benefit someone," she says.

Kasinski hopes to accomplish both goals while studying lung cancer, which kills more men and women than breast, colon and prostate cancers combined. When diagnosed while the cancer is still localized within the lung, the five-year survival rate is around 50 percent.

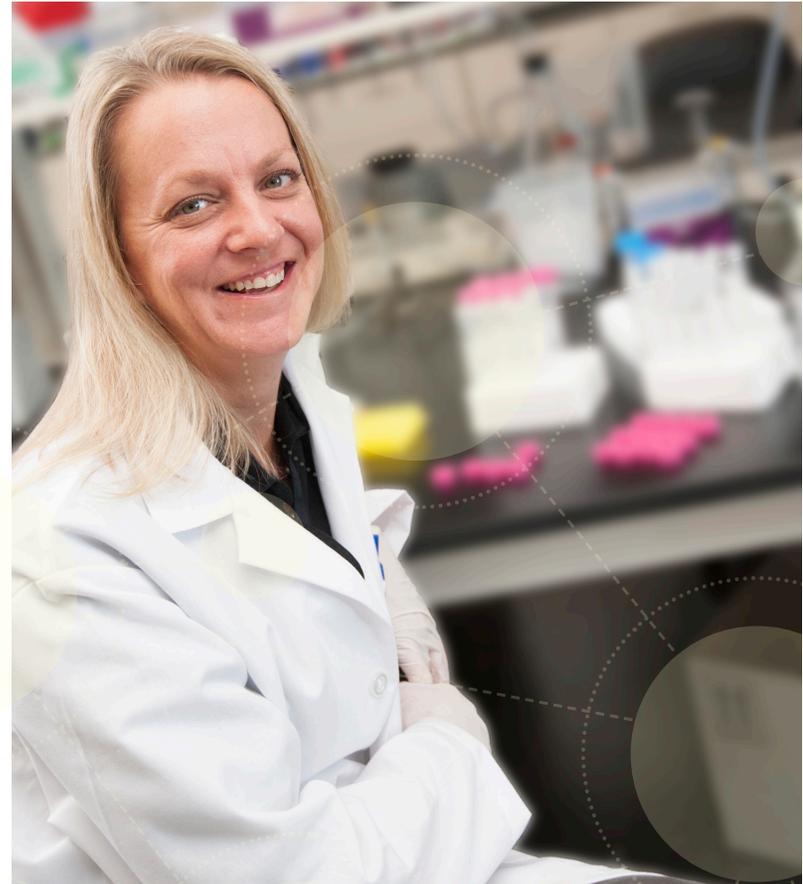
But 85 percent of lung cancers are diagnosed after they've spread to other organs, and five-year survival rates among those patients is only 4 percent. That's in large part because as the cancer metastasizes, it mutates into varieties often resistant to available drugs.

Kasinski believes that microRNAs could hold the key to future treatments. Discovered 21 years ago, these small, non-coding RNA molecules are now known to bind to certain genes even if they're not perfectly complementary, so a single miRNA is theoretically capable of affecting several different genes that are causing cancer to grow.

Around three years ago, Kasinski determined that restoration of a particular miRNA has a therapeutic effect on lung cancer in mice. Now she's collaborating with clinicians and Mirna Therapeutics to study the miRNA in a handful of patients around the world. It's the very first clinical trial for an miRNA.

For purposes of the trial, patients with liver cancer are being studied. "But if this works — and we're optimistic — it will hopefully be useful in a variety of cancers, including lung," Kasinski says.

Although Kasinski did her postdoctoral work at a university with its own hospital and where she could attend case conferences whenever she wanted, the fact that Purdue is a basic cancer research center hasn't held her back at all. "I still work with many of the leading lung cancer physicians in the world," she says. "And if anything, I think the environment at Purdue promotes our work. Basic science fuels clinical application. Otherwise, you'd be going through blindly and cherry picking."



"The environment at Purdue promotes our work. Basic science fuels clinical application. Otherwise, you'd be going through blindly and cherry picking."

ANDREW MESECAR



“When my wife told me that she’d had a mammogram and the lump was potentially cancerous, I entered a completely different mindset. The world was suddenly different; I was now the husband of a patient with cancer.”

LIVING IN CANCER’S SHADOW

It was another warm September day and the sun had already begun to set, its descending rays casting pink and orange against an azure sky, when Andrew Mesecar drove home from work and discovered that his wife had found a lump in her breast.

“One minute, I’m a basic scientist studying the mechanisms of cancer and trying to find fundamental properties that could potentially lead to new therapeutics. I’m hoping what I do will make an impact later on, but I’m not necessarily thinking about what individuals with cancer go through daily, even though I know because I’ve talked to patients over the years,” says Mesecar, the Walther Professor in Cancer Structural Biology and deputy director of the Purdue University Center for Cancer Research.

“But when my wife told me that she’d had a mammogram and the lump was potentially cancerous, I entered a completely different mindset. The world was suddenly different; I was now the husband of a patient with cancer.”

Cancer is indiscriminating, invading cells wherever it finds the means and the opportunity, and yet the Mesecars had the added defense of Andy’s 20-plus years as a cancer researcher. Andy knew where to go and whom to ask for a second opinion, and he knew how to look at data objectively.

One physician practice advised Gail to get a mastectomy, while another suggested a lumpectomy. “I realized how easy it is for people to make decisions purely based on emotion without really looking at the evidence,” he says.

Delving into the latest research, the couple examined pros and cons of each option. Andy withheld his opinions until Gail had decided for herself. Independently, they each concluded a lumpectomy was her best option.

After surgery, Gail underwent chemotherapy, then radiation therapy. This summer, her hair grew back into a short style, and her wig went back into a box.

And Andy is now back to his daily laboratory routine without the added doctor visits and patient advocate appointments, but he’s forever changed. “It was a very eye-opening experience for me,” he says.



Gail and Andy Mesecar at The Challenge in 2014.

MICHAEL WENDT

FINDING NEW OPTIONS FOR BREAST CANCER CARE

Michael Wendt was on a trajectory toward medical school, studying biology in a small liberal arts college along the banks of a meandering river and staying up late to prepare for his MCAT entrance exams, when a rotation in a local emergency room stopped him in his tracks.

"I liked working with the patients, but the work itself just wasn't that interesting," says Wendt, who realized that his previous stint in a laboratory at the Medical College of Wisconsin, spending long hours studying cell cultures in petri dishes, had been far more appealing. "What interested me more was the science behind the care — what you could do to lead to a product or a drug that could immediately affect a person's health."

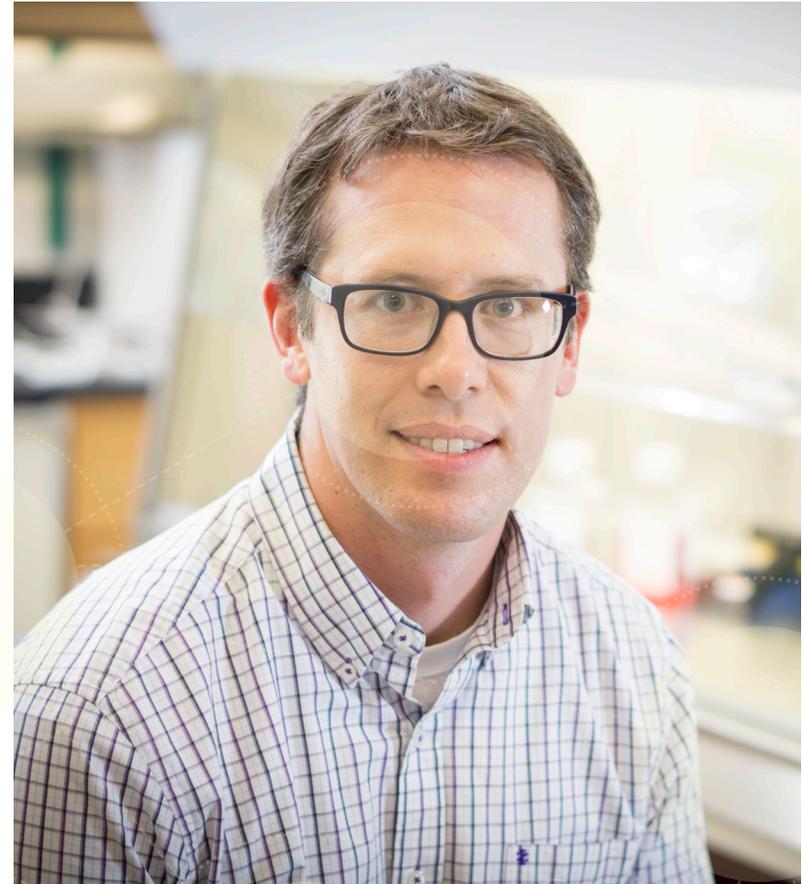
So Wendt switched career paths, ultimately landing at Case Western Reserve University in urban Cleveland, where he studied the phenomenon of epithelial-mesenchymal transition (EMT), a process researchers are now learning makes metastatic breast cancer more difficult to treat.

When tumors are removed from the breast, any stray cells that have migrated away from the original tumor site metastasize and become resistant to currently available therapies. That's because of EMT, which causes them to change characteristics as they leave the breast.

"The primary tumor you are getting the diagnosis from is not what you're trying to treat," says Wendt, an assistant professor of medicinal chemistry and molecular pharmacology. "That is removed via lumpectomy. These metastases are really, really different, and clinically that correlates with the failure of a lot of therapies."

So Wendt is studying exactly when and how spreading tumors change and become resistant to available treatments. Establishing cell lines that have undergone EMT and acquired resistance to currently available medications, he's discovered several potential targets that may be responsible for the EMT process and resistance.

"The goal of our lab is to understand the plasticity of tumor cells and get to the heart of that," Wendt says. "Breast cancer is a great example of the potential of personalized medicine; the clinical oncologist has a big bag of drugs that can target very specific growth factor pathways, but once those fail, women are limited to general toxic chemotherapy. The future of personalized medicine lies in the appropriate application of therapeutics that target very specific aspects of cancer cell biology."



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THE CHALLENGE



The Challenge 5K annual run/walk celebrated eight years in 2015.

The race, which began as a way to raise awareness and research funds, has now yielded hundreds of thousands of dollars for high-potential cancer research at Purdue.

At this year's event, Darrell Hazell, honorary chair and Purdue's head football coach, welcomed the crowd of over 1,750 participants. Thanks to these participants, along with generous sponsors and fundraising teams, the race raised over \$120,000. Many participants united as teams in a friendly competition to raise the most money or simply to honor or memorialize a loved one.

Fundraising award winners were:

Cuonzo Martin Student Team Challenge Award
Alpha Sigma Phi – Shear Madness (team captain, Connor Goodheart)

Community Team Challenge Award
Sisters for Life (team captain, Lorraine Hubert)

Leroy Keyes Faculty/Staff Team Challenge Award
Team Kickin' It (team captain, Andrea Bridge)

Top Individual fundraiser
Alan Karpick

Each year, proceeds from the race fund research grants for select members of our center. The grants kick-start innovative research with high potential to progress into life-saving diagnostics or treatments.

Three faculty members were funded this year. They are:



Claudio Aguilar
Associate Professor and Assistant Head, Department of Biological Sciences
A Chimeric EGF-Targeted Bacterial Toxin as Therapeutic Agent against Bladder Cancer



R. Graham Cooks
Henry Bohn Hass Distinguished Professor of Chemistry
Ambient Mass Spectrometry for Clinical Diagnosis of Oral/Pharyngeal Cancer



Yoon Yeo
Associate Professor, Industrial and Physical Pharmacy
Associate Professor (by courtesy), Weldon School of Biomedical Engineering
Intraperitoneal Drug Delivery System for Post-Surgical Chemotherapy of Ovarian Cancer

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SMALL GRANTS

AWARD	PI NAME	PROGRAM	YEAR	PROJECT TITLE
Challenge	Claudio Aguilar	CIS	2015	A Chimeric EGF-Targeted Bacterial Toxin as Therapeutic Agent against Bladder Cancer
Challenge	R. Graham Cooks	DDMS	2015	Ambient Mass Spectrometry for Clinical Diagnosis of Oral/Pharyngeal Cancer
Challenge	Yoon Yeo	DDMS	2015	Intraperitoneal Drug Delivery System for Post-Surgical Chemotherapy of Ovarian Cancer
Innovative Pilot	Ann Kirchmaier	CIS	2015	Quantitative Sensors for Oncometabolites Leading to Defects in Epigenetic Processes in AML, Gliomas and Other Cancers
Innovative Pilot	Alex Wei	DDMS	2015	Defining the Role of the Protein Corona in Cell Uptake: New Insights for Nanoparticle Delivery to Tumor Cells and Tumor-Activated Macrophages
Robbers	Qing Deng	CIS	2014	Understand How mir-223 Regulates Neutrophil Reverse Migration
Robbers	GuangJun Zhang	CIS	2014	Translational Regulations on Cancer Driver Genes by Ribosomal Proteins
Shared Resources	Humaira Gowher	CIS	2014	Determining the Genome-Wide Changes in DNA Methylation that Are Affected by Impeding Histone Demethylation by Inhibitor Treatment during Differentiation
Shared Resources	Christine Hrycyna	CSB	2014	Substrate-Based Inhibitors of Ras Carboxyl Methyltransferase as Potential Therapeutics for Pancreatic Cancer
Shared Resources	Chang-Deng Hu	CIS	2014	Discovery of Novel PRMT5 Target Genes Conferring Radioresistance in Prostate Cancer Cells
Shared Resources	Chang Kim	CIS	2014	Double Transgenic Mouse Line GFPCRE/Flox-STOP-Flox-ROSA tdTomato for In Vivo and Ex Vivo Tracking of CCR9+ Immune Cells
Shared Resources	Barbara Stefanska	CIS	2014	Preventive Role of the Dietary Polyphenol Pterostilbene in Hepatocellular Carcinoma Triggered by a Methyl Donor-Deficient Diet in Rats
Shared Resources	Yoon Yeo	DDMS	2014	In Vivo Evaluation of Novel Hydrogel Systems for Intraperitoneal Chemotherapy
SIRG	R. Graham Cooks	DDMS	2014	Rapid Characterization of Resected Surgical Renal Cell Carcinoma Using Touch Spray Mass Spectrometry
SIRG	Stephen Konieczny	CIS	2014	The bHLH Transcription Network Promotes Acinar Cell Differentiation and Reverses the Growth Potential of Pancreatic Ductal Adenocarcinoma
SIRG	Andrew Mesecar	CSB	2014	Probing the Role of Human Sulfotransferase 2b1b (SULT2B1b) in Prostate Cancer by Small-Molecule Antagonism
Summer Undergraduate	Jennifer Freeman	MC	2014	Effects of a Developmental Atrazine Exposure on SIK2 Expression: A Gene Important in Mitotic Regulation and a Mediator of MITF Expression
Summer Undergraduate	Stephen Konieczny	CIS	2014	Defining the Importance of Foxp2 to Pancreatic Cancer Initiation
Summer Undergraduate	Wangjing Liu	CIS	2014	A Translational Pharmacogenetic Study on Aromatase Inhibitors in the Treatment of Breast Cancer
Summer Undergraduate	Joseph Ogas	CIS	2014	Transgenic Chd5 in Zebrafish
Summer Undergraduate	Keith Stantz	DDMS	2014	Anti-Angiogenic Therapy on Cancer Stem Cell (Csc) Biomarkers
Summer Undergraduate	Barbara Stefanska	CIS	2014	DNA Methylation Biomarkers in Risk Prediction in Primary Liver Cancer
Summer Undergraduate	Elizabeth Taparowsky	CIS	2014	Characterization of the BATF Transcription Complex
Summer Undergraduate	David Thompson	CSB	2014	Gd3+:DOTA-CD Polyrotaxanes and Paclitaxel Loaded in Rhdl for Imaging and Therapy of Early Stage Liver Tumors
Summer Undergraduate	Alex Wei	DDMS	2014	Gold-Coated Magnetic Nanoparticles for Cancer Cell Imaging and Photothermal Therapies
Summer Undergraduate	Yoon Yeo	DDMS	2014	Surface Modification of Polymeric Nanoparticles for Drug Delivery to Cancer
Summer Undergraduate	Craig Goergen	DDMS	2015	Optimization of Photoacoustic Imaging to Assess Breast Tumor Margins
Summer Undergraduate	Ann Kirchmaier	CIS	2015	Genetic and Molecular Characterization of Oncometabolite Production
Summer Undergraduate	Stephen Konieczny	CIS	2015	Establishing a Critical Role for SOX9 in Pancreatic Cancer Malignancy
Summer Undergraduate	Barbara Stefanska	CIS	2015	DNA Methylation Biomarkers of Early Detection in Primary Liver Cancer
Summer Undergraduate	David Thompson	CSB	2015	Development of Targeted Gene Delivery Vehicles for Bladder Cancer Therapeutics
Summer Undergraduate	Vikki Weake	CIS	2015	Determining the Binding between SAGA and Spliceosomal Components
Summer Undergraduate	Alex Wei	DDMS	2015	Studying the Effects of Fetal Bovine Serum on Folate-Nanoparticle Development, Recognition and Cell Uptake
Summer Undergraduate	Yoon Yeo	DDMS	2015	Developing Near-Infrared Dye-Polymer Conjugate for Optical Tracking of Nanoparticles In Vivo

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