A Tribute to Dr. John Kersey’s Legacy

Masonic Cancer Center
University of Minnesota
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Dear Friends,

Many of you have probably heard of the critically acclaimed television series “The Big C,” about a suburban wife, mother, and teacher coping with a terminal cancer diagnosis. As I reflect on the achievements and activities of the Masonic Cancer Center over the past year, another “Big C” comes to mind: Collaboration.

Collaboration has always been at the core of our work; this year we’ve taken it to a whole new level with the opening of the Cancer & Cardiovascular Research Building (CCRB) in the University’s Biomedical Discovery District. Already, more than 18 Masonic Cancer Center researchers and their research staff, students, and post-doctoral fellows have moved into this state-of-the-art facility to work together on new ideas. Together, they will focus primarily on environmental causes of cancer, the discovery of new cancer targets using mouse models of cancer, and improved therapies based on this new knowledge. Truly a “big” collaboration!

Collaboration is also the central component of our National Cancer Institute (NCI) designation as a Comprehensive Cancer Center, which we first earned in 1998. This year, we completed the peer review process to renew this designation and we were awarded a “high impact” score. We are awaiting final notice of the award expected in the first quarter of 2014. Recognition of collaboration and teamwork is the key to the successful awarding of this designation; the Masonic Cancer Center is the only facility in the greater Twin Cities area, and one of only 41 in the country, to hold this honor.

Pilot funding got a boost this year, with faculty receiving over $1 million in support for more than 50 promising new projects. This is a reflection of the Masonic Cancer Center’s commitment to discovery, as well as a testament to the talent of our researchers and their ability to carry out this vision. In addition to new pilots, other ongoing “team” projects have been submitted for funding. The Masonic Cancer Center awarded special pilot funding to teams headed by David Largaespada, Ph.D. and Yoji Shimizu, Ph.D. Largaespada and colleagues, including laboratories in the CCRB and University of Minnesota Duluth, are unlocking the genetic origins of colorectal cancer. Dr. Shimizu’s team aims to enhance anti-cancer immunotherapies and is housed in the Wallin Medical Biosciences Building which is directly connected to the CCRB.

It is impossible to think about collaboration at the Center without thinking of our colleague and friend John Kersey, who we lost unexpectedly last year. Dr. Kersey’s vision and drive made the Masonic Cancer Center possible. His dedication to teamwork was first and foremost and is a lasting legacy for us.

I hope this report sparks a desire to learn more about our work. More information can be found on our web site at cancer.umn.edu, and I invite you to e-mail us with questions or comments at ccinfo@umn.edu.

Sincerely yours,

Douglas Yee, M.D.
Director, Masonic Cancer Center,
University of Minnesota

FROM THE DIRECTOR
University loses friend, mentor, Masonic Cancer Center pioneer

The University of Minnesota, as well as the world of cancer research and treatment, suffered a significant loss with the death of John Kersey, M.D., in March, 2013. A key figure in the history of the University’s Medical School and the creation of the Masonic Cancer Center, Kersey left a lasting mark as a researcher, physician and mentor to those who will now carry on his work.

Kersey was a native Minnesotan who earned his undergraduate degree from Dartmouth College and his medical degree at the University of Minnesota. Following an internship and residency in pediatrics and pathology, he joined the faculty, where he rose from assistant professor to professor in six years.

Kersey had a passion for discovery, and he translated that passion to out-of-the-box thinking and big, bold ideas. Always, his underlying goal was to improve outcomes for cancer patients, and his efforts truly changed the field when it came to the treatment of blood cancers. He was the founder of the University’s Blood and Marrow Transplant program, serving as director from 1974 to 1995. In 1975, Kersey led the team that completed the world’s first successful transplant for malignant lymphoma.

“The work we do at the Masonic Cancer Center is a direct result of the leadership of John Kersey,” said Douglas Yee, M.D. “The world has been positively changed by John’s scientific, educational and clinical contributions.”

Beginning in the late 1980s, Kersey worked tirelessly to realize his vision of a comprehensive cancer center at the University. Ultimately, he was the founding director of this institution we now know as the Masonic Cancer Center, and was instrumental in achieving its National Cancer Institute (NCI) designation.

Kersey was president of the International Society for Experimental Hematology and the American Society for Blood and Marrow Transplantation. He held continuous funding from the National Institutes on Health from 1977 through 2010, and was the recipient of an Outstanding Investigator Award from the NCI from 1991 to 2001.

His colleagues, however, say it was his generosity as a friend and collaborator that set him apart.

“John Kersey was a wonderful friend, mentor and colleague to many in the University and far beyond,” said Wes Miller, M.D., head of the department of medicine in the Medical School. “John was driven by an insatiable curiosity. He asked questions and found answers that amazed me.”

Throughout his career, Kersey was a mentor to generations of investigators who now work at transplant and leukemia centers throughout the world. He was generous with his time and expertise, and provided sage advice and counsel in a manner that was always kind, enthusiastic and focused on endless possibilities.

“John was the driving force that helped the University of Minnesota become internationally recognized for excellence in cancer treatment and research,” said Aaron Friedman, M.D., former senior vice president for health sciences. “His enthusiasm for his work was contagious, and his passion for bringing people together to solve problems changed the way cancer research is conducted.”

Memorials may be directed to the John H. Kersey Chair in Cancer Research, Fund #1149, at the University of Minnesota Foundation.

Left: Open House for the new Cancer Cardiovascular Research Building
A man who loved history, John Kersey is an unforgettable part of our past

by Emily Hagens

I began studying the history of the Masonic Cancer Center in 2011 while John Kersey, M.D. was just wrapping up a project with Aimee Slaughter, a Ph.D. candidate in the History of Science, Technology and Medicine program. Their work culminated in a paper published in Minnesota Medicine discussing a 1925 gift of $250,000 to the University of Minnesota for the establishment of a cancer institute, including x-ray and radium technology. At a time when radical surgeries were the gold standard for the treatment of cancer, the availability of radium at the University opened up a world of possibility.

The concluding lines of the article reveal Dr. Kersey’s fascination with and great respect for the early history of cancer research at the University of Minnesota:

“In many respects, the Cancer Institute was on the leading edge of medical and social efforts to fight cancer. It had a matrix structure, a director with authority, philanthropic partners, institutional support, and a multidisciplinary approach to care and research.”

Cancer research and treatment continued to blossom between the early and late 20th century, thus Dr. Kersey turned the focus of his history project to the development of the University of Minnesota Cancer Center, now known as the Masonic Cancer Center. Research into the history was conducted in large part in the University Archives, located in the Andersen Library, and in the Masonic Cancer Center’s current files. We gathered significant information from meeting notes, memoranda, correspondence and official publications but, ultimately, we decided the best way to gain insight was to conduct oral history interviews.

Center built on spirit of collaboration

During the interviews, the Masonic Cancer Center’s strong tradition of collaboration became clear. In fact, it played an important role in achieving our National Cancer Institute (NCI) designation.

In 1988, Dr. Kersey began to have discussions about obtaining “comprehensive” designation from the NCI. He and others involved in the planning knew the Center would need to specifically address issues of authority and department loyalty in order to create a space for fruitful collaboration, especially after a failed attempt at gaining NCI designation in the 1970s. Dr. Kersey’s work at the time with the Bone Marrow Transplantation Program with colleagues Norma Ramsay, M.D. and Philip McGlave, M.D. provided a foundation from which the development of the larger scale collaboration that would ultimately assist in the University’s application to the NCI. Interviews with Drs. Kersey, Ramsay, and McGlave, as well as nurse coordinator Joanne Howard, highlighted the unique nature of their combined adult and adolescent trial program. Persevering through periods of severe failure and threats of nurses refusing to conduct trials on more patients, Kersey, Ramsay, and McGlave eventually developed successful treatments for lymphoma using several types of transplantation procedures.

Drs. Kersey, Ramsay and McGlave “tested and succeeded in a model of interdisciplinary research where individuals from multiple departments and specialties worked together as a unit, as a program or as a center,” reflected Mary Sumpmann, M.S., associate director of administration.

The translational and collaborative cross-disciplinary nature of their work served as themes for Dr. Kersey and me as we continued to consider how the University of Minnesota’s Cancer Center was established.

Birth of a comprehensive cancer center

Dr. Kersey continued to initiate meetings on campus to discuss how to develop an NCI-designated center. In addition to the interdisciplinary translational research he promoted among his colleagues, he also worked to encourage conversations within the Twin Cities community about how to support cancer research. In particular, interviews with Dr. McGlave and Bruce Johnson, M.D., Ph.D. shed light on the importance Dr. Kersey saw in making the Center’s work accessible to the community. Others, particularly the Minnesota Masonic Charities, agreed – and from the beginning of the 20th century to its major gift in 2008, the Minnesota Masonic Charities has been instrumental in the continuing support of cancer research at the University.

The progress of the Cancer Center is relatively clear: Dr. Kersey’s initial meetings with David Brown, Ph.D. and other University leaders in 1988, the University designation of the Cancer Center in 1991, construction of the Masonic Cancer Research Building in 1996, the NCI designation in 1998, and the Minnesota Masonic Charities’ gift of $65 million in 2008. The stories Dr. Kersey and I heard while working on this project, however, demonstrate that the subtle negotiations and cooperation taking place behind the scenes between colleagues, friends and community supporters were the building blocks from which the Masonic Cancer Center eventually gained success.

From left: Quanzhi Li, Ph.D., senior research associate in Dr. Kersey’s lab; David Stahl, recipient of the world’s first successful BMT for Burkitt’s Lymphoma, in 1975; and John Kersey, M.D.

Emily Hagens is a Ph.D. candidate in the History of Science, Technology and Medicine at the University of Minnesota, where she is currently working on a dissertation that examines knowledge transfer and domestic medical practice in 16th century Italy. The article by Aimee Slaughter and John H. Kersey, titled “Philanthropy and Scientific Medicine: The History of the University of Minnesota’s Cancer Institute,” can be found in the September 2011 issue of Minnesota Medicine.
From lab to law: melanoma research helps protect teens from indoor tanning

In 2010, DeAnn Lazovich, Ph.D. and her research team made headlines with a study that proved frequent indoor tanning increased melanoma risk, regardless of device used and age when indoor tanning began.

Yet, every year in the U.S., nearly 30 million people continue to tan indoors. Of these, 2.3 million are teens. Melanoma rates among young women have increased 50% since the 1980s, a trend that parallels the use of indoor tanning.

Hopefully, this trend is about to change, as more and more lawmakers use the Lazovich study to build a case for more restrictive laws on indoor tanning. So far, California, Illinois, Nevada, Oregon, Texas and Vermont have passed laws banning the use of commercial tanning devices for all minors under the age of 18. Another 29 states require parental permission for minors.

Just about every major health group – including the World Health Organization, the American Medical Association, the American Academy of Dermatologists and the American Pediatric Association – has called for a complete ban on the use of indoor tanning devices for minors. The team looked at the effects of regulated fibers, namely asbestos, in causing mesothelioma. The team is currently expanding its focus to examine other possible causes of disease and other disease types, including non-malignant respiratory diseases caused by asbestos fibers, non-mesothelioma lung cancers, and the effects of shorter mineral fibers (such as those in taconite dust and silica) in relation to mesothelioma.

The more time spent on the job, the more likely a Minnesota Iron Range worker is to develop mesothelioma, a rare and deadly lung cancer thought to result exclusively from exposure to the long, needlelike fibers in asbestos. Taconite workers are exposed to asbestos at higher levels compared to other types of employment. These facts and other information gleaned from a state-commissioned study will help health officials understand the health effects of taconite mining.

Identifying the exact substances and exposures causing harm is more complicated. Initially, Jeff Mandel, M.D., M.P.H. and his team looked at the effects of regulated fibers, namely asbestos, in causing mesothelioma. The team is currently expanding its focus to examine other possible causes of disease and other disease types, including non-malignant respiratory diseases caused by asbestos fibers, non-mesothelioma lung cancers, and the effects of shorter mineral fibers (such as those in taconite dust and silica) in relation to mesothelioma.

“We are exploring those differences, though they are difficult to sort out when you consider all the different exposures a person may have had over a lifetime,” said Bruce Alexander, Ph.D. The process, he explained, involves collecting many samples from various plant locations and stages of the mining process, then carefully overlaying with exposure data over the course of a worker’s career.

For more information, visit taconitemining.umn.edu

Public Health study aims to find specific disease risks in taconite mining

“We’re looking at giving survivors some tools to cope with the aftermath which can be overwhelming.”

Blaes just completed a survivorship study, supported by the Hourglass Fund, to test the effects of an integrated mindfulness and meditation program on quality of life. Initial results show improvements in mental health. This success has led to additional grants to provide the program to the community, as well as test it with specific survivor populations.

After the cure: healing mind and body

We know the life expectancy of a cancer survivor is shorter than those without cancer. Worries about recurrence, the physical and emotional stress of treatment, lingering or permanent side effects, susceptibility to other diseases, the toll of illness on finances and career – are all factors that can lead to depression and anxiety, and diminished quality of life.

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Second-hand-smoke exposure in children prompts parents to quit smoking

Common wisdom suggests one of the best ways to reach adults is through their children. In terms of smoking cessation, Anne Joseph, M.D. and her team found this timeless adage to have a measurable effect on encouraging parents to seek help for their habit.

Participating children lived with at least one parent who smoked. Measurable cotinine was identified in 93 percent of the children tested. More parents in the intervention group (versus the control group) sought smoking cessation treatment, and more parents reported abstinence from smoking at eight weeks.

More information can be found in “A Pilot Study of Concurrent Lead and Cotinine Screening for Childhood Tobacco Smoke Exposure: Effect on Parental Smoking,” published in the American Journal of Health Promotion, September 2013.

Low-dose CT scans superior to chest x-rays in detecting lung cancer

Results from an extensive study by the National Lung Screening Trial (NLST) research team showed that low-dose CT scans are better at detecting lung cancer than chest x-rays. The multi-year study, led by Tim Church, Ph.D., enrolled 53,439 asymptomatic participants with a history of smoking in 33 locations throughout the United States. The participants agreed to undergo annual screening using either low-dose CT scans or chest x-ray for three years.

Lung cancer was diagnosed in more CT-scan participants versus those in the x-ray group, suggesting that a reduction in mortality from lung cancer is achievable by screening with low-dose CT scans.

This study appears in the New England Journal of Medicine under the title, “Results of Initial Low-Dose Computed Tomographic Screening for Lung Cancer.”

New look at pathology samples may find cancer links to diet, environmental chemicals

Trapped inside pathology samples from cancer patients is a wealth of information for understanding the role chemicals in the diet and environment in causing cancer. But, until now, there was no reliable way for researchers to access that information on a large scale. Previously, such measurements could only be taken from fresh, frozen cancer tissue, and those biospecimens are not easily obtainable for large human studies.

Thanks to the groundbreaking work of Robert Turesky, Ph.D., researchers now have a way to measure human exposure to suspected carcinogens in archived tissue samples.

The method uses formalin-fixed paraffin embedded (FFPE) tissues, a process of preserving tissue by embedding it in a block of wax. Paper-thin slices are shaved off, which are examined for likely cancer-causing chemicals using mass spectrometry. Dr. Turesky’s team also developed an approach to recover the DNA and examine it for biomarkers, called DNA adducts, which are pieces of DNA bound to a carcinogen. The bonding may mean the start of cancer.

“This may help epidemiologists add another piece of data to their tool kits to help assess carcinogen exposure and take into consideration other cancer-causing chemicals we might not have known about,” said Dr. Turesky.

Initially, this approach will be applied to examine FFPE tissue specimens of subjects who are exposed to potential carcinogens in tobacco smoke and grilled meats.

Hair used to measure carcinogen exposure

Epidemiology studies have reported that frequent consumption of well-done cooked meat can increase the risk of developing cancers of the colon and prostate in men and mammary glands in women. The cooking of meat at high temperature forms carcinogenic chemicals called heterocyclic aromatic amines. Until now, there has not been a reliable method to measure these carcinogens in humans.

After eating cooked meat, a carcinogen called PHIP is absorbed into the body and a portion of the chemical accumulates in the hair shaft. Dr. Turesky and his team have developed a method to isolate PHIP from a few strands of hair. The hair is broken down and the PHIP released can be measured by sensitive mass spectrometric methods, allowing researchers to determine the extent of exposure to PHIP in cancer patients. The measurement of the levels of PHIP in hair can help us to understand a person’s eating habits and may determine the link among well-done cooked meat consumption, PHIP exposure and cancer risk.

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Smokeless tobacco database goes global

There are literally hundreds of brands and varieties of smokeless tobacco available in the United States alone. To make it possible to evaluate this known carcinogen, Irina Stepanov, Ph.D. has been using her chemistry background to create an extensive database of the chemical carcinogens found in these products.

“A major challenge to understanding the cancer risk posed by smokeless tobacco is the vast differences in its chemical composition,” explained Stepanov.

After creating a national database of close to 500 varieties available in the United States, Stepanov has spent the last year expanding the database globally. Her team, composed of long-time collaborators in Africa and India, is focusing initially on Africa and India, where smokeless tobacco is used extensively, and the staggering diversity of products makes evaluating their risks particularly challenging. Two thirds of the world’s smokeless tobacco users reside in India, and its rates for oral cancer are among the highest in the world.

“Companies are supposed to report the make-up of their product,” noted Stepanov. “But results depend on how it’s tested and analyzed.” The database, she added, provides a consistent and accurate record. This work is funded by the NIH and will ultimately result in a published paper that will assist the FDA in its evaluations.

Research points to possibility of a “safer” smokeless tobacco

Smokeless tobacco is presented by some as an alternative mode of tobacco use associated with less harm. Yet, the products are a known cause of oral cavity cancer. Thousands of the estimated quarter million new cases each year worldwide attributed to its use. The disease can impair vital functions such as speech, taste and swallowing, and is often fatal.

In a recent study, Stephen Hecht, Ph.D. was able to identify the specific form of the carcinogen present in smokeless tobacco, in the hopes that its removal could make the product less harmful.

All smokeless tobacco products contain high amounts of the carcinogen N’-nitrosonornicotine (NNN). NNN exists in two chemically distinct forms called (S)-NNN and (R)-NNN, with (S)-NNN being the predominant form in tobacco.

In the study, (S)-NNN and (R)-NNN were tested for their carcinogenic activities in rats. The results clearly showed that (S)-NNN is a powerful oral cavity carcinogen, inducing multiple benign and malignant oral cavity tumors, while the opposite form (R)-NNN was only weakly active. Thus, (S)-NNN was identified for the first time as the only strong oral cavity carcinogen in smokeless tobacco products indicating that its reduction or removal from the product could significantly reduce its cancerous effects.

Breast cancer culprit also found in multiple cancers

Researchers have long wondered why breast cancers are relatively rare in the Pacific Islands and Asia, and particularly Japan. The reason may have to do with APOBEC3B, an enzyme that is genetically absent in these populations.

Earlier this year researcher Reuben Harris, Ph.D. and his colleagues published evidence that APOBEC3B is a major source of cell mutation and was found in more than half of breast cancers.

“This is the first clear example of enzyme-induced mutations in human cancer,” said Harris. “With this knowledge, we now have a chance to do something about it.”

An obvious next step, added Harris, is to determine how early APOBEC3B starts contributing to mutation in breast cancer, and figure out ways to suppress the accumulation of these mutations. This could have a major impact, for instance, in decreasing the chance of tumors developing resistance to therapeutic drugs.

A double-edged sword

APOBEC3B belongs to a family of enzymes called APOBECs (A’po-becks). Earlier work in Harris’s lab found their ability to mutate DNA. In white blood cells, they act as a first line of defense against viruses and other parasitic elements.

But despite its antiviral properties, APOBEC3B isn’t essential for life – as its absence in Asian populations shows.

Harris would like to know how the absence or presence of APOBEC3B and its gene correlates with cancer risk and other factors. Also, he hopes to find a way to block the enzyme from mutating DNA. By focusing on APOBEC3B, researchers may be able to zero in on factors that act earlier in the sequence of events leading to cancer.
### A calling card for cancer

Harris and his colleagues have extended their findings to other cancers. In a study encompassing 19 different cancer types and a million mutations, the researchers found similar evidence for APOBEC3B as a contributor to mutations in five additional types of cancer: bladder, cervix, head and neck, and two forms of lung cancer.

“We are very excited about these discoveries because they indicate that a single enzyme is one of the largest known contributors to mutagenesis in cancer,” says Harris. “We are confident that our findings will trigger a domino effect of additional research and clinical studies that result in better outcomes for patients with many forms of cancer.”

For a full report of these study results, see “APOBEC3B is an enzymatic source of mutation in breast cancer,” Nature, February 21, 2013.


### Study identifies new link between genetic diseases

Fanconi anemia (FA) and Bloom syndrome (BS) are genetic diseases that cause genome instability and cancer. FA and BS patients carry mutations in a distinct set of genes, the true function of which has remained elusive. It has been known that FA and BS patients share certain chromosomal abnormalities, suggesting partial overlap between the biochemical pathways that are defective in the two diseases. Alexandra Sobeck, Ph.D., and her team have now demonstrated that both FA and BS genes are required to restart “stalled” replication forks. Her team showed that functional FA proteins are required to promote the assembly of the so-called BS-complex, which is recruited to stalled forks so that cells can finish copying their genome and pass a complete set of chromosomes on to their daughter cells. These findings will help pave the way to identify specific target points for therapy useful in treating both diseases.

### Researchers develop virus aimed to kill pancreatic and ovarian cancer cells

The protein mesothelin is a tumor marker that is highly expressed on the surface of pancreatic and ovarian cancers, making it a prime candidate for targeted cancer therapy. Recent work by Julia Davydova, M.D., Ph.D. and Masato Yamamoto, M.D., Ph.D. have brought us one step closer to delivering a deadly blow specifically to these tumors while sparing normal cells of the body. The two researchers have developed a highly enriched virus that exclusively attacks mesothelin-expressing pancreatic cancer cells. Not only did the virus cause tumors to disappear in mouse models, the tumors failed to emerge after treatment. The team is now poised to move this work to Phase 1 clinical trial.

### New imaging technology allows earlier detection in mobile organs

While magnetic resonance technologies have great potential for imaging tumors, they have limits – one of which is a poor ability to image tumors in organs that are in motion. This includes the lungs and bones, common sites for tumor metastases. TME member Michael Garwood, Ph.D., has developed and patented a new imaging technology he calls SWIFT (Sweep Imaging with Fourier Transformation) for high-resolution imaging of mobile organs such as the lungs. Dr. Garwood has reached an agreement with General Electric to license SWIFT for use in the company’s clinical MRI instruments. This has the potential to greatly enhance the ability of clinicians to identify small tumors, allowing for earlier detection and treatment.
Researchers apply engineering principles to understand tumors

The interactions between cells and their influence on the tumor microenvironment drive the process of metastasis by inducing cell migration. David Wood, Ph.D., is examining this phenomenon using a microfluidic system that simulates tumor physiology. His work suggests cell migration leading to metastasis is based on a motor-clutch model of cell traction. This mechanism-based understanding will aid in the development of targeted therapies to treat cancer.

New imaging techniques improve tumor detection, pain management

Bin He, Ph.D., is developing magneto-acoustic imaging for the detection of tumors and tumor metastases, using combined quantitative EEG and structural MRI to quantify pain. If successful, this work would be a major advancement in detecting deep and smaller metastases, as well as quantifying pain objectively to improve therapy.

Research aims to find target for difficult-to-treat breast cancer

Triple negative breast cancer (TNBC) is a collection of tumor subtypes that lack targetable markers, making treatment a major clinical challenge. Collaborative studies published by Jim McCarthy, Ph.D. have demonstrated a surface protein expressed by TNBC, named CSPG4, that can be targeted with antibodies to limit cancer growth in animal models. Dr. McCarthy is working with Kaylee Schwerfeger, Ph.D., Douglas Yee, M.D. and Andy Nelson, M.D., Ph.D. to determine the role CSPG4 plays in tumor growth and promoting resistance to chemotherapy. The longer term goal is to identify key molecular features of CSPG4 to improve treatment outcomes in TNBC patients.

Studies examine negative effect of opioids in treating cancer

With support from the Masonic Cancer Center Seed Grant Program, Kalpna Gupta, Ph.D. made the initial discovery showing opioid painkillers can stimulate the growth of malignant tumors in mice. Opioids (such as morphine) work by binding to opioid receptors which cause both the benefits and side effects of the drug. More recently, the team found a type of opioid receptor is expressed in human lung and prostate cancers. In conjunction with Pankaj Gupta, M.D., they found an elevated amount of this receptor in prostate biopsies was associated with worse outcomes in patients with advanced prostate cancer. Dr. Kalpna Gupta has received NIH funding to further examine the effects of opioids, and develop alternative analgesics to use with cancer treatment.

The art of persuasion: convincing the immune system to eliminate cancer

Scientists know certain types of lymphocytes effectively target and kill infections. But to do their work, they must be properly activated. The trick is to figure out how these valuable allies can be finessed and manipulated to learn to eliminate cancer cells.

Professor and Center for Immunology Director, Matthew Mescher, Ph.D. and his research team have made significant strides in understanding more about what it takes to activate lymphocytes, specifically T cells. They knew T cells require a signal from a cytokine, specifically interleukin-12 (IL-12) or interferon type I (IFN-α), to function. In comparing the effectiveness of the two cytokines, they discovered T cells stimulated by IL-12 were significantly more effective in controlling tumors.

“This wasn’t predicted, really, because when you analyze the cells in the lab, they appear to be identical,” said Mescher. “This tells us that we want to promote an environment where IL-12 is available.”

The next step in the research was to find out why IL-12 and IFN-α are so different in their ability to activate T-cells to control tumors. This is where programmed cell death protein 1 (PD1) becomes part of the story. Expressed on the surface of the T cell, PD1 can turn off its killer function so cancer can grow. What Mescher discovered is that IL-12 induced less PD1 on the surface of T cells than IFN-α stimulation.

(continued on page 18)
Spotlight on T cells

In addition to the work of Matthew Mescher, Ph.D., several other studies are adding to our understanding of the role of T cells in cancer immunotherapy.

The CD8+ T cell is a type of white blood cell that kills cells damaged by cancer, a virus, or other forms of disease. The CD8+ T cell population contains many subsets, and a recent study led by Stephen Jameson, Ph.D. sought to identify exactly which subset was most responsible for protecting the body against infection or tumor growth. The team’s data suggests long-lived effector CD8+ T cells persisted to become T cells and are optimal for protective immunity against pathogens.

Another study looked at CD4+ T cells, called helper T cells, which assist other white blood cells in their various functions. Following an infection, the effector CD4+ T cells produce a consistent ratio of effector T cells that mount an effective immune response by activating macrophages or helping B lymphocytes produce antibodies. This study examined the mechanism underlying this division of labor by tracking the progeny of a single T cell.

Results of these studies can be found in the following publications:
- Immunity, June 27, 2013, “Effector-like CD8+ T cells in the memory population mediate potent protective immunity”
- Cell, May 9, 2013, “Single naive CD4+ T cells from a diverse repertoire produce different effector cell types during infection”

The art of persuasion, continued

“One of the real excitement in tumor immunotherapy is the use of antibodies that can block the PD1 inhibitory pathway, and promising clinical results are being obtained. Our results suggest that activating the T cells in the presence of IL-12 may allow this approach to be even more effective,” explained Mescher, “and animal studies are being used to test this.”

On a basic science level, Mescher is asking the question: “Why does IL-12 induce lower expression of PD1 on T-cells than IFN-α?” The answer has the potential for creating even more possible pathways for cancer treatment.

A different piece of the puzzle is another type of lymphocyte: the natural killer (NK) cell. NK cells are much better than T cells at recognizing tumors and killing them. However, unlike T cells, which need specific receptors, NK cells are not very good at identifying specific cancer cells to fight.

“The idea is to make NK cells as specific as we know a T cell can be,” said Jeff Miller, M.D., “and to make NK cells more effective.”

As Deputy Director of the Masonic Cancer Center, Miller is helping to shape the future focus of immunotherapy research at the Masonic Cancer Center.

“The goal of immune-based therapy is to replace chemotherapy with something that is more specific. But science doesn’t yet know exactly how to manipulate the immune system to fight cancer,” he explained. “We are going to continue our excellence in exploring this up-and-coming modality and drive the field.”

Details of Mescher’s study can be found in Journal of Immunology, August 1, 2013, “Cutting edge: IL-12 and type 1 IFN differentially program CD8 T cells for programmed death 1 re-expression levels and tumor control”

Research aims to enhance therapy for advanced-stage prostate cancer

For decades, the standard treatment for advanced prostate cancer has been the use of endocrine or hormone therapy to suppress testosterone in the body. While being quite effective at promoting cancer regression, the therapy eventually stops working as the cells develop a resistance to the treatment.

Understanding what happens on a molecular level in this resistance stage is the focus of Scott Dehm, Ph.D. The challenge was to find out how the testosterone-dependent cancer cells can adapt to a complete lack of testosterone and begin to proliferate autonomously without this hormonal signal.

In order for prostate cancer cells to grow, testosterone must dock onto an androgen receptor. Now engaged with a testosterone molecule, the androgen receptor binds to DNA and drives a program needed for the prostate cancer cells to divide and thrive.

In the treatment-resistant stage of the disease, Dehm and his research team discovered the receptor protein is able to bind to DNA even in the absence of testosterone. They found those cancer cells will eventually make a variant form of the receptor without a testosterone docking site, allowing these proteins to bind with the DNA on their own.

“This is an important finding because it provides knowledge about how resistance develops that could reveal opportunities for new therapies,” said Dehm. For example, he added, “There may be a way we can block the interaction between the androgen receptor binding to the DNA.”

The National Center for Biotechnology Information has published several recent studies by Dehm on this topic. The most recent, titled “TALEN-engineered AR gene rearrangements reveal endocrine uncoupling of androgen receptor in prostate cancer” was published October 22, 2013 in the Proceedings of the National Academy of Science U.S.A.
Pancreatic cancer drug enters Phase I clinical trial

Ashok Saluja, Ph.D. has established a robust research program as principal investigator on five NIH RO1 grants to identify mechanisms by which pancreatic cancer resists therapies. His laboratory recently identified heat shock protein 70 (HSP70) as an important protein protecting cancer cells from treatment. In collaboration with Selwyn Vickers, M.D., Dr. Saluja showed inhibiting HSP70 with triptolide (a plant-based compound) causes cancer cell death and enhances response to therapeutic agents. This study is the first to demonstrate the effectiveness of this approach in pancreatic cancer. Masonic Cancer Center development funds were used to develop a drug (Minnelide) for treatment based on this finding. Phase 1 clinical trials for Minnelide are underway.

Anti-retroviral drug shows promise in treating breast cancer

David Potter, M.D., Ph.D., is investigating the mechanisms by which the anti-retroviral drug ritonavir inhibits AKT kinase pathways in breast cancer. AKT is a protein associated with tumor cell growth and survival. Notably, Dr. Potter has shown ritonavir inhibits chaperone molecules and may affect the stability of AKT kinase and other key client proteins important in breast cancer survival. This finding has led to the development of a Phase 1/2 clinical trial funded by Susan G. Komen for the Cure.

Continuing his work targeting lipid metabolism in breast cancer, Dr. Potter (in collaboration with Stephen Sigal, Ph.D. at the University of Illinois at Champaign-Urbana) is also using cell-based assays and CYP nanodiscs to identify novel inhibitors of EET biosynthesis in breast cancer cells. These novel approaches are based on highly sensitive targeted lipidomics assays for EETs developed in Dr. Potter’s lab. A candidate biguanide molecule has been identified as an effective tumor inhibitor and is being developed for future therapeutic use.

Cancer metabolism study signals hope for leukemia treatment

Some of the most promising research in understanding and treating leukemia focuses on the regulation of metabolic pathways in cancer cells. This is the work of Ameeta Kelekar, Ph.D., who is currently investigating the potential of a regulatory protein, Noxa, to serve as a therapeutic target against the disease. The recognition that cancer cells exhibit an altered metabolism, diverting glucose toward anabolic pathways conducive to cancer cell growth, also points to therapeutic strategies directed at manipulating the metabolic pathways.

Leukemia treatment with cord blood now faster, more effective

Umbilical cord blood is a source of blood and marrow-forming stem cells commonly used for transplantation in leukemia patients after high-dose chemotherapy and radiation. The goal of the transplant is to prompt the body to resume production of healthy blood cells in the patient’s bone marrow.

While the primary benefits of umbilical cord blood are rapid availability and reduced tissue-matching requirements, its use has been limited by the low number of stem cells in a single cord blood unit.

Recently, scientists at the Genomic Institute of the Novartis Foundation found a way to solve this limitation. They discovered a small molecule, StemRegenin-1 (or SR1) could externally expand the number of regenerative stem cells in cord blood. After the development of a clinical-scale manufacturing method at the University of Minnesota’s Molecular and Cellular Therapeutics Facility, John Wagner, M.D. initiated a first-in-human clinical trial in 15 adults with high-risk leukemia and myelodysplasia.

In combination with several growth factors, SR1 yielded a remarkable 300-1000 fold increase in blood and marrow-forming stem cells. In the clinical trial, all patients received a double umbilical cord blood transplant with one cord blood unit placed in expansion culture and one unit left un-manipulated. No patient has had detectable significant side effects from the expanded product.

(continued next page)
Leukemia treatment, continued
In the 10 patients in whom the expanded unit predominated, time-to-white-blood-cell recovery was shortened by 10 days on average. In contrast to the average of 26 days to recovery, patients have had recovery times as short as 5 days – a stunning achievement!

These results were presented at the American Society of Hematology meetings in December 2013. On the basis of these remarkable results, the next phase of the study will include children and adults age 10-70 with leukemia, myelodysplasia, lymphoma or multiple myeloma. Trials are also being planned for patients undergoing transplant for non-malignant diseases.

Tregs a promising weapon against GVHD
Research performed by Claudio Brunstein, Ph.D., John Wagner, M.D., and Bruce Blazar, M.D. to limit the occurrence of graft-versus-host-disease (GVHD) using Regulatory T-cells (Tregs) continues with a study to identify target doses. Of the four patients enrolled with engraftment, all remain GVHD-free. Plans are underway to develop a Treg bank for treatment of GVHD, and a Phase 1 clinical trial has been re-initiated to further identify the most effective dosages.

Researchers look to make the most of natural killer cells
Interleukin-15 (IL15) continues to be one of the most promising cytokines under development because it induces the proliferation of CD8+ T cells and NK cells without stimulation of Treg. Jeffrey Miller, M.D., and his research colleagues at the Masonic Cancer Center are near completion of a dose-finding study in which IL15 is combined with NK cells to treat acute myeloid leukemia, a fast-growing cancer that starts inside bone marrow and interferes with the production of normal white blood cells.

Robert Turesky, Ph.D.
The Carciogenisis and Chemoprevention program welcomed Robert Turesky, Ph.D. to its team of researchers in 2013. Prior to joining our faculty, Turesky was associate professor at State University of New York, Albany, and a research scientist at the Wadsworth Center, New York State Department of Health. Prior to that he was Division Director of Chemistry for the National Center for Toxicological Research, United States Food and Drug Administration in Jefferson, Arkansas.

Turesky’s current research focus is on analyzing by mass spectrometry exposure and the resulting DNA damage, of cancer patients. Specifically he is studying exposure to well-done cooked meats. After eating cooked meat, a carcinogen named PhIP is absorbed in the body and accumulates in the hair shaft. Turesky has developed a method to isolate PhIP from a few strands of hair and measure a patient’s extent of exposure to PhIP. This can help us to understand a person’s eating habits and may strengthen the link among well-done cooked meat consumption, PhIP exposure and cancer risk.

Turesky earned his undergraduate degree in biochemistry from the University of Massachusetts, Amherst and his doctorate in nutrition and food science from Massachusetts Institute of Technology.

Jill Siegfried, Ph.D.
Jill M. Siegfried, Ph.D., the new head of the Department of Pharmacology and Frederick and Alice Stark Endowed Chair, was appointed Associate Director for Experimental Therapeutics at the Masonic Cancer Center in September, 2013.

Siegfried was a professor in the Department of Pharmacology and Chemical Biology at the University of Pittsburgh. While there, she held the University of Pittsburgh Medical Center Endowed Chair for Lung Cancer Research and co-led the lung cancer program at the University of Pittsburgh Cancer Institute (UPCI). She also directed the Specialized Program of Research Excellence (SPORE) in Lung Cancer, a grant supported by the National Cancer Institute, for the past 12 years at UPCI.

Siegfried’s primary research focus is the biology of lung cancer, including analyzing new therapeutic targets, the causal effects of tobacco exposure, and possible biomarkers associated with the disease. She examines the relatively unexplored area of hormones in lung cancer, and has researched estrogen-receptor-positive lung cancers as can be found in breast cancers in which estrogen promotes cell growth, tumor formation, and malignant cell survival. Recently, her research group completed a first-of-its-kind clinical trial using the combination of an anti-estrogen medication with a medication targeting the epidermal growth factor receptor to treat lung cancer. This work shows great promise and she looks forward to continuing her research at the University of Minnesota.
A significant and prestigious source of funding for the kind of interdisciplinary, comprehensive research taking place at the Masonic Cancer Center (MCC) comes from the National Cancer Institute through its Specialized Programs of Research Excellence (SPORE) and Program Project (PO1) grants.

In 2011, the MCC set a goal to pursue these highly competitive grants and created an internal funding mechanism towards that end. The mechanism, called SPORE/PO1-Pilot/Planning (SP3) award, supports multi-disciplinary teams of investigators to develop a research program meeting all the criteria necessary to receive an outstanding evaluation on their SPORE or PO1 application.

Two major SP3 projects are currently underway, leveraging the two powerful disciplines of immunology and genetics to unlock the mysteries of cancer.

Getting personal: Genetics may lead to individualized, more effective colorectal cancer therapy

A major obstacle in the treatment and understanding of cancer is the fact almost no two patients’ cancers are alike. However, scientists are finding a promising future in the use of genetic signatures to gain information about a person’s specific cancer to better inform clinical decisions in colon cancer.

A group of researchers at the Masonic Cancer Center, led by David Largaespada, Ph.D., Robert Cormier, Ph.D., Timothy Starr, Ph.D. and Edward Greeno, M.D. are pairing this movement toward personalized cancer medicine with the clinical need for better treatments for colorectal cancer (CRC). Currently, there are no curative therapies for late stage CRC and prevention and survival rely primarily on screening and early detection.

“The hope is that, based on genetics and genomics, we can use information about a patient’s cancer to predict how it will respond to a specific therapy, manage the disease more effectively, and hopefully develop new targeted therapies that can extend patient survival, possibly turning some advanced lethal cancers into chronic diseases that can be managed therapeutically” said Cormier.

A goal of this research, said Cormier, is to develop a clinical tool that serves as a “prognostic predictor.” For example, in the future, it is hoped, the genomic mutation signatures of a patient’s cancer could be analyzed to determine at an early stage which patients will survive CRC surgery alone, and which patients will benefit from the addition of chemotherapy or possible new therapies.

“Currently, we have limited tools to guide these critical treatment decisions,” said Cormier.

To determine which genomic signatures predict certain outcomes, the team is sequencing DNA from 160 carefully annotated matched normal colon and early stage colorectal cancer samples obtained from collaborators at the VU University Medical Center in Amsterdam. Each sample comes with long-term clinical information such as type of treatment and survival rate. Bio-statisticians are analyzing the raw data to find genetic differences between the samples and outcomes. The objective is to identify a genomic signature, a set of mutations associated with cancer relapse, which can predict disease progression. Future funding will allow the team to validate the results against a second larger set of samples.

Another key aspect of this project is the identification of novel genetic mutations (fusion oncogenes) not picked up in normal gene sequencing. The fusion of two genes forms a chimera, creating its own unique properties and, therefore, treatment implications. Until fairly recently, scientists believed these mutations were uncommon in cancers like CRC. However, new sequencing technology and bio-analysis software readily permits identification of these fusions. Cormier, Largaespada, and their team have identified more than 800 novel fusions, about half of which appear to represent transcription-induced chimeras. Additionally, the team has identified more than 80 gene fusions in CRC, with about 20 of those as having a high probability of causing disease based on statistical analysis.

According to Cormier, this is the first large-scale study of human fusion transcripts for CRC, and results will be published this year. The next step is to link these fusions to specific clinical outcomes.

““There is potential here for new therapeutic targets,” explained Cormier. “These fusions are not made in normal cells, and thus are unique. Therefore, drugs can potentially be developed that will only target the specific chimeric transcript, and leave healthy cells alone.”
T cells: unlocking the potential of the body's immune system to fight cancer

The goal of this second SP3 project is to gain a greater understanding of how T cells work to control cancer growth, and to identify opportunities where T cells could be manipulated to provide very targeted cancer-specific treatments. The hope is to find an alternative and better approach to traditional chemotherapy, which affects both normal healthy cells and cancers.

Yoji Shimuzu, Ph.D. is project director, working collaboratively with Steve Jameson, Ph.D., David Largaespada, Ph.D. and Matthew Mescher, Ph.D. The program consists of four projects aimed at identifying the parameters responsible for activating and generating tumor-controlling T cells.

Highlights in 2013 included an automated bioinformatics tool, developed by Largaespada, which provides the first step in identifying neoantigens, the body’s first immune response to cancer. Mescher’s research has found differences in how CD8 T cells respond to certain signals. He discovered that T cells stimulated by interleukin 12 (IL 12) were more effective at controlling tumors. Also working with CD8 T cells, Jameson has shown that different subsets of these cells show distinct functional properties and capacity to control infection. Additionally, Shimuzu used photon imaging to gain more insight into the regulation and interaction of T cells.

“The immune system as a natural tool to treat cancer is a huge area of research,” said Shimuzu. “Many of these principles have relevance to cancer, but how can we help the immune system be better equipped to recognize and deal with altered normal cells when it is used to dealing with cells that are foreign? These are basic questions for us to answer.”

2013 Pilot Activities by MCC Members

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<tr>
<th>Award Program</th>
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<td>MCC Internal Grant Program</td>
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<td>CTSI Pilots</td>
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Award descriptions on following pages.
**2013 Masonic Cancer Center Internal Grant Program**

**Brainstorm Awards – $50,000**
- Anja Bielinksy, Ph.D., Eric Henderson, Ph.D., Alex Sobeck, Ph.D., Naoko Shima, Ph.D. & John Wagner, M.D.
  - “Comparative analysis of repair and checkpoint capacities of Fanconi anemia cells”
- Venkatram Mereddy, PhD, Lester Drewes, PhD
  - “Development of Novel Monocarboxylate Transporter-1 Inhibitors for the Treatment of Gliomas”

**Cancer Detection, Treatment and Survivorship Award - $25,000**
- Melissa Geller, M.D.
  - “Website-based hereditary cancer risk assessment for ovarian cancer patients”

**Cancer Prevention & Control Award - $25,000**
- Fekadu Kassie, Ph.D.
  - “Inhibition of lung tumorigenesis by combinations of myo-inositol and iloprost in A/J mice”

**Gynecologic Oncology Translational Working Group Seed Grant Award - $25,000**
- Amy Skubitz, Ph.D.
  - “Validation of Novel Prognostic Biomarkers for Serious Ovarian Cancer”

**Hematologic Malignancy Innovations Award – $25,000**
- Vivian Bardwell, Ph.D. & David Largaespada, Ph.D.
  - “Transposon based screen for Hodgkin’s lymphoma cancer genes”
- Jaime Modiano, Ph.D.
  - “A Comparative Assessment of the Role of the Alternative NFkB Pathway in DLBCL”

**Hourglass Integrative Therapies Cancer Research Award – $25,000**
- Annie Heiderscheit, Ph.D.
  - “Feasibility & acceptability of an active music making method with BMT patients and their parents”

**Minnesota Chemoprevention Consortium (MC²) Award - $50,000**
- Naomi Fujioka, M.D.
  - “Assessment of glucobrassicin/I3C uptake via a whole food matrix using urinary DIM”

**Translational Breast Cancer Research Award – $25,000**
- Elizabeth Wattenberg, Ph.D., Kaylee Schwertfeger, Ph.D.
  - “A New Model for Studying Collective Cell Migration and Invasion in Breast Cancer”

**Translational Pediatric Cancer Research Award - $25,000**
- Zigang Dong, M.D.
  - “Wilms Tumor 1: Tumor Suppressor or Oncogene”

**2013 CTSI Internal Funding**

**F&T Pilot Grant Program (Fellow & Traineeships) - $16,000**
- Caroline Diep, Fellow (Carol Lange, Ph.D. laboratory)
  - “En vivo modeling of primary ovarian cancer cells in 3D culture systems”

**New Investigator Pre-K Career Development Program - $52,000 over 2 years**
- Guatam Jha, M.B.B.S., M.S.
  - Primary Mentor: Jeffrey Miller, M.D.
  - “Potentiating of Cetuximab by Tregs Depletion With Metronomic Cyclophosphamide in Metastatic Squamous Cell Cancers of Head and Neck”

**K to R01 Transition to Independence Program - $50,000 over 2 years**
- Julie Ostrander, Ph.D.
  - Primary Mentor: Douglas Yee, M.D.
  - “PELP1 Localization as a Biomarker for Early Mammary Carcinogenesis and Response to Chemoprevention”

**R to R Pilot Grant - $75,000 over 2 years**
- Robert Cormier, Ph.D.
  - Collaborators: Gerrit Meijer, Ph.D.; Kevin Silverstein, Ph.D.
  - Project Title: Discovery of Fusion Oncogenes in Colorectal Cancer
- Joseph Gaugler, Ph.D.
  - Collaborator: Philippe Gaillard, Ph.D.
  - Project Title: The Residential Care Transition Module: Pilot Evaluation
- Reuben Harris, Ph.D.
  - Collaborators: Yen-Yi Ho, Ph.D.
  - Project Title: Determining clinical correlates of Apobec3 over-expression in breast cancer
- Usanadri Hui, Ph.D.
  - Collaborators: Chap Le, Ph.D.; Yan Zhang, M.S.
  - Project Title: Developing novel bio-markers to assess comprehensive bone loss in cancer patients
- Janet Thomas, Ph.D.
  - Collaborators: Hongfei Guo, Ph.D; Jasjit S. Ahluawalia, M.D., M.P.H., M.S.
  - Project Title: Exploring “Lose & Win” Contests to Promote Weight Loss among Overweight College Students
2013 OVPR Funding

2013 Minnesota Futures Research Grant Awards - $250,000
- Benjamin Hackel, Ph.D.
  "Targeting Metastatic Breast Cancer with Dual Specificity"

2013 Spring Grant-in-Aid Awards – est. $25,000
- Susanta Hui, Ph.D.
  "Functional imaging to assess cellular proliferation in hematological malignancies"
- Ameeta Kelekar, Ph.D.
  "Biophysical analysis of the structural dynamics of Bcl-2 protein, Noxa"
- David Largaespada, Ph.D.
  "Direct generation of tumor specific memory CD8 T cells"
- Timothy Starr, Ph.D.
  "Karl Storz Mouse Colonview Endoscopy System"
- Vaiva Vezys, Ph.D.
  "Immunity to SIV infection"

American Cancer Society Institutional Research Grant

2013 Pilot Awards - $30,000
- Julie Ostrander, Ph.D.
  "PELP1 protein interactions that promote early mammary carcinogenesis"
- William Pomerantz, Ph.D.
  "Polarity Switching Peptides for CREB:KIX inhibition"
- Anindya Bagchi, Ph.D.
  "Role of tumor suppressor CHD5 in DNA damage repair"
- Emil Lou, MD, Ph.D.
  "Tunneling Nanotubes as a Mechanism for Intercellular Transfer of microRNAs and Cellular Contents in Colon Cancer"
- Da-Qing Yang, Ph.D.
  "Translational Regulation of p53 Induction in Response to Cellular Stress"

2013 Academic Health Center Awards

Transition Grant Award - $30,000
- Erin Dickerson, Ph.D.
  "SMURF1 Maintains the Cancer Stem Cell Population by Reglating the BMP Switch"
- Scott McIvor, M.D.
  "Targeting Gene Therapy for Athabascan SCID"
- Michael Verneris, M.D.
  "Repair of Secoondary Lymphid Tissues Using Lymphoid Tissue Inducer (Lti) Cells"

Minnesota Partnership - $636,000 ($318,000 to MN)
- Lester Drewes, Ph.D. (Aaron Johnson, Ph.D., Mayo Clinic partner)
  "Development of Novel Drugs for the Treatment of Gliomas"

UMF Medicine and Health Faculty Bridge, Equipment, and Research Grants Program

Small Research Grants
- Michael Kyba, Ph.D. - $40,000 award
  "Regulation of Hematopoietic Development by Hox Proteins"
- Michael Olin, Ph.D. - $14,170 award
  "Glioma secreted exosomes suppress RGS3 protection from the immunosuppressive effects of TGF-beta"
- Naomi Fujikawa, M.D. - $15,000 award
  "Pilot analysis of unbound sorafenib: relevance to efficacy and toxicity in a Phase I trial and to in-vitro cytotoxicity"

Small Equipment Grants
- Timothy Starr, Ph.D. - $15,000
  "Modeling Colon Cancer in Mice"

2013 CETI Funding (MCC)

CETI Pilot Funding - $75,000
- Bruce Blazar, M.D./Mark Osborn, Ph.D.
  "Chimeric Antigen Receptors (CAR) Development"
**Prevention and Etiology Publications**


**Carcinogenesis and Chemoprevention Publications**


Sangaranu D, Goggins M, Walker V, Swenberg J, Tretjakova NY. NanoHPLC-nanoESI(+)-MS/MS quantitation of bis-N7-guanine DNA-DNA cross-links in tissues of B6C3F1 mice exposed to subppm levels of 1,3-butanediene. *Anal Chem.* 2012;84:1732-1739. PMCID: PMC3298759


**Genetic Mechanisms of Cancer Publications**


Oh S, Wang Y, Zimbic J, Hendrickson EA. Human LIGIV is synthetically lethal with the loss of Rad54B-dependent recombination and is required for certain chromosome fusion events induced by telomere dysfunctions. Nucleic Acids Res. 2013 Feb 1;41(3):1734-49. PMID:PMC3561972


**Tumor Microenvironment Publications**


Immunology Programs Publications


Krentz AD, Murphy MW, Zhang T, Sarver AL, Jain S, Griswold MD, Bwdwell VJ, Zarkower D. Interaction between DMRT1 function and genetic background modulates signaling and pluripotency to control tumor susceptibility in the fetal germ line. Dev Biol. 2013 Mar 6. PMID:23473982


Cell Signaling Publications

Böttner PB, Polenovsky VA. Attacking a nexus of the oncogenic circuitry by reversing aberrant eIF4F-mediated translation, Mol Cancer Therapy, 2012;11(5):1061-1069. PMCID:PMC3349966


Krentz AD, Murphy MW, Zhang T, Sarver AL, Jain S, Griswold MD, Bwdwell VJ, Zarkower D. Interaction between DMRT1 function and genetic background modulates signaling and pluripotency to control tumor susceptibility in the fetal germ line. Dev Biol. 2013 Mar 6. PMID:23473982


Transplant Biology and Therapy Publications


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Deborah J. Hennrikus, Ph.D.
Keli L. Hippen, Ph.D.
### 2013 Masonic Cancer Center Research Members

<table>
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