Cancer Research Center

Annual Report 2015
Volume 12 Issue 1

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CRC

A private, non-profit organization since 1962
At CRC, we are searching every day for a healthier tomorrow. Our extensive cancer research is funded in large part by the citizens and businesses of central Missouri who desire a solution to this devastating disease. Because of the extensive cancer research that is being performed all over the world, including right here in Columbia, we are going way beyond poisoning, radiating, and cutting out cancer cells. We are developing procedures to stop cancer before it ever starts and researching innovative treatments to avoid destroying healthy cells.
Message from the Director

As I look back on the past year I am filled with excitement for all we have accomplished. The CRC staff, volunteers, and Board members have played a diligent roll in our progress and are maintaining this momentum for even more success in the coming year.

Each member of the CRC staff has a talent and they all intermingle to create an efficient and effective team. Regardless of the areas in which we each excel, we share a common goal of improving the situation for cancer patients. Our current research is showing great promise in a new treatment for cancer. Our therapeutic Salmonella strain has proven to be effective against prostate and other types of cancer, and now appears to be a possible therapy for pancreatic cancer. Read more about our current research and the newest work on pages eight through 14. See how we are working to treat cancer without making the patient feel miserable.

A secondary mission for CRC is our Roma Eisenstark Scholars Program. As an example of his love for research, Dr. Abe established this fund. Due to his own generosity, students come to our laboratory and are given a research project of their own. They are graduate students, undergraduate students, and even high school students. Many of them continue to make important discoveries as career cancer researchers. Read about these talented young scientists on pages 15 through 17.

This research would not be possible without funding. The various individuals, foundations, organizations and businesses that give to CRC make the research possible. Many donors and volunteers come together with Jack Bozarth once a year to plan and execute the Jim Kidwell Memorial Gala. Without them, the evening would not be a success. The 2015 event honored Bill Powell, an accomplished attorney and Missouri Tigers Football legend. See pictures and read about this event beginning on page 20.

Behind every successful organization is solid leadership, and CRC is no exception. Our Board of Trustees is a diverse group of individuals who donate their time, expertise, and financial resources to our mission. They truly have CRC’s best interest at heart and are dedicated to helping CRC move the Salmonella bacterial therapy from the laboratory bench to the patient bedside. We cannot thank them enough for their dedication.

Whether donating to the Jim Kidwell Memorial Gala, responding to our annual mailing, or sending a memorial or tribute to a loved one, the dollars given to the Cancer Research Center are spent in our laboratory in Columbia, Missouri. With your help, we will one day be treating cancer without poisoning the patient. Thank you for your generosity in supporting our work.

With gratitude,

Marnie H. Clark
Administrative Director
**Meet the CRC Staff**

**Abraham Eisenstark** is the Research Director of the CRC. Previously, he was a Byler Distinguished Professor and Director of the Division of Biological Sciences, University of Missouri - Columbia. He has served as Program Director of the Molecular Biology Section, National Science Foundation, Washington, DC. His career includes years of collaborative research at other institutions, including universities at Copenhagen, Denmark; Leicester, England; Paris, France; Leiden, Netherlands; and Brookhaven National Laboratories. He is a native of Kansas City, MO. He received his BS, MS, and PhD. in Microbiology from the University of Illinois. He is married to the former Joan Ragsdell of Columbia and is the father of three children.

**Marnie Clark** is the Director of the CRC and has been with the organization for more than 18 years. She has served as Development Director from 1994 to 1999, and was a member of CRC’s Board of Trustees from 1999 to 2001 while working at William Woods University. She has extensive experience in public relations and association management. Marnie is a member of Columbia Metro Rotary, Fraternal Order of Eagles Auxiliary, Columbia Elks Lodge and Cosmopolitan Luncheon Club. She is an active member of the Columbia Chamber of Commerce where she has Chaired the Chamber Ambassadors, as well as various committees. She was a 2003 recipient of the 40 under 40 in Columbia Award and is a graduate of Leadership Columbia. She earned a BFA degree from William Woods College. Marnie lives in Fulton with her husband Michael. They have four children.

**Jack Bozarth** is the Director of Development at the CRC. He is responsible for fundraising and public affairs. He is a retired Air Force Officer who was the Public Affairs Officer for the Commissioner of Military Affairs of the state of Alaska. He graduated from the Defense Department’s Defense Information School with honors. He is married to the former Ann Freese of Columbia and has three children and four grandchildren. Jack was born in Kansas City and raised in Raytown, Missouri. He is a graduate of Central Missouri State University and was awarded a MS degree by Embry-Riddle Aeronautical University. He is a member of the Columbia Elks Lodge No. 594, Missouri Aerie 2730 of the Fraternal Order of the Eagles, and Twilight Lodge No. 114 AF&AM.

**Alycia McGee** is the Executive Assistant and joined the CRC team in July of 2008. She is dedicated to managing the database, photographing special events and lab research projects along with designing the Annual Report and advertisements throughout the year. She was born in Mexico, MO where her father still resides. She graduated from Centralia High School and earned her Bachelor’s degree at Columbia College in Columbia. Through the years, she found her passion for photography after the loss of her mother to breast cancer. Since then, she has worn the hats of an artist, a photographer and an office manager and is proud to combine all of her talents at the Cancer Research Center. She resides on a quiet little street in southern Columbia.
Jacki Kian Mehr was born and raised in Jefferson City, MO. She is the youngest of six children. Jacki attended Jefferson High School and graduated in 1984. While in high school, she worked on a research project on embryo transfer. Jacki attended CMSU and there she met her husband of 30 years. They have four girls ages 29, 27, 14 and 12 and two grandchildren ages 6 and 2. Along with being a homemaker, Jacki was an advocate for the disabled. Since then she has returned to her love of research at the Cancer Research Center.

Alison Fea is the Senior Technician and Laboratory Manager of the CRC. A New Jersey native, she attended Stephens College in Columbia prior to joining the CRC in 2002. During her time as an undergraduate, she served as the Chemistry Laboratory Assistant for the college’s Natural Science Department and served as an officer in several honor societies. The summer of her junior year she was elected to Sigma Xi, the Scientific Research Society, for her HIV-1 research work when she was an infectious disease intern in Galveston, TX. She graduated Magna Cum Laude from Stephens in 2002, with a BS in Biology and a minor in Chemistry. She is the eldest of three; her family now resides in Lawrence, KS.

Dr. Robert A. Kazmierczak came to CRC as the Raymond W. Freese Fellow. He now serves as Senior Investigator. He received his BS in Bacteriology at the University of Wisconsin, studying regulation of Vitamin B12 production by Salmonella enterica (serovar Typhimurium) and interning at Upjohn Pharmaceuticals. He earned a MA and PhD in Microbiology from the University of Illinois, during which time he held an NIH Cell and Molecular Biology Training Grant Fellowship to research chronic viral infections. He later studied at Washington University in St. Louis. At the CRC he is conducting research to characterize and develop therapeutic Salmonella enterica as a treatment for prostate cancer.

Dr. Bakul Dhtagat Mehta joined CRC as the Raymond W. Freese Fellow in October, 2012. Bakul earned her PhD degree in Biochemistry from Michigan Technological University, Houghton, MI. She graduated with a Masters of Science in Chemistry from India. Currently, here at the CRC, Bakul is studying protein interactions that occur between therapeutic Salmonella and their target human protein prostate cancer cells in order to understand the underlying mechanisms responsible for Salmonella’s targeting towards cancer cells. Bakul lives in Columbia with her husband Ravish and two children, Gauri and Meera.
Reaching out to the Community

Thank You, Rita Doten for designating the proceeds of your Cancer Fun Day Event in Florida to CRC.

On behalf of CRC, Senior Investigator, Dr. Robert Kazmierczak accepts a check from Grand Madam President-Elect Penny Skinner in the amount of $30,000 at the Fraternal Order of Eagles National Convention.

Thank you for your generous gift of support!

Ashley Jones-Kaufman, Jerry Zimmerman and Marnie Clark visit at the Missouri State Employee Charitable Campaign kick-off in Jefferson City.

Our many thanks to Missouri Employers Mutual’s Community Involvement Committee for supporting our continued success in researching the cause and effects of cancer. Yolanda Burnett presents a check to Jack Bozarth at the CRC laboratory.
Message from the Research Director

Good News:
Cancer deaths in the USA continue to decline. The decline is 1.8% each year. To the relatives and friends of the recovered, we share your joys! Our sincere condolences to family and friends of the less fortunate.

Not the Best News:
Scientists everywhere, including ours at CRC, are frustrated that we have yet to find the magic bullet that would result in perhaps an 80% drop in cancer deaths within the next decade but we are trying hard, and we are proud of our promising and hopeful recent discoveries. But hold on! There is a more optimistic promise!

CRC Is Vigorously Pursuing This Goal:
As reviewed elsewhere in this Annual Report, we are continuing to use genetically engineered bacterial organisms to destroy tumor cells without harming normal cells. There is a sharp optimistic turn among scientists, based in part, on experimental activities in our CRC labs [see Dr. Kazmierczak's research in the following pages]. Note particularly our improvements in our Salmonella tumor-seeker and tumor destroyer. Note also that our tumor destroying cargo will include the venom genes of rattlesnake and the toxin genes from a Brazilian bacterium. Also, by use of super computer bioinformatics, we are identifying critical tumor involvement genes. Finally, the hottest item in cancer therapy out there that is getting a lot of public press is CRISPR TECHNOLOGY, a candidate for the Nobel prize that allows the editing and deletion of one identified tumor gene at a time.

My personal joy is to witness the enthusiasm of the various CRC participants as we pursue this goal. First, there are the researchers who design and execute each facet of our cancer experiments. It is a pleasure to share their passion and determination as they observe the destruction of cancer cells. In support of the day-to-day bench research, CRC is fortunate to have a devoted administrative staff and Board of Trustees.

A third component in our mission to reduce cancer mortality and morbidity is the financial support we receive from our many donors. Thank you, generous supporters!!! You are, indeed, a vital factor in our research progress.

In addition to our in-house research, CRC is always proud of its student scholarship program. As in the past, our high school and college undergraduate trainees, with their passion for careers in cancer research, are destined for positions in the best laboratories. Note their faces in the Scholars to Scientists section of this Annual Report.

As a special note: We are fortunate to have some of the brightest High School students as interns in our lab, thanks to Pam Close. Pam has been named the top science teacher for the State of Missouri. I remember the teachers from my youth. Pam's students who interned in our lab are now also on their way to finding cures for cancer.

Thank you so much for your continued confidence in our experiments aimed at reducing cancer mortality. With our best wishes for your good health, including that you will be cancer free.

Abraham Eisenstark
Byler Distinguished Professor, Univ. Missouri [emeritus]
Our current cancer research focuses on three topics:

1) **Early Detection.** Cancer detected early is easier to treat and almost always results in complete recovery.

2) **Targeted Treatment.** If you can target cancer-killing drug therapies so they invade tumors but not healthy tissue, you can concentrate powerful, effective drugs at tumors using smaller chemotherapy dosages, killing the cancer while minimizing or eliminating the unwanted side effects of chemotherapy.

3) **New, Effective Chemotherapy.** Although different types of cancer result in the same problem (uncontrollably growing tumors), each cancer type in the body is different and reacts differently to anti-cancer drugs. Discovering new and powerful drug combinations to treat the many types of cancer is critically important.

Research Report: Recruiting Effective Anti-Cancer Compounds For Delivery by Cancer Targeting, Tumor Infiltrating *Salmonella*

Our research in 2015 paves the way for bringing *Salmonella*-based bacterial cancer targeting therapy or “*Salmonella* bacteriotherapy” to the cancer clinic. Our genetically modified, non-toxic *Salmonella* specifically target, infiltrate, and persist in mouse, canine, and human tumors but not normal, non-cancerous cell tissues. We have engineered our cancer-targeting *Salmonella* to carry or generate anti-cancer drugs that cannot target cancers directly to maximize their cancer killing effects while minimizing the unwanted side effects on non-cancerous tissues.

We are expanding our current treatment efforts on prostate cancer, breast cancer, and melanomas to include pancreatic cancer and blood cancer (leukemia). Alison Fea has spearheaded the effort to use our therapy to target pancreatic cancer, which you can read about later in this annual report. We are also working with the Veterinary Oncology department at the University of Missouri to treat B cell leukemia in dogs.

Working through the 2015 spring, summer, and fall, we concentrated on three different research projects with the same overarching goal: To put an effective *Salmonella* cancer targeting therapy into the clinic to eliminate cancer. Here are the relevant details of our progress this year.

**Spring 2015: Using *Salmonella* Bacteriotherapy to Successfully Target Canine Leukemia.**

In our last Annual Report, we announced the start of our collaboration with Dr. Jeffrey Bryan and Dr. Carolyn Henry in the University of Missouri Veterinary Oncology department. This partnership enabled us to expand our animal testing to include canine (dog) cancer models. Our first goal for testing *Salmonella* bacteriotherapy in dogs was to test how effectively our tumor-targeting *Salmonella* targeted and killed cancer cells typically found in dogs. Once we confirmed that our therapy effectively targeted and killed cancers found in dogs, we could then proceed to establish a clinical treatment program for dogs that are diagnosed with cancer at the veterinary clinic.
In the spring of 2015, Dr. Kazmierczak and University of Missouri Discovery Fellow Caroline Dunn successfully demonstrated Salmonella-mediated killing of canine leukemia (blood cancer) B cells at the Cancer Research Center. Caroline presented the preliminary findings at the Life Sciences Undergraduate Research Opportunity Program (LSUROP) in July of 2015 (Figure 1) and this data is currently being prepared for publication in scientific journals.

Summary: In 2015 we successfully killed canine leukemia cells in the lab using therapeutic Salmonella. In 2016 we are partnering with the Veterinary Oncology department for preparing clinical tests of our Salmonella bacteriotherapy in dogs diagnosed with leukemia at the University of Missouri veterinary clinic. This will enable us to determine therapeutically effective dosage levels in mammals similar in size to human patients.

Summer 2015: Demonstrating Long-Term Safety of Tumor-Targeting Salmonella at the Genetic Level

Our previous animal model studies demonstrated the safety of our Salmonella bacteriotherapy. In the summer of 2015 we began a project that analyzes the genomic DNA of our non-toxic bacteria that have already successfully targeted and colonized prostate cancer in our mouse models for up to three days in order to definitively show that they remain non-toxic and safe at the genetic level. This safety analysis is essential for us to get permission to use our therapy and drive acceptance of our therapy in the human cancer treatment clinic. When we prove the safety of our clinical treatment at the genetic level, physicians are more likely to partner with us to use our cancer therapy to help patients, whether they be dogs suffering from leukemia up to human patients who need targeted cancer therapy.

To speed up the genetic analysis process, Dr. Kazmierczak and University of Missouri Biological Engineering undergraduate, Duy Nguyen, teamed up with Dr. Aaron Best, the Harrison C. and Mary L. Visscher Professor of Genetics, at Hope University, Michigan. Dr. Best has already been of great help to the Cancer Research Center by assembling the genetic sequences of the Salmonella extracted from prostate tumors, and additionally providing training resources for personnel at the CRC to do their own analyses.

Genetic sequence analysis is a rapidly advancing area of science and it is very easy to become overwhelmed by the gigabytes to terabytes of data that modern genetic analysis produces. However, with Dr. Best’s guidance, we are tracking and analyzing each of Salmonella’s 4000+ genes to demonstrate the safety and efficacy of our non-toxic, tumor-targeting Salmonella before, during, and after our therapy has completed.
Summary: Genetic analysis of our non-toxic, tumor-targeting *Salmonella* before and after invasion of tumors will definitively show efficacy and safety of our cancer targeting therapeutic.

**Fall 2015: Using Bacterial Cancer Targeting and Tumor Infiltration as a Delivery System for Known Cancer Killing Drugs**

Regular injections of *Salmonella* bacteriotherapy alone into our prostate cancer mouse models, which have been genetically designed to develop prostate cancers (Figure 2), reduce the size of these prostate cancers by more than 30% in under 4 months. In the Fall of 2015, we submitted these findings for publication in the scientific journal PLOS One.

In order to get complete cancer remission using our *Salmonella* bacteriotherapy, we are investigating what other anti-cancer therapeutic drugs, specifically ones that cannot target tumors on their own, would be most effective when delivered using our cancer targeting *Salmonella* bacteriotherapy.

We have previously engineered *Salmonella* bacteriotherapy to carry or synthesize anti-cancer drugs that cannot specifically target tumors. By targeting and concentrating these drugs at the tumor site, we expect to amplify their anti-cancer properties and reduce the amount of unwanted side effects that would occur if they were allowed to accumulate throughout the patient’s body without tumor targeting. The ability of *Salmonella* bacteriotherapy to infiltrate throughout the tumor mass gives our therapy an advantage over other therapies, as it can deliver carried anti-cancer drugs evenly throughout the tumor mass, ensuring a uniform, clinically effective dosage.

In the fall of 2015, Dr. Kazmierczak continued our testing of Violacein, a chemotherapeutic with anti-tumor properties that has been isolated from sources in the Amazon. Our *Salmonella* can overproduce this characteristically deep violet anti-tumor chemical (Figure 3) and we are in the process of determining if the combination of *Salmonella* and Violacein kills human tumor cells in a synergistic fashion – better together than individually. Initial testing shows that Violacein does kill our human prostate cancer cells and we are planning work in 2016 to determine the optimal dosage levels for use of this potent chemotherapeutic.

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**Figure 2.** Stained cross section of mouse seminal tube (pink circle) invaded by prostate cancer (purple mass). Alone, our *Salmonella* cancer therapy shrinks these tumor masses by a third or more. We expect to eliminate these tumor masses entirely using the *Salmonella* combination cancer therapies discussed.

**Figure 3.** *Salmonella* bacteriotherapy strain CRC2631 genetically engineered to produce Violacein chemotherapeutic (Violet).
Additionally, animal-derived venoms have been in the cancer research news lately, and the Cancer Research Center is involved. In the fall of 2015, Dr. Eisenstark and Dr. Kazmierczak established a partnership with Dr. Elda Sanchez at the National Natural Toxins Research Center at Texas A&M to deliver Mohave rattlesnake snake venom to tumors using our *Salmonella* cancer-targeting therapy. This snake venom, called r-Mojastin1, is highly effective at inhibiting human pancreatic cancers from spreading, a primary target of our anti-pancreatic cancer research. In 2016, we will re-engineer our cancer-targeting *Salmonella* to make this chemotherapeutic and evaluate its anti-cancer effects on prostate and pancreatic cancers.

**Conclusion:**

In 2015, we have successfully shown that our *Salmonella* bacteriotherapy targets and kills canine leukemia cells, allowing us to continue our partnership with the University of Missouri Veterinary Oncology department for eventual clinical treatment of canines with leukemia. This important step allows us to prove safety and clinical effectiveness of our cancer targeting *Salmonella* bacteriotherapy in large mammals.

Our genetic analysis of *Salmonella* bacteriotherapy before and after successful targeting and invasion of prostate cancers in our mouse cancer models is essential for showing the safety of our therapy and will ensure acceptance of the therapy in veterinary and human cancer clinics.

Finally, we have begun synthesizing and delivering proven anti-cancer drugs that cannot target cancer cells on their own using our cancer targeting *Salmonella* bacteriotherapy. Carried by our cancer targeting *Salmonella*, this ensures delivery of the potent anti-cancer drugs to tumor sites without non-specific targeting to normal, non-cancerous tissue. Our initial tests in 2015 focused on showing that these anti-cancer drugs are still effective when delivered using our tumor-targeting *Salmonella*. Once effectiveness has been established, we can then proceed to test them in animal models.

We eagerly look forward to continuing the development of cancer-targeting *Salmonella* bacteriotherapy in 2016 and are immeasurably grateful for your support.

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**Recent Publication Submissions by Cancer Research Center Scientists**

*Salmonella* bacterial therapy reduces autochthonous prostate tumor burden in the TRAMP mouse model.  
Authors: Robert A. Kazmierczak, Bettina Gentry, Tyler Mumm, Heide Schatten and Abraham Eisenstark  
Journal: PLOS One

Strains, mechanism and perspective: *Salmonella*-based cancer therapy.  
Authors: Cheng-Zhi Wang, Robert A. Kazmierczak and Abraham Eisenstark  
Journal: International Journal of Microbiology  
(In Press)

Solar Ultraviolet Radiation and ROS: Observations from Studies with Bacteria  
Authors: Abraham Eisenstark and James Hoerter  
Book Title: Reactive Oxygen Species in Biology and Human Health  
Volume Editor: Shamim Ahmad.  
Book Publisher: Taylor & Francis Group

Life in Science: Abraham Eisenstark  
Bacteriophage  
www.ncbi.nlm.nih.gov/pmc/articles/PMC4116385/
CRC2631 Takes on Pancreatic Cancer
By: Alison Fea

A cancer diagnosis is life altering enough but a pancreatic cancer diagnosis is downright terrifying and rightly so. The National Institutes of Health report that from 2005-2011, the most current data available, that the 5-year survival rate for pancreatic cancer was 7.2%. By comparison, the 5-year survival rate for female breast cancer over the same period was 89.4%. To put these rates in perspective, the lifetime risk of a woman developing breast cancer is 12.3% and female breast cancer makes up 6.8% of all cancer deaths, while the lifetime risk of developing pancreatic cancer for men AND women is only 1.5% (8x less) yet the disease makes up a nearly identical 6.9% of all cancer deaths.

A 89.4% 5 year survival rate for breast cancer among women speaks to the great strides that have been made in cancer treatment in the last couple of decades. However, pancreatic cancer patients have largely failed to benefit from these advances. Pancreatic cancer remains something of an “orphan disease.” Receiving far less funding and attention than most other cancer types and current treatments (chemotherapy, radiation & surgery) are often unable to gain the upper hand against this swift moving cancer. At the Cancer Research Center we find this disparity in research efforts and treatment tools a call to action.

Thinking back over our successes with melanoma, prostate, breast and colon cancer we realized that our therapeutic Salmonella strain CRC2631 might just be what the pancreatic cancer treatment field has been waiting for. To put CRC2631 to the test we first chose two pancreatic cell lines to serve as a test model for how a patient’s body would react to this developing treatment. The first cell line, PANC-1 is a normal pancreas duct cell line and the second hTERT-HPNE, is a cancerous pancreatic duct cell line.

The first hurdle CRC2631 needed to clear as a viable pancreatic cancer treatment was to demonstrate an ability to invade pancreatic cancer cells while differentiating cancerous cells from normal cells. To do this, a pilot study was conducted in which normal and cancerous pancreas cells were incubated with CRC2631 for 30 minutes and two hours to allow the therapeutic Salmonella the opportunity to invade the pancreas cells. After the designated time had elapsed the media was removed, the cells were washed and new media containing the antibiotic gentamicin was added. After incubating for an additional 40 minutes the antibiotic media was removed and the pancreas cells were broken open, serially diluted and plated.

In this elegantly simple system, the antibiotic kills all therapeutic Salmonella that are not “safely” inside a pancreas cell at the end of the incubation. Therefore, when the pancreas cells are broken open and the cell slurry is diluted and plated, any bacterial colonies that grow overnight are derived from therapeutic Salmonella that have successfully invaded. A series of controls and standards allows us to use these colony counts to calculate the percentage of the bacterial population able to successfully invade the pancreas cells.
Reviewing the data from the invasion assays revealed several familiar patterns illustrated in the figure below. The first pattern to emerge was the invasion of normal pancreas cells (blue) by CRC2631 levels off between 30 minutes and 2 hours. This is a very good sign that there is nothing actively attracting CRC2631 to the normal pancreas cells. This also fits with what we observe in successful time course experiments with other cancer types. With certain cancer types, melanoma for example, we observe an initial attraction and a small reduction in the number of normal cells and then CRC2631 “loses interest” and the normal cell population rebounds.

The second familiar pattern was the invasion of pancreatic cancer cells (red) by CRC2631 increases two fold between the 30 minutes and 2 hours. This a very good sign that the cancer cells have attracted CRC2631’s “attention.” The increasing invasion of CRC2631 into the pancreatic cancer cells over time fits with the progressive targeting and killing we have observed in time course microscopy experiments with other cancer types.

The final familiar pattern is the invasion percentages themselves are similar to those we have seen with other cancer types. This is a good indication that CRC2631 will successfully target pancreatic cancer cells just as it has successfully targeted the other cell types we have tested.

The next hurdle in our quest to hone CRC2631 into a viable pancreatic cancer treatment is to demonstrate its pancreas tumor targeting prowess in a time course microscopy study. In this study, CRC2631 will be incubated with normal and cancerous pancreas cells over 24 hours and samples taken at regular intervals to provide snapshots of the interaction. The appearance of the pancreas cells (indicates cellular health), where the Salmonella chooses to congregate (shows targeting) and changes to the cell population size over time (killing or growth) will provide much insight into the efficiency of CRC2631 as a pancreatic cancer treatment.

Each time we expand the range of CRC2631 as a therapy to a new cancer type we are standing on the shoulders of all we have learned thus far. In this way, even though pancreatic cancer is an uncharted territory we are not without a North Star. The Cancer Research Center is very grateful to our generous donors for providing the funding that allows us to continue to explore and build on our successes as we close in on the ultimate goal of sharing CRC2631 with the world as a non-toxic cancer treatment.
Discovering New Communication and Tumor Destruction Mechanisms
By: Dr. Bakul Dhagat-Mehta, Raymond Freese Fellow

Followers of our research may recall that we are trying a multifaceted approach to understand how our therapeutic strain of bacteria specifically targets, infiltrates, and persists in mouse, canine, and human tumors but not normal, non-cancerous cell tissues. Our approach takes full advantage of the latest DNA, RNA, and protein analysis techniques towards understanding this mechanism.

In 2008 a group of scientists (Nabil Arrach, et al) reported that specific Salmonella gene promoters were preferentially activated inside tumors. Promoters are a region of DNA (gene) that initiates expression of protein coded by that gene(s). Assisted by our students Bethanie and Nathan, we have constructed tools for some of these genes that would help us over-express the proteins that are coded by these genes. Since these promoters are known to be activated in tumor tissue we predict that the genes that they initiate may have a role in Salmonella’s targeting mechanism. Now that we have confirmed overexpression of the desired proteins with the help of these tools, we are in the process of determining if overexpression of these proteins would influence our therapeutic bacteria’s ability to target cancer cells.

In the last annual report we mentioned exploring proteomic tools like Mass Spectrometry (MS) in order to get insight into Salmonella’s targeting of prostate tumor cells. With the help of MS, we have discovered proteins that are differentially expressed in Salmonella treated cancer cell lines as opposed to normal cell lines. Currently, 2-dimensional SDS-PAGE, a form of protein separation procedure commonly used to analyze protein mixtures on basis of two properties in two dimensions and its analysis are in progress. This is for confirmation of the differentially expressed proteins that have been previously identified by mass spectroscopy. Along with this, we are simultaneously working to develop tools that can control the expression (production) of these proteins in vitro, thus enabling us to determine if they would influence the invasion and/or targeting of Salmonella towards cancer cells that are grown on plates. This proteomic analysis has helped us identify cancer proteins that might be potential targets of bacteria, and the global analysis of protein alterations can help understand a drug’s (in our case Salmonella) mechanism of action. After we have confirmed that these proteins are involved in cancer targeting at the cell culture level, our next step would be to move on to animal model.

Summary:
In the coming year we will look at the bacterial (Salmonella) proteins to determine if they influence our therapeutic bacteria’s ability to target cancer cells. We will also evaluate effects of differentially expressed prostate cancer cell proteins specifically on invasion and killing of cancer cells by Salmonella. Between these two approaches we hope to potentially identify new molecular targets that could be optimized for improved bacterial targeting of prostate cancer.
Training the Next Generation of Medical Researchers

In addition to our primary focus on developing novel cancer therapies and moving them to the clinic, CRC researchers devote significant time to train and mentor talented students to become the next generation of medical researchers. Students that have had a research “apprenticeships” at the CRC have become cutting-edge researchers in the scientific fields of genetics, biochemistry, bioengineering and nanotechnology. Not only are we proud to have played a role in the beginning of our students’ professional development, many of these fully-trained researchers are eager to collaborate with the CRC in the search for better cancer therapies. We are happy to share some of the research progress of our students.

Caroline Dunn

was born in Houston Missouri to Tom and DeeDee Dunn. She is entering her sophomore year at Mizzou where she is pursuing a degree in biology with the intention of working in research and perhaps a professorship at a university in the future. Her time at Cancer Research Center was her first exposure to scientific research. She tested the CRC’s therapeutic Salmonella on canine cell lines. She has learned a lot in the past year and will continue to do so in lab classes, and in her extra curricular activities which include tutoring, science clubs, and art clubs.

She is now studying bacterial morphology under Dr. Pamela Brown at Mizzou.

Allegra Kerns

from Columbia, Missouri was accepted into the Roma Eisenstark Student Scholar Program in the summer of 2015. She is a senior at Hickman High School. Allegra plans on attending a university and working toward a degree in biology, however she has not yet decided where she will study. She plans to then continue her education by attending medical school. Allegra is a very well rounded student taking part in choir, school musicals and volunteering clubs as well as being a member of the National Honors Society and the varsity dance team while maintaining a 3.5 grade point average. Allegra says she is extremely thankful to have been accepted into the Eisenstark Student Scholar Program. While studying at the Cancer Research Center, Allegra has learned lab procedures, lab safety and research standards. Her work has been evaluated by Dr. Eisenstark and awarded a grade and three hours of credit toward a microbiology or chemistry degree at UMC.

Duy Nguyen

Duy is a senior at the University of Missouri studying bioengineering. He was born in Ho Chi Minh City, Vietnam and immigrated to Kansas City in 1999. His current research at the Cancer Research Center involves sequencing of several Salmonella strains and using bioinformatics to compare their genomes with one another. With this knowledge, we will be able to identify if there are any genetic changes before, during, and after tumor invasion.

Duy chose to intern at the CRC as he has always seen bacteria and viruses as a necessary part of life. While public perception may view them as negative, he tends to see all of these microorganisms as having the potential to be life saving. Discovering that the CRC used bacteria to achieve a curing effect was something that he had never heard of but always knew was possible. With his background in bioengineering, he hopes to apply the skills he has attained at the CRC to further his future goals of research and development in an industry setting.
Over the years a multitude of young researchers have launched their careers through the Roma Eisenstark Student Scholar program at the Cancer Research Center. This unique hands on program gives talented high school and undergraduate students the opportunity to gain laboratory skills and participate in real research projects. Summer student scholars receive a stipend and during the school year arrangements are made for student scholars to receive class credit for their work and required semester manuscript.

Overwhelmingly, the students participating in this program are undergraduates in their second or third year of college. That just seems to be when interest, drive and maturity combine to produce the concentrated talent, dedication and passion needed to fuel the success of a young researcher in a working laboratory. However, some students are just ahead of their class.

One such student, Allegra Kerns, joined the CRC as a Roma Eisenstark Student Scholar in the summer of 2015 after her talent caught the eye of award winning Hickman High School science teacher Pam Close. Pam approached the CRC looking for a research experience for an exceptional Hickman student eager to learn research skills. We had no idea just how exceptional.

Over the summer of 2015 Allegra’s skills grew by leaps and bounds as she learned laboratory safety, sterile technique and basic microbiology with flying colors. Before the summer was out she was integrated into an ongoing research project working alongside CRC research technician Jacki Kian Mehr. The two became fast friends as they spent the summer surveying bacterial DNA for the presence of genes related to competition and survival. This would have been impressive enough had Allegra not also been dancing at 7am, attending a competition dance team camp and attending practice for multiple roles in PACE Youth Theatre Company’s production of Legally Blonde the Musical. As a featured dancer she treated the audience to a nine minute jump rope solo. That is about 100X more jump roping than her labmates have done. Ever.

High school students have much less control over their schedules and as a result CRC almost always says goodbye to their high school students after the summer. So, once school started in the fall we expected Allegra would have to leave the lab and go back to class. However, we were excited to find that she was able to arrange her schedule to be able to come to the CRC and continue her research for course credit!
Just as it did in the summer, Allegra’s day starts early. When most of us are hitting snooze she is hitting the dance floor for a 7am dance class. Then it’s off to the Career Center for her “Biomedical Innovations” class, a Project Lead the Way national STEM initiative class at the Career Center. Then it’s off to the lab to work with Jacki on the day’s microbiology project before going to Hickman for the rest of her day’s classes. After an hour’s break it’s back to school for play rehearsals. Early days, quitting time is at 8pm but on basketball game nights dance team practice courtside calls her name till 10pm. If that weren’t enough she is also the president of Trireme, a senior girls volunteer group at Hickman, where she organizes and participates in service projects around the community.

While Allegra has outstanding parents who are very supportive, her drive is most definitely internal. We have had enough students pass through the lab doors to know the difference. No one is prodding her to do any of this. She is naturally curious, ambitious and driven. She is also a joy to work with, always smiling and up for whatever challenge comes her way. Allegra is perkier in the lab after a 7am dance class that most of our undergraduates are at noon. Quite frankly it’s amazing, but you won’t hear it from her. She is down to earth and seems a little surprised when someone complements what is apparently just Allegra being well, Allegra. As a senior this year, currently applying to colleges and with aspirations to be a pediatric thoracic surgeon we know we don’t get to keep Allegra forever. However, we are having a great time mentoring her to the next great thing while she is with us as a Roma Eisenstark Student Scholar.
Catching up...

Kelly Edwards

CRC had the pleasure of visiting with one of their own this summer. Dr. Kelly Edwards stopped by with daughter, Olivia and grand-daughter, Avery.

After her visit Dr. Edwards reflected upon meeting “Dr. Abe” Eisenstark and working at the CRC. “I first met Dr. Abe near the “projected” end of my graduate program at Mizzou. When my sponsor ran out of grant money and my committee asked for some additional data, Dr. Abe offered to take me in at the CRC and help me find funding to finalize my experiments and defend my thesis. In exchange, I helped in the lab at the CRC and learned the most important lessons of my scientific life under his influence. I was pregnant with my 3rd child during this time and the people at the CRC became our extended family. Dr. Abe always encouraged me to follow my scientific dreams and to break through barriers with my skill and desire to better myself. He saw my family as an asset and anchor in tough times rather than a liability. Even though my education took a traditional course from the CRC to a post-doctoral fellowship with the USDA in Clay Center, NE, I ultimately decided to pursue a somewhat non-traditional career path for someone with my education and experience. I felt empowered to choose a career in the pharmaceutical industry that allowed me to expand my scientific experience in clinical research and achieve healthy work-life balance at the same time. I have devoted the last 10 years to this industry and see it as one of my best professional choices. The baby that was born at the beginning of my Dr. Abe experience is now 16 years old and was excited to take a day trip with me to Columbia recently to catch up with the CRC family. In my family, we have always privately referred to Dr. Abe as my “Yoda” because of his unique way of imparting wisdom. On the way home, my daughter turned to me and said how lucky I was to have him as “my Yoda.” She couldn’t have been more right.”

Elizabeth Choe

Elizabeth currently runs the MIT+K12 Videos Program, an educational media outreach initiative in MIT’s Office of Digital Learning / Strategic Educational Initiatives, in addition to supporting Institute-led and MIT community K-12 projects. She gets to create, produce, and research original webseries and video experiences designed to spark curiosity and a love of science/technology/engineering/math in middle and high school students. She also teaches a course on digital media literacy and leveraging video and media to spark learning for everyone from MIT staff and graduate students to middle school students! And on the side, Elizabeth has been producing a web series for National Geographic on the chemistry of everyday objects.

Even though she is not working at the bench anymore, She still spends quite a bit of time in labs, trying to show the excitement of science to young people much like how Dr. Abe did for her when she first came to the CRC as a high schooler. She is amazed how much she still uses many of the things she learned while working at the CRC in her current projects!
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Marnie Clark, Jack Bozarth, Alycia McGee & Alison Fea
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Don Stamper & Garry Banks draw the raffle winner!

Joyce Evans, Dulcenia Kidwell, Rhonda Durham and Stacy Tatiersky

Suzy & Steve Lee

Bill Barnhouse from Crazy Music
Bill Powell was a very accomplished man and yet a humble man. In fact, if he were here, he wouldn’t approve of this honor. He would, however ignore his personal shyness to help others as the Cancer Research Center is trying to do. He was a man whose purpose in life was to sacrifice personal comfort to help others.

Bill developed his personality and integrity growing up in the small river town of Mokane, Missouri. He spent his childhood working on the farm, fishing the Missouri River, and learning how to be a man. His dad, James “Buck Powell,” was a hard-working man who owned the Mokane Lumberyard. Buck was a pillar in the community living a simple life, save the time he tried out for the St. Louis Browns baseball team. Buck made the team, but had to forego a career in baseball to help run the family businesses. He took pride that on the day of try-outs Buck could hit off Dizzy Dean.

Bill lost his dad to colon cancer while a young man and always recognized the importance of cancer research. Bill’s mom, Helen was a high school math teacher who earned her doctorate in mathematics. Helen was brilliant, and disciplined her children to have the same feeling for academic achievement. Bill began his academic training early, helping his mom grade high school calculus papers when still in elementary school. Bill’s mom proved her toughness and fortitude as she battled breast and skin cancer successfully.

The dedication to hard work and excellence Buck passed down to Bill served him well as he grew up. Playing football in Jeff City for the legendary coach, Pete Atkins, forged him into a tough and heralded player. On a storied football team that was undefeated during all four years of Bill’s time with the Jays. He was a leader and tenacious defender.

Bill earned a scholarship to play football at Mizzou, playing guard and becoming captain his senior year. He was selected to play in the Blue and Grey All-Star Game and in the Senior Bowl as well. In his senior year, his Missouri team beat Florida and their Heisman-winning quarterback Steve Spurrier, 20 to 18 in the Sugar Bowl.

Kerri, his oldest child attributes her passion for gardening to her dad. She remembers hating the hard work of hoeing and pruning in the garden while her friends were swimming and otherwise enjoying the summer. Later she realized the discipline of growing a garden was even more valuable than the wonderful vegetables harvested in the fall. Later in life, Kerri realized that gardening was a release for her dad from the demands of a law office and a chance to just “be” with his kids. With dirty hands and sweaty brow, two stubborn souls melded together.

Bill cherished the time spent with his sons, Doug and Scott, taking them fishing, hunting and camping. Throughout the experience of bonding, he would impart his wisdom of how hard work brings you everything, and how honesty and integrity only reside in men of worth. He believed in working hard and instilled this trait in Doug when working in the yard or workshop. Doug’s work ethic today was developed as a boy who wanted to be just like dad.

With eleven beloved grandchildren: Allie, Spencer, Marley, Carson, Rhenn, Will, Myla, Emery, Reece, Jack and Celia, “Oompoo” and Cathe felt their mission was to spoil the grandchildren.

And they did. Whether making toy train tables or swing sets, letting them ride the John Deere “Gator” around the property or sitting through their countless school and sporting events, the proud grandparents were there.

In town, most Saturdays would find Bill with friends at Lawn and Leisure sharing food and playing cards with the boys in the back room. And every summer for years, Bill happily helped cook for the annual Bar Association Barbeque. There, stories of courtroom antics and back room negotiations were told and retold while feasting on prime rib, potato salad and more than a few cocktails.

Dad had a special bond with Amy, his youngest child. He spent most of his time with her late in his career. Amy became his “right-hand partner” as he wound down his businesses. She was invaluable to her dad as he transitioned into retirement.

As much as Dad loved his kids, there was only one true love of his life, his wife and partner, Cathe. They were introduced when he was 20 and she was 18. They decided that day to be together for eternity. Bill and Cathe were married June 10, 1966 in the Stephens Chapel. Through the early years of marriage, they struggled to build their family, finish school and begin a career. They worked hard, sacrificing personal needs to create an amazing life for themselves and their children. Through it all, Bill lived to bring security and happiness to his beloved wife. His comfort was defined by her well-being and happiness.

Bill’s family would like to thank the Cancer Research Center for honoring him at this year’s Jim Kidwell Memorial Gala. We appreciate all those who attended and for your generous time and money spent to help fund this research. The Cancer Research Center exists to fight a disease that leaves no life untouched.
The Powell Family

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Since 1990, the annual Cancer Research Center (CRC) banquet has been named in memory of Jim Kidwell.

Mr. Kidwell was a lifelong resident of Boone County and he graduated from Hickman High School. In 1965, he met Howard Eiffert and Raymond Freese and became an employee of Boone County Lumber Company.

In 1984, Mr. Kidwell was recruited by his good friend Mr. Freese to assist with the annual CRC banquet. Mr. Kidwell had been diagnosed with cancer, and he was relentless in his efforts to raise funds for CRC’s local cancer research. He was honored numerous times for having sold the most tickets to the annual dinner - regularly over 200 single-handedly.

In 1990, Mr. Kidwell succumbed to cancer.
Hope

is the thing with feathers
That perches in the soul,
And sings the tune without the words,
And never stops at all.

- Emily Dickinson
Michelle Becker-Hapak, Abraham Eisenstark and Robert Kazmierczak

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A sampling of the area’s finest restaurants have provided gift certificates for your dining pleasure. Great for hosting out of town guests, business clients or just making the rounds of these favorites yourself!
Donated by: Area Restaurants & Gala Volunteer Committee Members
Purchased by: Travis Burnett

2. Stihl Chain Saw
Fire up the Honey Do List with this Stihl chain saw. Comes ready for action with MotoMix High Performance Fuel Mix and bar oil to get you started!
Donated by: Travis Burnett
Purchased by: Melissa Quast

3. Choice Spirit Wagon
Take your pick of two high quality Radio Flyer wagons filled with top shelf spirits. Winner of second wagon determined by a card raffle.
Donated by: Bill Burnett & Gala Volunteer Committee
Purchased by: Chelsea Braun

4. Kindle Fire HDX Bundle
Donated by: Travis & Yolanda Burnett
Purchased by: Emily Brady

5. Weekend at the Kansas Speedway!
Donated by: Lloyd & Kathy Farris, and CRC
Race Weekend A (Night races!)
Purchased by: Steve Hughes
Purchased by: Gary Workmeister

6. Private Columbia Culinary Tour for up to 10 Guests
Enjoy Columbia’s newest social and culinary experience!
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Purchased by: Steve Hughes

Donated by: Billy Burnett
Purchased by: Kerry Bush

8. Child’s Ride with Truman the Tiger on Truman’s Taxi Before an MU Home Football Game
Donated by: Boone County Fire Protection District
Purchased by: Brad Wright

9. Weekend Bobcat Rental
Donated by: Bobcat of St. Louis-Columbia
Purchased by: Steve Erdel

10. Springfield Armory XD .40 Pistol
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11. Paul Jackson Eyes of the Tiger Framed Giclée Print
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Purchased by: Adam Patchett

12. Carl Edwards Rookie Season Collage
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13. Magnavox - V Series 46” 1080p LED TV
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Joe Machens Toyota Scion is proud to support The Cancer Research Center and its search for a cure. Everyone has been touched in some way by this disease and we make it a priority to help fund finding the cure. Toyota as a whole has contributed millions of dollars all over the world to help find a cure and we are glad to do our part here in Columbia, MO.
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Opportunities for Giving

Donations to the Cancer Research Center, unless otherwise directed, go to three main funds.

**Roma Eisenstark Scholarships and Internships.**
In conjunction with our research mission, Dr. Eisenstark engages promising students in order to enhance their scientific backgrounds. We have programs for high school students, undergraduate and graduate students and postdoctoral fellows. Each category has opportunities to participate in our research to one degree or another. For more information, contact Dr. Abraham Eisenstark.

**Ray Freese Memorial Fellowship in Cancer Research.**
This Fellowship supports a postdoctoral scientist who engages in basic research at CRC in the development of a professional career finding ways to reduce cancer deaths. Dr. Bakul Dhagat-Mheta is the most recent Raymond W. Freese Fellow at the CRC.

**The Pamela Dunn Legacy of Hope.**
Due to her dedication and contributions to cancer research, the CRC’s Dr. Pamela Dunn Legacy of Hope was created in her honor. The legacy is used to recognize individuals, businesses and foundations who demonstrate a tangible interest in supporting the CRC. Income from these funds provide for instruments, books, and support for our scientists who receive fellowships, stipends and other financial help based on their training and experience.

We are very fortunate to receive tremendous support from fraternal organizations around the state. The Fraternal Order of the Eagles, The Order of the Eastern Star, and the Cosmopolitan Luncheon Club of Columbia have for years generously supported our work. Friends of the CRC frequently obtain their employer’s help to make outright donations or participate in a company’s matching funds programs. When you participate in our annual Jim Kidwell Memorial Gala, whether by buying a table or sponsoring the event, your contribution goes to our biggest fund raiser of the year. Donations can be made through our once yearly direct mail appeal, through our website’s PayPal page or with a memorial donation in memory of a loved one. An additional way you can contribute to our research is through a simple bequest in your will.

Your generous bequest can bring us all closer to the day when the terrible disease of cancer is finally eradicated from our society. It doesn’t matter whether your bequest to the Cancer Research Center is quite small or very large. All bequests have the real potential to save lives and to help thousands of people avoid the physical, mental and emotional suffering of cancer. We invite you to take advantage of the free gift planning services of our Development Office.

Our experienced and knowledgeable staff can help you plan a bequest or trust that will accomplish all your specific estate objectives and give you the great personal satisfaction of knowing you have made a truly meaningful contribution to America’s ongoing war against cancer. Your personal situation will determine whether any type of bequest would be advantageous to you as well as the Cancer Research Center.


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Raymond Freese, a local builder, developer, and president of Boone County Lumber Company, was a member of the CRC Board of Trustees for 21 years, beginning in 1973. He worked tirelessly to secure funding and support for various CRC projects and was especially devoted to the CRC Gala. Ray lost his sister and several close friends to cancer and decided to do what he could to fight this lethal disease. Unfortunately, he lost his own battle with cancer in 1994. After his death, the CRC Board of trustees set up the Raymond W. Freese Memorial Fellowship. This fellowship is awarded to promising postdoctoral scientists for an initial one year appointment, with reappointment for additional years based on performance. The stipend is comparable to those awarded by the Health Sciences Center at the University of Missouri - Columbia. The major research project is prostate tumor therapy with genetically altered Salmonella. Applicants are expected to have (1) expertise in molecular genetics of bacteria, (2) willingness to develop a mouse testing model, (3) skills in writing grant proposals and manuscripts, (4) skills in presenting research results at national meetings, and (5) skills to develop projects independently and creatively.

Resumes may be submitted via one of the following:
Dr. Abraham Eisenstark
E-mail with attachments to eisenstarka@missouri.edu
Fax to 573-443-1202 or
Mail to: Cancer Research Center, 3501 Berrywood Dr., Columbia, MO 65201

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Save the Date!

2016
Jim Kidwell Memorial Gala.

The Plaza Event Center Parkade Plaza
601 Business Loop 70W, Columbia, MO
Saturday, April 9th
Event Begins at 5:30 pm

For more information contact:
Jack Bozarth
jackbozarth@cancerresearchcenter.org
(573) 875-2255

cancercrc.org

All proceeds will benefit local cancer research projects through the Raymond Freese Memorial Fellowship Fund.

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