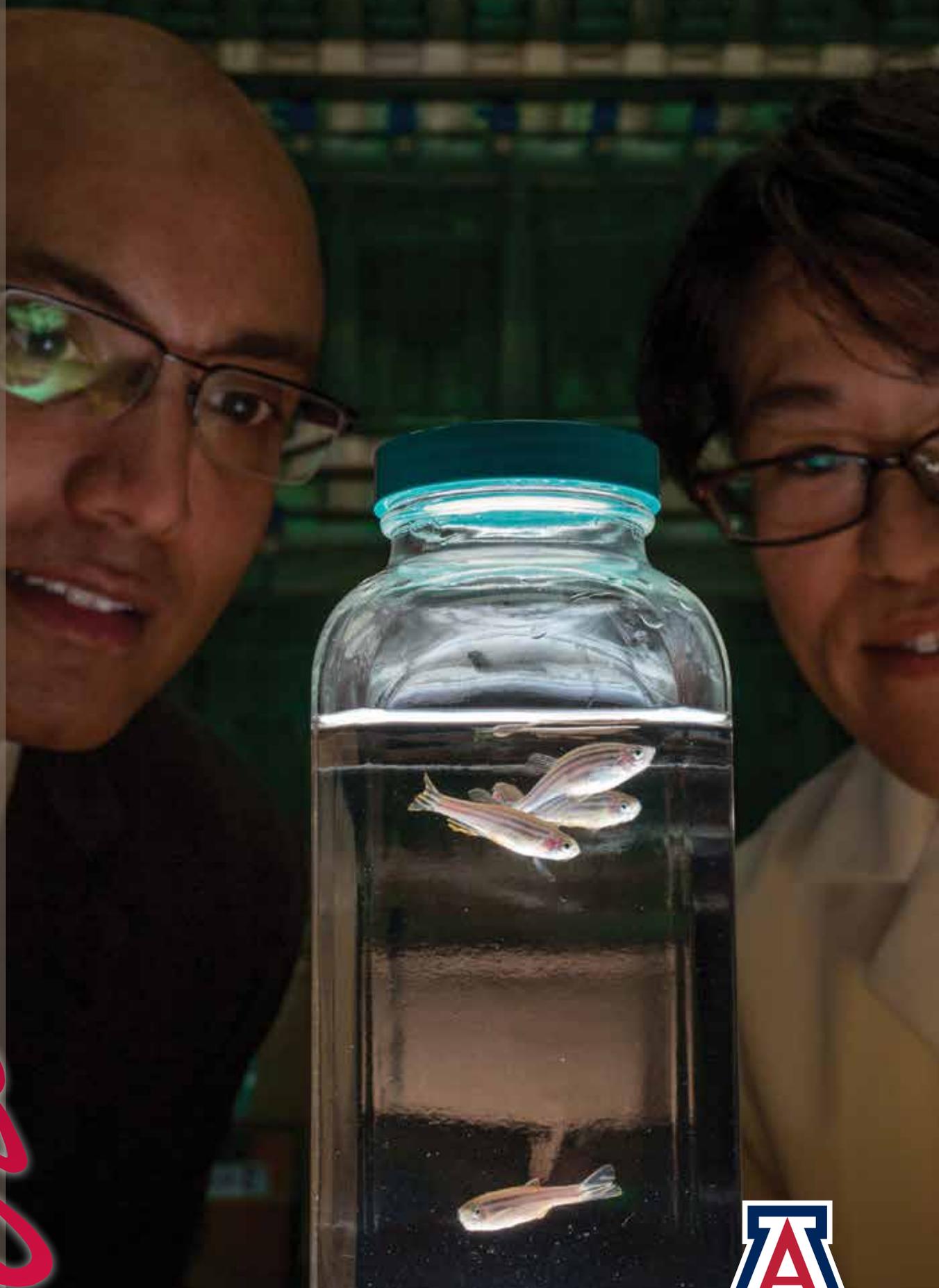


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AGAINST CANCER™



A publication of the University of Arizona Cancer Center

WINTER 2015



A Note *to* our Readers

As I am settling into my new job as Director of the University of Arizona Cancer Center, and my wife and I are becoming acclimated to the beauty of the Sonoran Desert, I want to express my deepest appreciation for the warm welcome we have received here in Arizona. I am looking forward to accomplishing great things at the University of Arizona.

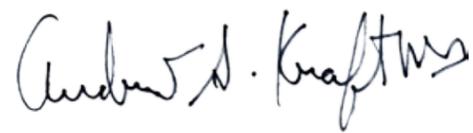
As the UA Cancer Center approaches its 40th anniversary next year, we all are working hard to assure that our center is redesignated a comprehensive cancer center by the National Cancer Institute, a designation we first earned in 1990. That means taking a hard, honest look at the science we are doing each and every day, and how our resources are allocated to make sure that our science is cutting-edge, bringing us closer every day to achieving our mission to prevent and cure cancer.

The NCI requires its comprehensive cancer centers to demonstrate greater depth and breadth of research in three major areas: laboratory, clinical and population-based science, including enhanced public education, training, and outreach activities.

We have extremely talented and experienced scientists, physicians, researchers, and staff members at the UA Cancer Center. Our work is nationally and internationally recognized for its excellence. We must ensure that our work remains on the forefront and that the UA Cancer Center reaches the top-tier of comprehensive cancer centers nationally.

I am particularly interested in cancer immunology, genetics and drug discovery, along with cancer disparities, an area which holds great promise for all of Arizona and the Southwestern United States. It is in these areas that all of us in the cancer research world can expect to see great progress and make big strides.

Thank you for your support of the University of Arizona Cancer Center.



Sincerely,
Andrew S. Kraft, MD
Director, University of Arizona Cancer Center

On the cover:

UACC scientists Abraham Jacob, MD, and Maki Niihori, PhD, study zebrafish, found to serve as an effective model for a number of human cancers.

photo by csrichards.com

The University of Arizona Cancer Center is a Comprehensive Cancer Center designated by the National Cancer Institute. The primary responsibility of a NCI-designated Comprehensive Cancer Center is to conduct research that will lead to the reduction of cancer morbidity and mortality.

Produced by the UACC
Office of Public Affairs
Director ~ Sara Hammond
Associate Editor ~ Nick Prevenas
Designer ~ Kayla Coe, MA
Printer ~ AlphaGraphics CPS

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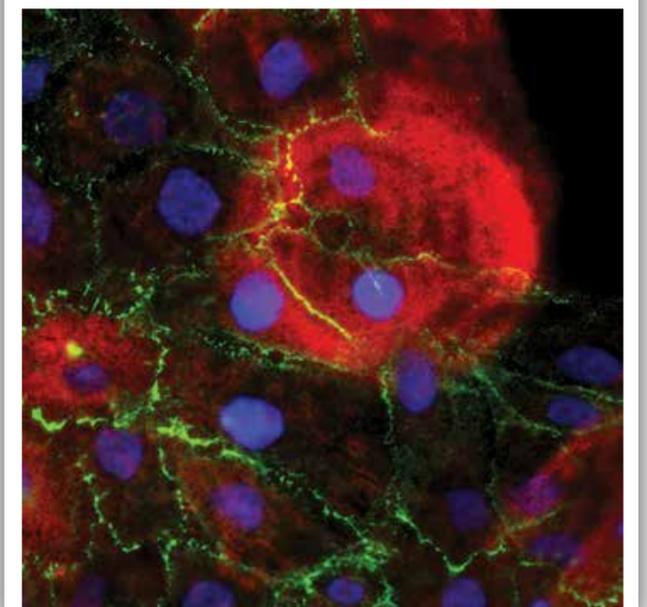
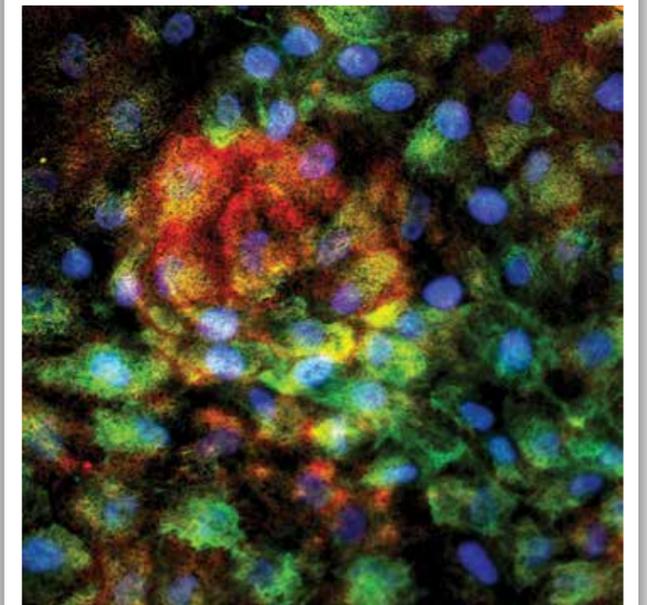
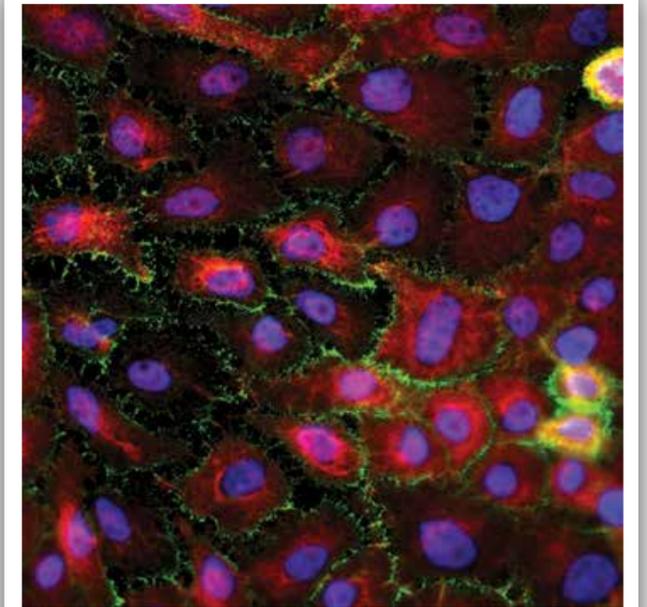
SCIENCE AS ART

There has long been a connection between science and art, one that can be traced back to the Egyptian pyramids. History proves that the two disciplines cannot exist without each other, enduring in constantly changing and evolving relationships, on both small and large scales.

WATCHING HEMIDESMOSOMES

Researcher Sangita Pawar, PhD, treated human tumor cells with antibodies specific to laminin-5 and $\alpha 6$ -integrin (hemidesmosome proteins) to prevent cancer metastasis. Hemidesmosomes anchor cells to surrounding tissue and are modified in cancer allowing the cells to move to distant sites.

(images courtesy of the Cress Lab)



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Abraham Jacob, MD, and Maki Niihori, PhD, work with zebrafish specimens.

FISHING FOR ANSWERS

Cancer researchers are constantly searching for innovative ways to develop life-saving therapies as quickly as possible. The possible key to unlocking these cures can be found at any pet store throughout the world.

It's only about four centimeters long and a few grams in weight, but thanks to a wide variety of genetic and biological factors, it has emerged as an invaluable member of the scientific research community.

What is this wonderful organism?

The zebrafish.

Scientific articles in many top peer-reviewed journals have touted the zebrafish's effectiveness and versatility for nearly two decades, but recently, a group of University of Arizona researchers has applied the zebrafish's unique research capabilities toward discovering potential solutions for chemotherapy-related hearing loss (ototoxicity).

Chemotherapy-induced damage to the inner ear can rob patients of their hearing and even balance function. At the University of Arizona Cancer Center, researchers are looking to an unlikely ally in their fight to find drugs that prevent hearing loss.

"Zebrafish orient themselves in water much like the way the human's inner-ear cells evolved to orient themselves to sound waves," said Abraham Jacob, MD. "When we simulate ototoxicity with zebrafish, we are able to generate so much more data than with any other model."

In recent years, the zebrafish has been found to serve as an effective model for a number of human cancers, as well as post-treatment side effects. According to the National Institutes of Health, "major technical advances have been essential for the generation of zebrafish cancer models relevant to human diseases. These models develop tumors in various organ sites that bear striking resemblance to human malignancies, both histologically and genetically. Further exploration of the zebrafish cancer models not only will generate unique insights into underlying mechanisms of cancer but will also provide platforms useful for drug discovery."

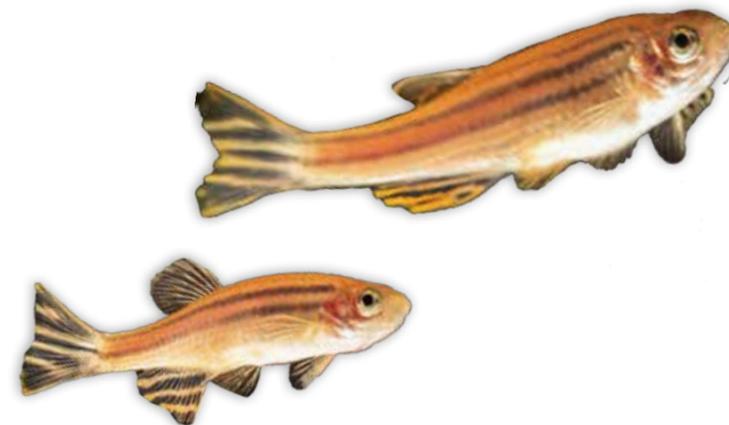
Before zebrafish entered the picture, these experiments required higher-order species, such as birds or mice. These projects were costly and time consuming — so much so that it was next to impossible to generate the amount of data required to make any statistically relevant conclusions, let alone develop any effective interventions.

Zebrafish changed all that. Information that took years to gather could be done in weeks. For example, thousands of zebrafish larvae can be used each month to test promising hearing-protective drugs.

"We have the data to show that a change in the zebrafish's behavior is a biomarker for inner-ear damage," Dr. Jacob said. This information is presented in a journal article titled "A High Throughput Ototoxicity Assay in Zebrafish: Drug Development Platform Targeting Hearing Loss."

So what is the potential impact?

Hearing loss has become one of modern cancer therapy's most prevalent side effects. In fact, hearing loss is among the most underreported, yet potentially devastating, side effects endured by many chemotherapy patients. Often, these patients don't realize that their hearing has been





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compromised until it is too late to receive treatment. Dr. Jacob started the Hearing Conservation Program to educate chemotherapy patients about their risks for hearing loss, while suggesting possible interventions to prevent hearing loss or to recover a patient's hearing.

Dr. Jacob is an Associate Professor with Tenure and Vice Chair of the Department of Otolaryngology, as well as a member of the University of Arizona Cancer Center and the BIO5 Institute.

"It doesn't even occur to most cancer patients that their treatment could impact their hearing," said Dr. Jacob, who, in addition to his role with the UA Cancer Center, is the director of the University of Arizona Ear Institute, which is dedicated to the prevention, detection, treatment, and rehabilitation of ear disease through clinical care, research and education.

Postdoctoral Research Associate Maki Niihori, PhD, is

responsible for much of the data analysis, and says that these fish can start to tell a story once you observe them long enough.

"It's remarkable how consistent their behavior remains from test to test," Dr. Niihori said. "They're ideal for this kind of research."

Dr. Niihori's experience with experimental fish analysis dates back to her days as a student at the Graduate School of Humanities and Sciences at Ochanomizu University in Tokyo, Japan. She was among those studying the development and swimming activity of Japanese rice fish (referred to as "medaka fry") during spaceflight aboard the Space Shuttle Columbia.

These experiments took place as part of JUSTSAP — the Japan-US Science, Technology and Space Application Program — during the early 2000s, with their findings published in 2003 and 2004.

Dr. Niihori's background in small fish study has helped make this current chemotherapy-related hearing-loss study one of the most exciting and innovative projects at the University of Arizona. She joined the UACC in April 2012, with the zebrafish program beginning just a few months later.

"We've built this program from the ground up," Dr. Niihori said.

"We've built this program from the ground up."

~ Maki Niihori, PhD

Collaboration has been crucial to the success of this program. Dr. Jacob's lab is working closely with Donna Zhang, PhD, and Eli Chapman, PhD, of the University of Arizona College of Pharmacy to develop clinical trials that would test the efficacy of various therapeutic interventions that could help save a cancer patient's hearing.

Further collaborations with Jeffrey Rodriguez, PhD, in the University of Arizona College of Engineering, Marvin Slepian, MD, at Sarver Heart Center, and personnel in the University of Arizona Cancer Center's Bioinformatics Shared Resource will go a long way toward translating this data from a spreadsheet full of numbers into personalized patient care.

"Now that the data gathering is so much more streamlined, we can apply that to therapeutic development, as we can quickly administer, test, and rank the various drug combinations in ways we never could without these zebrafish," Dr. Jacob said.

With more and more people living full, rich lives well beyond that initial cancer diagnosis, survivorship care will continue to move toward the forefront of cancer research. These zebrafish find themselves in a unique position to assist with cutting-edge research in every facet of our fight against cancer.

~ Nick Prevenas



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ALL ABOUT ZEBRAFISH

The zebrafish, *Danio rerio*, is named for the five horizontal stripes on the side of the body, which resemble a zebra's stripes. A full-grown zebrafish is typically 2 to 4 inches long, and can live as long as five years.

This breed of fish didn't become part of the scientific community until the early 1970s, when researchers in the Pacific Northwest discovered that these fish — natives of the Southeast Himalayan region — could potentially serve as ideal models for disease examination.

What makes the torpedo-shaped zebrafish so special?

First and foremost, the zebrafish has a backbone. Unlike the majority of smaller, high-volume test subjects (insects, larvae, etc.), the zebrafish is a vertebrate, which makes a world of difference when it comes to translating these research findings into possible human applications.

In addition, zebrafish live healthy, happy lives in close proximity with one another. The ease of breeding makes it possible to run large tests on statistically significant numbers, while keeping the zebrafish's response to stimuli consistent across the board.

It's a smart, resilient fish that adapts almost immediately to its surroundings. All of the studies conducted in Dr. Jacob's ototoxicity study are completely safe and comfortable for the fish.

NEWS & NOTES

UACC SCIENTIST WINS BTE GRANT FOR BREAST CANCER RESEARCH

Pavani Chalasani, MD, MPH, will receive a \$20,000 research grant from the University of Arizona Cancer Center's Better Than Ever (BTE) program to study novel biomarkers that might predict therapeutic response for breast cancer patients.



BTE is in its 15th year of helping people make walking, running, or cycling a regular part of life, and the 14th year of awarding grants. The fundraising efforts of BTE participants and their supporters have resulted in more than \$1.8 million in 50 research grants to UACC researchers. Grants are awarded through a competitive process managed by a scientific review committee led by Setsuko K. Chambers, MD.

Dr. Chalasani's study is titled: Correlation of PI3K/Akt/mTOR pathway activation with response to neoadjuvant endocrine therapy in POWER-PIINC trial.

"PI3K/Akt/mTOR pathway activation has been associated with resistance to endocrine therapy (or anti-estrogen therapy)," Dr. Chalasani says. "Recently, drugs targeting this pathway have been approved in treatment of metastatic breast cancer. However, there are no known markers that predict which tumors respond to such drugs and which don't. This project proposes to study such markers (known as biomarkers) and gather pilot data if they can predict response. We will be studying these markers on tissue collected in POWER-PIINC trial."

AZPM DOCUMENTARY FEATURES UACC PATIENT

"*Winning by Living*" A Cancer Story follows a young Tucson woman as she faces advanced pancreatic cancer. Michelle Kirlaw vows never to give up and to win, simply by enjoying the time she has with her family and living her life to the fullest.

This half-hour documentary, produced by Arizona Public Media, will premiere at a screening event March 23, 6 p.m., at The Jewish Community Center. The event is free and open to the public; however, an RSVP is required. Go to www.azpm.org/onecancerstory for additional information.

The documentary will air on PBS 6 March 29 at 6 p.m., followed by a panel discussion about resources for the newly diagnosed with cancer, moderated by Arizona Illustrated host Tom McNamara. Phone lines will be open for viewers to call with questions about community resources.

The documentary will air again April 1 on PBS 6 at 8 p.m., in conjunction with the Ken Burns' documentary event, *Cancer: The Emperor of All Maladies*, airing March 30 and 31 and April 1.



To view more news from the UACC, go to: azcc.arizona.edu/news

ROGERS LAB PUBLISHES PAPERS IN HIGH-IMPACT JOURNALS

Groundbreaking work originating from the laboratory of Gregory C. Rogers, PhD, is featured in the *Journal of Cell Biology* and the *Proceedings of the National Academy of Sciences*.

Dr. Rogers is an Associate Professor in the Department of Cellular and Molecular Medicine at the University of Arizona, and has been a member of the University of Arizona Cancer Center Cancer Biology Program since 2008. Dr. Rogers is also a member of the BIO5 Institute.

For the past handful of years, Dr. Rogers' lab has established itself at the forefront of the study of centrosome duplication and the role of the Polo-like kinase 4 (Plk4) pathway in cell regulation and genome instability. Both papers were spearheaded by PhD student Joey Klebba, who is now a postdoctoral researcher at the University of California, San Francisco.

Both studies were funded in part by a donation from the Phoenix Friends of the Arizona Cancer Center and are an extension from the lab's original article published in the *Journal of Cell Biology* in 2011, which covered Rogers' group's groundbreaking work involving the identification of several new molecules that regulate centrosome duplication through the Plk4 pathway.

UA-DISCOVERED DRUG FOR SKIN DISEASE APPROVED FOR PATIENTS IN EUROPE

A synthetic hormone developed by faculty at the University of Arizona Cancer Center and the UA's Colleges of Medicine and Science more than two decades ago that has been shown to offer relief for a rare skin disease has been approved for patients in Europe.

Clinivel Pharmaceuticals Ltd., of Melbourne, Australia, received permission Oct. 23 from the European Medicines Agency to market the drug, whose trade name is Scenesse. The company says it plans to seek approval for Scenesse from the U.S. Food and Drug Administration and also for patients in the Asia-Pacific region.

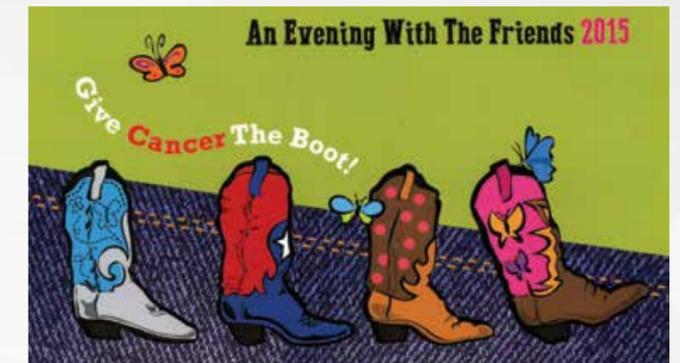
The molecule was developed, patented and initially tested at the UA under the name afamelanotide by UACC member Victor Hruby, PhD, Regents Professor Emeritus of Chemistry and Biochemistry; Robert Dorr, PhD, leader of the UACC's Therapeutic Development Program and Professor of Medical Pharmacology in the UA's College of Medicine-Tucson; and

the late Mac Hadley, PhD, a UA Cell Biology and Anatomy Professor. The UA licensed the molecule to a predecessor company, Melanotan Inc., in 1995.

"The discovery and development of this melanotropin compound for treatment of skin disorders and related medical applications had tremendous significance because it was a first of its kind and involved the very close collaboration of chemists, biologists and medical doctors who brought similar excitement and creativity to the problem but from different perspectives. These perspectives were all critical to the eventual success. Without this enthusiastic collaboration it would not have happened," Dr. Hruby said.

"This is the first pure melanotropin ever approved," Dr. Dorr said.

AN EVENING WITH THE FRIENDS 2015 — GIVE CANCER THE BOOT!



The Phoenix Friends of the Arizona Cancer Center are a group of compassionate and dedicated women who volunteer their talent and energy for the treatment and cure of cancer.

Help us support the outstanding tradition of so many generous women and join the Friends for the 29th annual **An Evening with the Friends gala March 21** to raise funds and support the cancer center's mission to prevent and cure cancer.

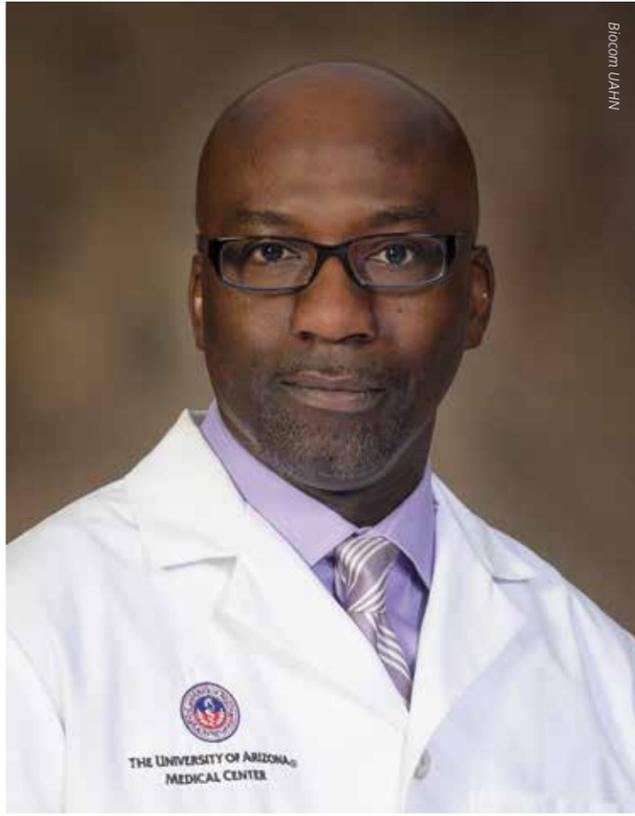
In addition to experiencing the joy of giving, enjoy an evening of friendship and the most imaginative and spirited silent auction in the Valley.

The Phoenix Friends have raised nearly \$6 million to help find a cure for cancer.

All proceeds stay within the state of Arizona for research at the University of Arizona Cancer Center.

Please visit phoenixfriends.org for more information.

NEW FACULTY



Rick Kittles, PhD

Cutting-edge cancer research can't take place until a scientist traces things back to the root of an issue. Nobody believes this more than Rick Kittles, PhD.

Dr. Kittles is a national leader on cancer health disparities and the role of genes and environment in disease, and a pioneer in DNA testing to trace the ancestry of African Americans. He joined the University of Arizona in July 2014 and brings with him years of expertise in a fascinating field of study.

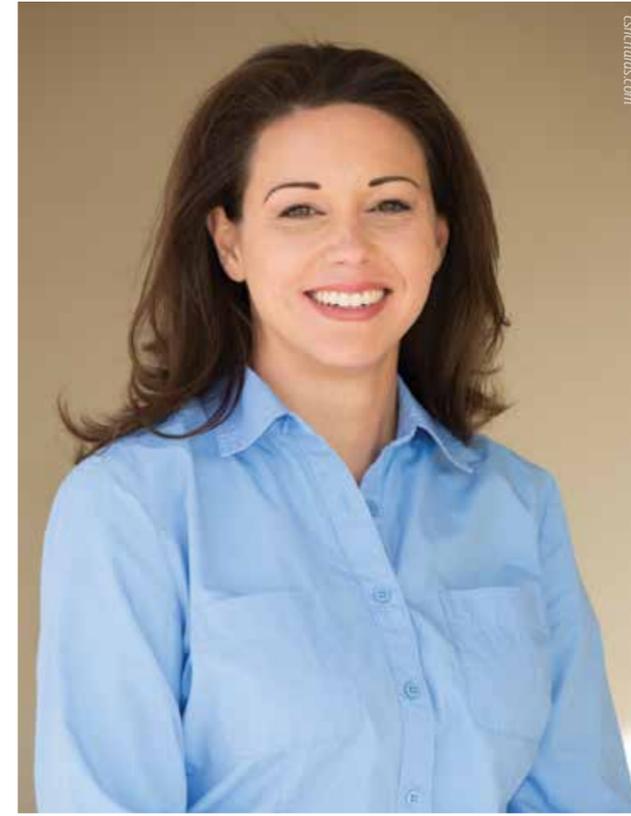
"These are very exciting times at the Arizona Health Sciences Center. I am extremely honored to be able to work with such talented researchers, clinicians, students, and staff," Dr. Kittles said. "The commitment to precision health crosses multiple disciplines, programs, and communities. Each of us will be challenged to help bring the vision to reality at AHSC."

Dr. Kittles is the Director of the Division of Population Genetics, part of the new Center for Applied Genetics at the Arizona Health Sciences Center at the University of Arizona. He has also been appointed Professor in the Department of Surgery Division of Urology at the UA College of Medicine – Tucson with a joint appointment in the Division of Health Promotion Sciences at the UA Mel and Enid Zuckerman College of Public Health. In addition, Dr. Kittles is a member of the University of Arizona Cancer Center and its Cancer Prevention and Control Program.

Dr. Kittles' research interests include prostate cancer risk and the role of genes and environment. His work on understanding the role of vitamin D in aggressive prostate cancer may lead to better treatments and prevention. His laboratory is focused on identifying genetic and environmental contributions to cancer risk and treatment outcomes, including understanding the complex issues surrounding race, genetic ancestry and health disparities.

Dr. Kittles is a co-founder of African Ancestry, Inc., a Washington, DC-based company that traces maternal and paternal lineages of African descent. His work has been featured in CNN's "Black in America" series about African American genealogy; the PBS documentary, "Oprah's Roots: An African American Lives Special;" the PBS documentaries, "African-American Lives" and "African-American Lives 2;" the BBC Television documentaries, "Motherland: A Genetic Journey" and "Motherland – Moving On;" and in a CBS "60 Minutes" interview about genetic ancestry by Leslie Stahl.

Prior to joining the UA, Dr. Kittles was with the University of Illinois at Chicago, where he was Director of the Institute of Human Genetics; Associate Director of the Office of Health Equity at the University of Illinois Cancer Center; and Associate Professor in the Department of Medicine and Division of Epidemiology and Biostatistics, School of Public Health.



Justina McEvoy, PhD

Justina McEvoy, PhD, is a big believer in the power of teamwork.

Dr. McEvoy knew early in her college career that she wanted to be involved in medical research in some way, and it didn't take long for her to see that truly transcendent work takes place in welcoming, collaborative environments.

"Everywhere I've been, I've been so fortunate to work with such brilliant, generous mentors who pushed me to be the best scientist I could be," Dr. McEvoy said.

It was this path that led her toward the University of Arizona Cancer Center, where she is an associate member in the UACC's Cancer Biology Program.

"As soon as I got to Tucson, I knew I'd be a good fit here," Dr. McEvoy said.

Her research deals with the regulation of differentiation programs during normal development and tumor formation in pediatric cancers. Dr. McEvoy hopes to shed light on the underlying biological mechanisms that separate normal cell development and tumor formation, while providing novel therapeutic approaches for these diseases.

Dr. McEvoy spent six years in the Department of Molecular Biology at Brown University as a graduate student research assistant before moving to St. Jude's Children's Research Hospital in 2007. In her seven years as a postdoctoral fellow, Dr. McEvoy became one of the nation's leading researchers in retinoblastoma — a rapidly developing eye cancer that begins in the retina and, if left untreated, can cause blindness and/or require the removal of the eye. Dr. McEvoy studies the role of the Rb tumor suppressor in regulation of differentiation pathways in this rare childhood cancer.

"Everywhere I've been, I've been so fortunate to work with such brilliant, generous mentors who pushed me to be the best scientist I could be."

~ Justina McEvoy, PhD

Additionally, she is studying the relationship between the genetic and epigenetic contributions in a pediatric cancer called rhabdomyosarcoma — a type of cancer, specifically a sarcoma, in which the cancer cells develop from skeletal muscle stem cells.

"These cancers are just devastating, and I want to do everything I can to help find cures for these diseases," Dr. McEvoy said.



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YOUR IMPACT

With your support, the University of Arizona Cancer Center (UACC) can fund new research initiatives as they emerge and accelerate our ability to prevent, detect and treat cancer.

Giving to the UACC provides opportunities for discovery, promotes education and enables our scientists and physicians to expand hope. Help us achieve these essential goals by choosing to become a partner. Together, we can save and change lives.

*For more information, please contact (800) 327-2873
or send an e-mail to development@uacc.arizona.edu.*