

The Hallmarks of



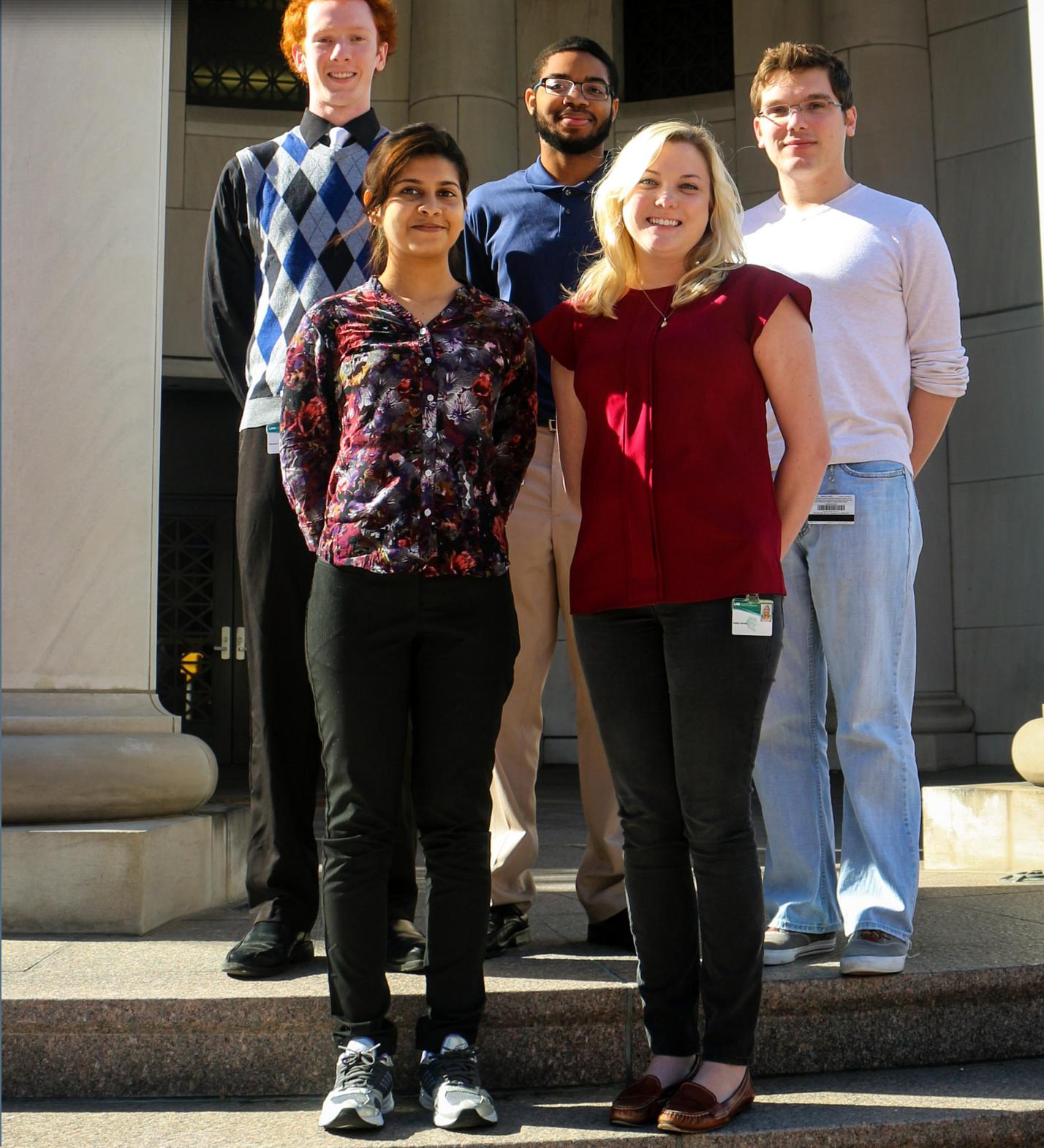
CANCER BIOLOGY

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FACULTY IN FOCUS: DR. EBEN ROSENTHAL & DR. KURT ZINN



WELCOME CLASS OF 2014





UAB GBS CANCER BIOLOGY THEME

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From the Directors

WELCOME to our Fall 2014 issue of The Hallmarks, where we have a lot of good cheers to share. In each issue we highlight our students' achievements, the current scene of events at UAB and most importantly, highlight the research, Faculty and the spectacular core facilities at UAB. We had a great start to the new academic year when we welcomed new students into our Theme and have also been proud to witness four of our senior students successfully defend their thesis. This Fall has been particularly event-packed with the Annual UAB Cancer Center Retreat, the Annual Pathology Research Day and the Komen Race for the Cure. Our students have provided you the highlights of these events. In this issue our guest contributor, Josh Fried, has authored an article on Alabama Drug Discovery Alliance (ADDA), while our Newsletter Committee Members have provided updates and articles to bring you up to speed on the latest and best that UAB and our students have achieved in terms of awards and publications. You'll agree that our students are high-achievers and also know how to give back to society. We invite you to sit back, relax and enjoy this issue. ●

Theresa Strong Ph.D. & Lalita Shevde-Samant Ph.D.



Visit our website: <http://www.uab.edu/gbs/cancerbiology>



Welcome, Blazers!

by ANN HANNA



Asmi Chakraborty

I earned my Biotechnology undergraduate degree from DY Patil University in Mumbai. Afterward, I worked for eight months in ACTREC cancer research institute as a research assistant in a diagnostic lab. It was a great experience, but I realized that I did not want to perform the same tasks daily, so I decided to apply to grad schools in the US and Germany that had Cancer biology programs. UAB extended me an interview and Dr. Strong and Dr. Shevde-Samant were always there to answer any queries and made me feel very **welcomed**. I ended up coming to UAB and I love the **environment** here!



Michael Dixon

I chose UAB for graduate school because as an undergraduate student, I was fortunate enough to work in various research labs in which I was able to see the **collaborative** effort between researchers and the many **opportunities** that could be provided to me. My interest lies in cancer immunology, and UAB has an incredible cancer biology and immunology program that allows me to combine the two to further enhance my knowledge. I interviewed at various other schools and I felt as though none of them offered a program and a community as enriching as ours. I am very proud to remain a Blazer.



Kaity Dorsett

My name is Kaity Dorsett, I grew up in Gadsden, AL just a short drive from Birmingham. I went to undergrad at Birmingham Southern College and graduated with a biology degree this past May. I chose to go to graduate school at UAB because I was incredibly impressed by the **faculty and students** here when I came for my interview. I really feel like this will be a great place for me to grow and develop into a knowledgeable and effective scientist!



Samuel Fehling

I grew up in a small town in Wisconsin called Elkhorn, so I really wanted to go out and experience the world. The reason I chose graduate school is relatively simple. Multiple times during my undergraduate career I would be in Biology lectures and really be enjoying the material. However, as soon as the subjects became really interesting, I would always hear the phrase "but this is beyond the scope of this class". Ultimately, I chose graduate school because of my pursuit for knowledge. UAB was the first graduate school to extend an interview. I came in not knowing what to expect, but when I got there, I was blown away by the students and faculty who were so **incredibly helpful and fun** to talk to. I had such a great experience that when I received an offer from UAB I knew this would be the school for my graduate career.



Brent Jones

I grew up in a small town, Forsyth GA, about an hour south of Atlanta. I got my BS and MS from Georgia College and State University in Milledgeville GA where I majored in Biology. I fell in love with research my senior year of undergrad, so to gain more research experience I stayed and got my Master's degree. For my thesis my research was in population phylogenetics, where I looked at a threatened species of crayfish and tried to use phylogenetic analyses to form a hypothesis as to how their populations moved across the landscape, and how each population was related to each other. I chose UAB for grad school, because I visited several times for various conferences, and several of my classmates came here so I knew it was a **great school**.

JOIN US. APPLY NOW!

We encourage you to apply for Fall 2015, beginning in August of this year. Applications are reviewed as they are received and interview sessions are scheduled based on receipt of applications. Priority deadline for domestic applicants is **December 1, 2014**; preferred deadline is January 15, 2015. Final deadline for international applications is **January 15, 2015**.

Our Cancer Biology Theme has two upcoming recruitment weekends, one is on January 22-24 and the other is February 19-21. The programs will start with dinner at Vulcan Park Thursday evening, faculty interviews on Friday, and end with an optional bus tour of the city on Saturday.

Visit us at <http://www.uab.edu/gbs/cancerbiology/admissions-information> for more information. •



Images of the Pioneers

by HAWLEY PRUITT



Dr. Eben Rosenthal



Dr. Kurt Zinn

In this issue, the faculty in *focus* section title has a double meaning; UAB researchers **Dr. Eben Rosenthal** and **Dr. Kurt Zinn** are pioneers in developing advanced imaging techniques for use in the operating room. The work of Dr. Rosenthal and Dr. Zinn has culminated into a Phase I clinical trial that is recruiting patients at UAB. The trial evaluates the safety of an antibody-dye conjugate, Cetuximab-IRDye800, on patients with head and neck squamous cell carcinoma. Cetuximab is an FDA approved antibody for the treatment of multiple cancers that binds the epidermal growth factor receptor. The use of cetuximab-IRDye800 allows surgeons to 'see' cancer and guides resection and obtaining negative margins in patients with aggressive malignancies. Positive surgical margins in patients with cancer generally results poor outcomes. The dye conjugate uses an infrared emission spectrum to avoid auto fluorescence of surrounding normal tissue thereby distinguishing tumor tissue, and allows the surgeon to resect cancer cells specifically. Real time fluorescence can detect subclinical islands of disease. Translation of this technique to the clinic will be streamlined by the fact that all reagents, including the SPY imaging platform and antibody are already FDA approved. This work will undoubtedly be used in the treatment of other cancers, especially cases where conservative surgery is essential for the quality of life of the patient. In preclinical models, this technology was successfully used to identify microscopic margins of breast tumors, brain tumors, melanoma and cutaneous cancers. The work done by Dr. Rosenthal and Dr. Zinn is an excellent example of the cutting edge **translational research** occurring at UAB through ongoing collaboration between physician and basic scientist directly benefits patients in the operating room.

Eben L. Rosenthal M.D. joined the UAB School of Medicine in 2001 and now is the John S. Odess professor of surgery as well as the Otolaryngology division director. His research interests include microvascular reconstruction of the head and neck, optical imaging in the OR, oncology and targeted therapy for head and neck cancer. Dr. Rosenthal received his medical training from the University of Michigan medical center followed by a fellowship at Oregon Health Sciences University.

Dr. Kurt Zinn received his undergraduate degree, Doctor of Veterinary Medicine (DVM) degree, and Ph.D. in biochemistry from the University of Missouri-Columbia. Shortly after, Dr. Zinn joined UAB in 1995. Dr. Kurt Zinn is a Professor in the Department of Radiology and a Director of the Division of Advanced Medical Imaging Research. In addition, he is a director of the Multi-Modality Imaging Assessment Laboratory and Small Animal Imaging Shared Facility.

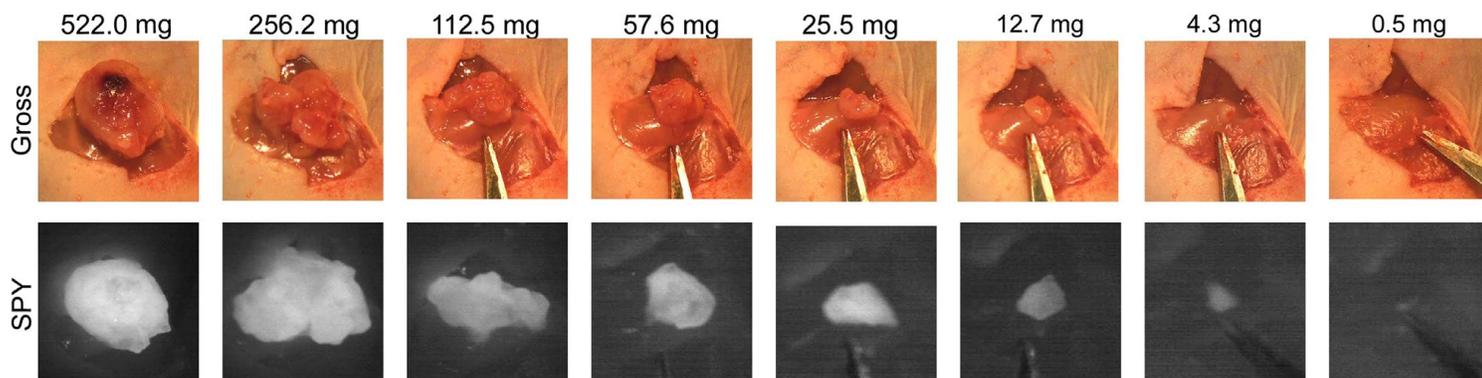


Figure: Serial tumor resection with panitumumab-IRDye800. Tumor was weighed, imaged, and resected in half until it could no longer be grossly divided. Panitumumab-IRDye800 allowed detection of the smallest fragment of tumor (0.5 mg). Note that tumor was imaged within the tumor bed to account for background fluorescence. Fluorescence decreased with decreasing tumor size, but was still greater than background with only 0.5 mg of tumor remaining.

(Adapted from Korb et. al. (05/2014). "Use of monoclonal antibody-IRDye800CW bioconjugates in the resection of breast cancer". *The Journal of surgical research.*)



Advanced Imaging Facility

TR24 Cyclotron and Radiochemistry Laboratory

Dr. Zinn has spearheaded the effort to install a cyclotron in the UAB Comprehensive Cancer Center so radiolabeled tracers for imaging purposes may be generated and delivered to patients with minimal transport time and cost. The cyclotron that now resides in the basement of the UAB Comprehensive Cancer Center is the largest in any academic research center in the United States. The close proximity of state-of-the-art PET/CT scanners and the cyclotron allow for the use of tracers that are virtually impossible for other medical centers to use including Carbon 11, Ammonia 13, and Oxygen 15. The installation of the cyclotron also allows for the development of novel experimental radiotracers that may better detect cancer in patients.

Small Animal Imaging Shared Facility

The Shared Animal Imaging Facility allows for advances in imaging animal models that will accelerate transition of treatments from the laboratory to the clinic. Equipment available in the facility include X-ray CT, microPET/CT, microSPECT/CT, bioluminescence, fluorescence, a 9.4 Tesla MRI instrument, and high frequency ultrasound imaging. These instruments have been utilized by over 85 UAB investigators conducting research on animal models of numerous diseases including cancer. ●



SPY system for imaging tumors

UAB for the Next Generations



UAB's **Community Outreach and Development (CORD)** was established to engage grade school students in the sciences. Via support from CORD and Birmingham City Schools, the Summer Science Institute (SSI) offers high school students the chance to dive into experimentation over the course of several summers. After learning about introductory experiments in their first couple summers, the students are placed into labs at UAB to perform an eight-week independent project under the guidance of faculty and staff. Students must also attend educational workshops and

scientific seminars. The interns must provide an original professional poster presentation highlighting the conducted research at the Closing Ceremony. With their summer programs motivated to encourage students to learn about science in their labs, CORD has been an important liaison between UAB and the community. Those interested in mentoring may contact Dr. Michael Wyss at jmwys@uab.edu. Please verify with your department whether you are permitted to accept a student into your lab and if any paperwork is required. ●



Visit program's website for more information

Best of luck in your future endeavors...

by ANN HANNA



Zachary Dobbin

It has been an exciting semester for the Cancer Biology Theme; four of our students successfully defended their dissertation and earned their PhD degrees.

On September 10th, **Zachary Dobbin**, the first MSTP student to graduate from the Cancer Biology Theme, defended his dissertation. Zach has worked under **Dr. Charles Landen** in the Department of Obstetrics and Gynecology focusing on chemotherapy resistant cancer stem cells in ovarian cancer. He developed a novel patient-derived xenograft (PDX) mouse model that characterizes tumor initiating cell populations and targets them for treatment.



Kyle Feeley

Kyle Feeley worked in **Dr. Scott Ballinger's** lab in the Department of Pathology on generating MNX mouse models with different genetic mitochondria while retaining their nuclear genetic background to study the effect of mitochondrial genetics on tumorigenicity, metastasis potential, and bioenergetic metabolism. Kyle has several original articles currently under review and has published in the journal Cancer Research .



Mark Stewart

Mark Stewart worked in **Dr. Ralph Sanderson's** lab in the Department of Pathology on characterizing the role of syndecan-1, which is a transmembrane heparin sulfate proteoglycan. Mark investigated the mechanism that the syndecan-1 present on the surface of myeloma cells uses to bind to normal cells in the bone marrow microenvironment and promote an aggressive tumor phenotype. Mark has published his research in several journals including Matrix Biology, PLoS One, and FEBS.

Vinayak Khattar worked in **Dr. Jaideep Thottassery's** lab at Southern Research Institute on the regulation of Csk1 protein turnover in breast cancer. Vinayak discovered that Csk1 turnover is governed by the tyrosine and lysine residues that stabilize the protein and could be modified post-translationally. Vinayak has published in the Journal of Cancer Therapy and the International Journal of Oncology. ●



Vinayak Khattar



Congratulations to the New PhD Candidates



Jason LeGrand

Entered Theme on 2011 (thru MSTP)
Thesis Advisor: **Christopher Klug, PhD**
Admission to Candidacy: March 2014



Alexander Bray

Entered Theme on 2012 (thru MSTP)
Thesis Advisor: **Scott Ballinger, PhD**
Admission to Candidacy: February 2014



Christopher Graham

Entering Class of 2012
Thesis Advisor: **Kevin Roth, MD, PhD**
Admission to Candidacy: August 2014

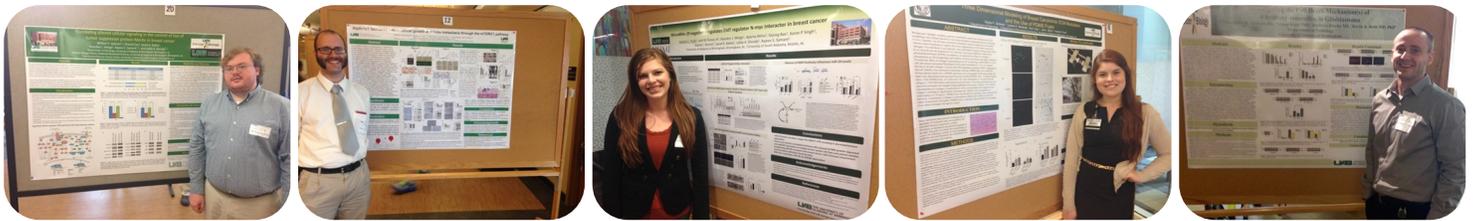
Pathology Research Day

by ANN HANNA

THE UAB Department of Pathology hosted its 10th Annual Pathology Trainee Research Day on October 10th. Graduate students, postdoctoral fellows, and medical residents within the department were all encouraged to display their research posters at the Edge of Chaos for a day full of scientific discussion. The event included two poster and two oral presentation sessions covering different topics from a wide range of fields of study. This provided a great opportunity for researchers to connect and share the latest advancements within the department.

The Cancer Biology Theme was well represented as eight of our graduate students participated in this event by presenting their research posters. Cancer Biology students

who showcased their latest research discoveries included: Ha-Ram Cha exploring the immunomodulatory role of CRAMP antimicrobial peptide in prostate cancer, Kayla Goliwas developing a model for 3D breast carcinomas, Christopher Graham investigating chemotherapy cell death mechanism in glioblastoma, William Jackson studying the role of Merlin in TGFβ/Smad signaling in breast cancer, Monica Lewis investigating roles of SIN3 scaffold proteins in breast cancer metastasis, Matthew McConnell characterizing the role of Atp6v1c1 in breast cancer metastasis, Hawley Pruitt investigating MicroRNA29 regulation of N-MYC in breast cancer, and Ann Hanna characterizing the role of hedgehog signaling in tumor associated macrophage polarization. ●



Comprehensive Cancer Center Retreat

by ABHISHEK GANGRADE

THE Comprehensive Cancer Center Research Retreat was held to provide a setting for interdisciplinary networking and to foster collaborations in cancer research. The 17th annual retreat, held at the Sheraton Hotel in Birmingham, drew faculty, trainees and staff. The theme for the retreat this year, personalized cancer care, was highlighted by outstanding presentations by renowned experts in the field. Dr. Mark Boguski of Harvard Medical School discussed the intricacies of cancer management inherent in genomics. Dr. Mark Kris of Memorial Sloan Kettering Cancer Center, presented his research linking identification of genetic traits in lung cancers with personalized

care. Dr. Donald Berry of MD Anderson Cancer Center discussed the innovative design of the I-SPY 2 Trial to determine more improved regimens against breast cancers. Dr. Paul Haluska of the Mayo Clinic presented ideas on use of mouse models for ovarian cancers. Dr. Philip Buckhaults (UAB) discussed the contribution of genetics to breast and colon cancers in African-Americans, and Dr. Christopher Willey (UAB) discussed the significance of kinomics in personalized care. Poster sessions underlining original work by UAB faculty and trainees revealed innovative research in various fields of cancer, demonstrating a promising strive to expand knowledge of the disease. ●

Kelly Kreitzburg won 3rd place for the John R. Durant Award for Excellence in Cancer Research at the Comprehensive Cancer Center Retreat. Her poster, entitled "Developing targeted therapy for the treatment of drug-resistant ovarian cancer," sheds light on the significance of the sphingosine-1-phosphate pathway in chemoresistance.



Giving back

Race for the Cure

by ABHISHEK GANGRADE

PINK adorned the ribbons, shirts, banners, tents, and the fountain water, symbolizing a sense of unity and spirit for the occasion. Since the founding of Susan G. Komen for the Cure in 1982, pink has been its color of choice. Held this year on October 11th, the **Susan G. Komen Race for the Cure** is an annual 5K run/walk held in Linn Park, Birmingham, aimed to raise funds and awareness for the battle against breast cancer. Dedicated to recognizing those lost due to the disease and to celebrating the valor of survivors, the Komen Race reminds cancer researchers of the importance of their roles. Over 11,000 participants were projected to take part in the 22nd annual event near City Hall in downtown Birmingham. 75 percent of the funds will be devoted to education, screening, and treatment programs, and 25 percent for innovative research. The event has raised nearly \$14 million for research for UAB since 2003. Several students participated in presenting posters on their research, underlining the impact of cancer research at UAB. The event certainly provides participants involved in cancer research valuable perspective of the disease outside the laboratory. Members of the public impacted by those affected by breast cancer shared their moving experiences to close the event. As survivors and supporters alike crossed the finish line with pride and glee, one feeling reigned above all: hope. ●

Run, Blazers Run!



The Blazer Bolt for Brain Cancer raised funds for the University of Alabama Birmingham (UAB) Division of Neuro Oncology research and support services for adult and pediatric patients battling brain cancer. Patients, family, and friends, joined by many UAB faculty, staffs and students, enjoyed a flat, fast 5K course through scenic Homewood neighborhoods in late autumn on Saturday, October 25th, 2014. Participants also had access to information and expertise from Dr. Pineda MD, founder of Cooking with Cancer. ●



Opportunities

The Alabama Drug Discovery Alliance: Propelling Alabama Forwards

by JOSH FRIED

The Alabama Drug Discovery Alliance (ADDA) is a partnership between the University of Alabama Birmingham (UAB) and the Southern Research Institute (SRI). The UAB Comprehensive Cancer Center (CCC) and UAB Center for Clinical and Translational Sciences (CCTS) are integral components of this partnership. The ADDA's objective is to combine the research efforts and assets of both institutions to promote drug discovery and development. This unique collaboration also provides funding and resources to researchers at these institutions, fostering exciting collaboration between UAB and the SRI. The ADDA grants UAB and SRI researchers the rare opportunity to progress their discoveries in the lab all the way to clinical trials, instead of having to sell their intellectual property to a pharmaceutical company.

The ADDA facilitates drug discovery by combining the innate strengths of the member institutions. UAB offers vast and diverse lab research and clinical knowledge along with research programs like the CCC and CCTS. Meanwhile, SRI lends its expertise in molecular target identification, high throughput screening (HTS), protein crystallography, medicinal chemistry, lead optimization, and other aspects of drug development. The combined efforts of these institutions ensure that crucial scientific findings in the lab go through all four major stages of drug development. While UAB provides the first (lab research) and fourth stages (clinical trials), SRI provides the second (drug discovery) and third (drug development). Both these organizations are spearheaded by excellent leaders, each bringing their unique expertise to drug discovery operations. SRI drug discovery activities are coordinated under stellar leadership of Dr. Mark Suto (VP, Drug Discovery Division), whereas Dr. Maaïke Everts (Research Project Director, ADDA; Associate Professor, UAB) oversees the ADDA affairs.

Developing a drug is costly, time consuming, and can also be rife with legal struggles. The ADDA furnishes support to researchers to minimize these difficulties. The ADDA provides funding to worthy projects. In addition, the faculty at SRI have years of expertise to help guide projects from conception to completion. SRI also has a

proven track record of successfully developing drugs, boasting seven FDA approved drugs with many more currently in development. Additionally, the ADDA imparts assistance in managing researchers' intellectual property through UAB's Institute for Innovation and Entrepreneurship. In addition to the scientific aspect of this organization, their outreach activities include educating researchers about the drug development process through a series of lectures and symposiums held at UAB.

The ADDA in partnership with the CCC, UAB Center for Emerging Drug Discovery, and CCTS bestows pilot funding to researchers in the form of two year grants providing \$50,000 per year. The grants can be used to support projects located anywhere in the drug development pipeline. If a project is awarded a grant, the ADDA will arrange a team of experts to help guide the project through the drug development process. Projects are not only judged on their science, but also potential for commercialization and marketability as a drug.

There are currently several funded projects ongoing in the ADDA. These projects cover several different research fields and clinical needs. Areas with currently funded ADDA projects include, respiratory illness, central nervous system and oncology. For example, some of the funded projects are: LRKK 2 inhibitors (Dr. Andrew West, Neurobiology), TXNIP inhibitors (Dr. Anath Shalev, Diabetes), and TSP-1 inhibitors (Dr. Joanne Murphy-Ullrich, Oncology).

In all the ADDA, ensures that investigators retain ownership over scientific ideas from their conception in the lab to their eventual translation to potential drugs that will be used to cure devastating diseases. The resources administered by the ADDA assist investigators in managing the non-scientific aspects of drug discovery, allowing them to better focus their efforts on the scientific aspects of the project. This partnership has and will continue to foster both the scientific and the economic growth of Birmingham and Alabama. ●



Dr. Mark Suto



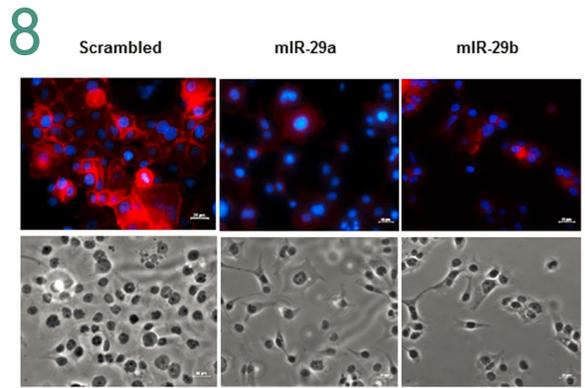
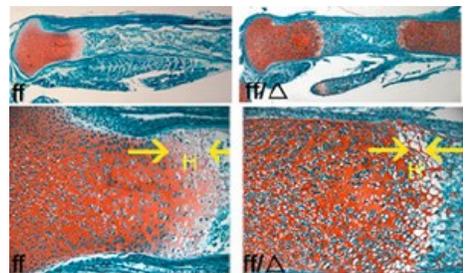
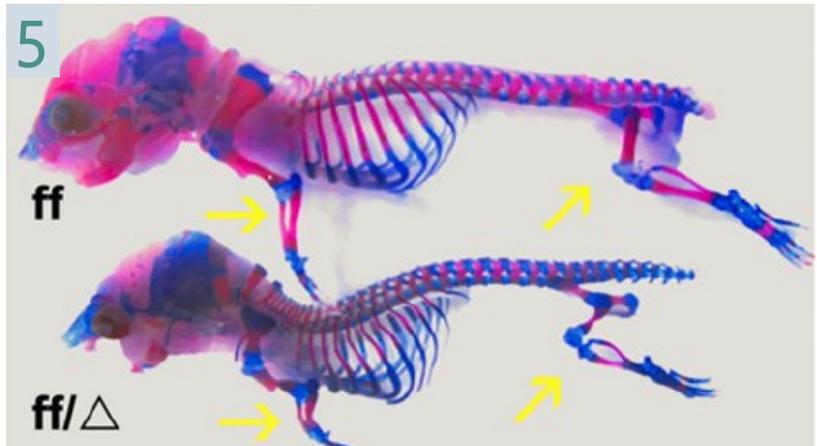
Dr. Maaïke Everts



The Celebrated Authors

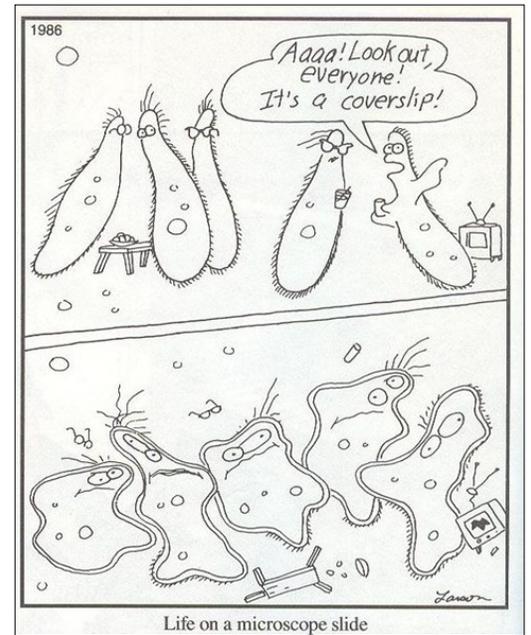
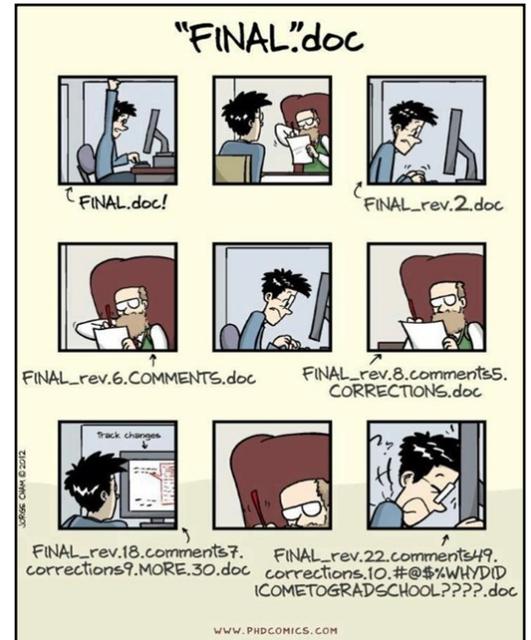
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From our publications:



#justphdthings

by ANN HANNA



Fun Fact :-)

Scientists at California Institute of Technology have been able to develop a technique that makes mice and their organs "see-through". The technique involves flushing chemicals through the dead mouse's body which make its internal organs block light and allow it to appear translucent. The original research was published in *Cell*. PMID: 25088144