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organization since 1962.

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## CRC Loses a Friend – Dr. Ben W. Papermaster

November 30, 1934 - December 22, 1999

By John E. McEntire, Ph.D.

A scientist, a mentor, a friend. All are words that describe Dr. Ben Papermaster, former Director of the Cancer Research Center. Dr. Papermaster died of cancer at his home in Coronado, California in December. He was originally from North Dakota, earned a B.A. in music from Harvard, an M.S. in anatomy and a Ph.D. in immunology from the University of Minnesota. Ben's work on the evolution of the immune system and the role of the thymus in immunology are still considered some of the most important findings in modern cellular immunology. He had a very successful academic career with faculty positions at Stanford, UC-Berkeley, Roswell Park Memorial Cancer Institute, and the University of Texas Medical Branch. Ben launched several science-based companies including Associated Biomedical Systems, IMBIC Corporation, and Kinex Corporation. Ben is survived by his wife, Sue Kwentus; his brother, Dr. David Papermaster; his children Gail, Steve, Mark and Adrienne; and seven grandchildren.

As with every other position he held, Ben's arrival at the Cancer Research Center in 1978 brought with it excitement, promise, new approaches to cancer treatment, and world-class cellular immunology. The people of Columbia and all of Missouri benefited from having this good man at the helm of CRC. Many exciting new programs were launched. Clinical trials of immune stimulators (lymphokines) were available in Missouri well before they became commonplace in other parts of the country. Cancer education and outreach programs, women's cancer screening programs, and basic research into the immunology of cancer were all begun or greatly enhanced under Ben's leadership.

Those of us who were then young,



Ben W. Papermaster

enthusiastic CRC scientists benefited even more directly. Ben was a huge influence on our careers and our lives. He taught us sound scientific principles, made sure that we met patients who were victims of cancer so that we understood the importance of our work, and taught us how to navigate the scientific "political" maze of grantsmanship, publishing, and peer review. In looking back on those ten years of working with Ben, I now realize that he taught us all many things that were much more important. We learned how to work as a true team, each of us contributing and encouraging others, focusing on tough goals. He constantly challenged us, taking risks by giving us much more responsibility and authority than we should have been able to handle. We all rose to the challenge, learned how to handle tough situations and realized that success was certainly preferable to failure, especially when cancer was the opponent.

Hardly a week passes that I don't find myself smiling and telling a "Ben" story to someone. Stories like coming home on my birthday and finding a crew of friends had painted my

house purple and were having a party in my living room ... returning from a trip and finding my office door removed and drywalled over (a sledgehammer in the hall had a welcome back note from Ben attached). The young kids I now take an interest in and mentor hear about the wonderful guy who once took a risk with me. They hear about how he took a skinny kid who had given up and become overwhelmed, gave him a job, and encouraged him to finish his doctorate. I learned from Ben to enjoy taking risks with those who don't seem to have gotten things right their first time around and watching them succeed. As friends, Ben and I helped each other through some tough personal times. We all felt the sting of failure as we watched his wife and my friend, Pam Dunn, die of breast cancer at a young age. The frustration of seeing the experimental drugs that Pam and I had co-developed not be the "silver bullet" we needed were almost unbearable for us all.

I still recall my days at CRC under Ben as a work environment where productive people laughed and couldn't wait to get back to work the next day. This special person opened my eyes to appreciate diversity, showed me that there was a much bigger world, and taught us all to think without limits. Ben really and truly made a difference in all our lives. I have never had another job that I enjoyed like the CRC one, nor have I ever had another friend that I knew really cared for people like Ben did.

As I attended Ben's memorial service in Austin a few months ago, I noticed one very striking thing. People were smiling, people were laughing, and people were feeling loved while recalling Ben's life. He would have liked that.

—Dr. McEntire was a former Scientific Director of CRC, and is currently a lifetime member of the Board of Trustees.

10th Annual  
Jim Kidwell Memorial Gala

Come sing with the kings of song,  
and dance with the legends  
of rhythm and soul



The Cancer Research Center (CRC) will be hosting the 10th Annual Jim Kidwell Memorial Gala on Saturday, April 29, 2000 at the Knights of Columbus Hall (2525 North Stadium Blvd., Columbia, Missouri). This year's event will remember Mr. Jim Kidwell and Mr. Ray Freese, two Central Missouri businessmen who were very much responsible for the successful history of this event.

The theme for this year's fundraiser is "The 1960s." A cash bar will open at 6 p.m. with appetizers followed by dinner at 7 p.m. The evening will include a silent and live auction; blackjack and craps tables; 1960s entertainment; and dancing to the music of legends.

It promises to be a wonderful evening full of fun and frolic. Tickets to this gala event are available to the general public through CRC for \$50 each. In addition, a table for eight can be purchased for \$400. CRC is a 501(C)3 non-profit organization, and all contributions to this event are tax-deductible to the extent the law allows. In addition, CRC is not affiliated with any national organizations, thus all proceeds from the gala stay in Columbia.

For more information, contact Ron Schmidt, CRC Development Director at (573) 875-2255.

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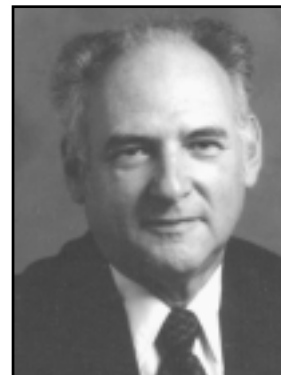
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## Cancer Research Center Staff and Board Update



Jim Cherrington



Dr. Abraham Eisenstark



Ron Schmidt

**D**uring its 1999 annual meeting, the Board of Trustees named Jim Cherrington Director of the Cancer Research Center (CRC). Effective January 1, 2000, Cherrington assumed the leadership role of CRC. He is responsible for the management of daily activities and personnel supporting the goals of cancer research, education and prevention. Cherrington had been serving as CRC's Manager of Business Operations since 1987.

Dr. Abraham Eisenstark, who had been CRC's Director for ten years, has stepped down to become the Associate Director for Research at CRC. Dr. Eisenstark will continue with his research program, as well as advise Director Cherrington on scientific matters. Prior to joining CRC, Eisenstark was Byler Distinguished Professor and Director of Biological Sciences at the University of Missouri-Columbia.

In January 2000, Ron Schmidt joined CRC as its new Director of Development. Schmidt will help CRC further its important mission by raising funds through the submission of grant applications and coordination of community fund-raising events, including the Annual Jim Kidwell Memorial Gala. In addition, he will be responsible for speaking to various service, church, civic, and work groups in Missouri about cancer research and prevention; coordinating CRC's involvement in area Health Fairs; and giving CRC facility tours.

Also joining CRC in January were three newly appointed members to its Board of Trustees. They are Dr. Jane Armer, Steve Lee, and Dr. Paul Lineberry.

Dr. Armer is the Co-Director for the MU School of Nursing's Office of Research. Dr. Armer, who has a Ph.D. in Nursing, is an acclaimed grant writer and has published numerous professional papers.

Lee has a long history in the local construction industry. He worked for Jim Kidwell, a former CRC volunteer, at Boone County Lumber, until Kidwell left to have a bone marrow transplant procedure. At that time, Lee assumed Kidwell's duties at the lumber company. Kidwell asked Lee to be involved with CRC in his absence, and he has. Lee has been very active in helping coordinate the Annual Jim Kidwell Memorial Gala, including serving as co-chair of this year's event, which will be held on Saturday, April 29.

Dr. Lineberry has B.S and M.S. degrees from MU, as well as a Ph.D. from Colorado State University. Dr. Lineberry has worked as a county extension agent, program analyst, with the Law Enforcement Assistance program, as well as the Division of Aging. Dr. Lineberry retired in 1990. From 1996 to 1998, he served in the Grand Family, Order of Eastern Star (OES). Cancer research has long been a primary charity of OES. Dr. Lineberry's goal is to continue OES support of cancer research in Missouri.

### First National Bank & Trust Company

#### Staff Charitable Fund Student Fellowship Award

In January 2000, the Cancer Research Center (CRC) was the recipient of a generous contribution by the First National Bank & Trust Company staff charitable fund. This is the second year CRC has been designated to receive funding from the bank located in Columbia, Missouri.

Donations from valued contributors such as these people are very important. Recognizing the high level of confidence and trust the FNB employees have placed in our scientific staff, we evaluated current research activities and determined the best use of this donation.

CRC has established the First National Bank & Trust Company Staff Charitable Fund Student Fellowship Award. CRC will use restricted research funds to match this contribution and apply the total amount to a student fellowship. This award will be renewed upon a yearly basis as funding is available.

For the inaugural award, CRC has selected Samantha Potter as the recipient. Samantha is a senior at the University of Missouri-Columbia in the School of Agriculture. She is cur-

rently working in the CRC laboratory on a Mutation Diversity project under the direction of Dr. Abraham Eisenstark. "Samantha is a brilliant student with a bright research future," stated Dr. Eisenstark. "She plans to attend medical school. Samantha's research experience will enrich her life as a physician."

We appreciate the support of the employees of First National Bank and Trust Company. Donations such as this have a major impact on our research efforts.



## What is CRC?

*The Cancer Research Center (CRC) of Columbia, Missouri is an internationally recognized institution serving the public since 1962. CRC is devoted to the field of cancer research, early detection, and education. While our work is scientific, our incentive stems from a genuine concern for cancer patients and the abuse of human dignity they endure.*

CRC is involved in the most advanced, innovative, and effective cancer research. Despite the many obstacles that exist in the study of cancer, dedicated institutions, like CRC, have made significant progress. Cancer, unlike many diseases, is highly individual, making it very difficult to detect and treat. In an effort to overcome this, CRC is developing a multitude of diagnostic tools.

Relying on the latest technology, CRC tailors diagnostic programs for individual cancers and has received worldwide recognition. CRC scientists believe it is possible to fight cancer by strengthening the body's natural disease fighting processes. We seek ways to detect cancer at its most basic stages and to deliver the benefits of science to individuals in their own communities.

### Want to know more?

Most people know CRC for its research, but we do a lot more. We also offer community outreach programs to educate church groups, civic clubs, and other organizations about our research and cancer prevention.

### Frequently asked questions are:

- Is cancer contagious?
- Can cancer be caused by an injury?
- Are all cancers inherited?
- Is cancer a disease of the elderly?
- Does personality or stress cause cancer?
- Is cancer always painful?
- Does cancer mean certain death?

Do you have your own inquiries about cancer? Would you like to know more about what we do at CRC? Or perhaps you just want to learn a little more about the research itself?

With one simple phone call, CRC scientists and research staff will gladly give a presentation to your club, organization, or church group at no charge to you. These presentations include not only informative speakers, but slides, graphs, brochures, and time to answer the questions that you may have concerning cancer and our center. Educating the public is important to us. Widespread knowledge of our research is key to finding a cure for this disease. We are happy to help you. To schedule a speaker, contact Ron Schmidt, CRC Development Director at (573) 875-2255.

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## Cancer is a Devastating Disease



The National Cancer Institute estimates that nearly 8.5 million Americans living today have a history of cancer, and over 1.2 million new cancer cases are expected to be diagnosed this year. Cancer is the second leading cause of death in the U.S. One out of every four deaths is from cancer.

In Missouri, the news is even less encouraging. According to the National Center for Health Statistics, Missouri's cancer mortality rate for males is 9.1 points higher per 100,000 persons than the U.S. rate (227.4 vs. 218.3), and the rate for females is 0.8 points higher than the national rate (143.1 vs. 142.3).

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## **This is how your donation leads to reduced cancer deaths**



*A number of promising new strategies are being developed by Columbia scientists for the prevention, diagnosis, and treatment of cancer.*

*The Cancer Research Center (CRC) provides additional funds for their projects.*

### THE SCIENTISTS AND THEIR STRATEGIES INCLUDE:

1. Radiopharmaceuticals to target and destroy tumors. In this strategy, developed at MU, drugs are linked up with radioactive metals that specifically attach to tumor cells. First, this can provide a visual image to pinpoint the tumor. Next, the energy emitted from the radioactive metal can then destroy tumor cells. These are the investigators who receive CRC support and who use this strategy, and their description of their research.

#### ■ **Pancreatic Cancer**

*Dr. Tim Hoffman, CRC award recipient*

Pancreatic cancer is currently the fourth leading cause of cancer mortality in the United States. Present limitations in conventional chemotherapy speak to the need to develop new therapies, coupled with improved diagnostic strategies, to enhance quantity and quality of life in patients diagnosed with pancreatic cancer. The research project being conducted with CRC holds the potential for development of one or more radiolabeled Gastrin Releasing Peptide (GRP) receptor-avid pharmaceuticals, that will be effective site-directed agents, for the diagnosis and/or treatment of patients with localized, as well as metastasized pancreatic cancer. Using appropriate radioisotopes, Tc99m for diagnostic purposes, one can prepare radiolabeled compounds with targeted radiodiagnostic/radiotherapeutic capabilities.

**Bottom Line — Using this selective targeting approach should lessen the toxic effects of drugs that are in current use.**

#### ■ **Malignant Melanomas**

*Dr. Thomas Quinn, CRC award recipient*

Malignant melanoma has become a serious public health problem due to an increase in incidence and the difficulties in discovering and treating melanoma metastases. Malignant melanoma is the eighth most common cancer in the U.S. In 1993, there were 6,800 deaths due to malignant melanoma and 32,000 new cases reported. Currently, 1 out of 105 Caucasians will develop malignant melanoma, and the rate is projected to be 1 out of 75 by the year 2001. Early melanoma tumor diagnosis and prompt surgical removal are a patient's best hope for a cure. Metastatic malignant melanoma is resistant to current chemotherapeutic and immunotherapeutic drugs. Combinations of chemotherapeutic agents or chemo/immunotherapeutic agents offer the best response rates. Despite recent advances in combination therapy regimens, the median survival for patients diagnosed with metastatic malignant melanoma is approximately six to nine months, with less than 10% surviving five years or more.

We have developed a novel family of peptide-based radiopharmaceuticals cyclized through the coordination of the radiometals Tc-99m or Re-188, that target a receptor present on the surfaces of malignant melanoma tumor cells. We have examined the tumor imaging properties of Tc-99m[CCMSH] in a mouse melanoma model system. The mouse image clearly shows high activity uptake in the melanoma tumor with very low background levels in the rest of the mouse. High tumor to background ratios will allow us to visualize melanoma tumors located throughout the body. Likewise, the analogous compound Re-188[CCMSH] has potential as a therapeutic agent in the treatment of malignant melanoma.

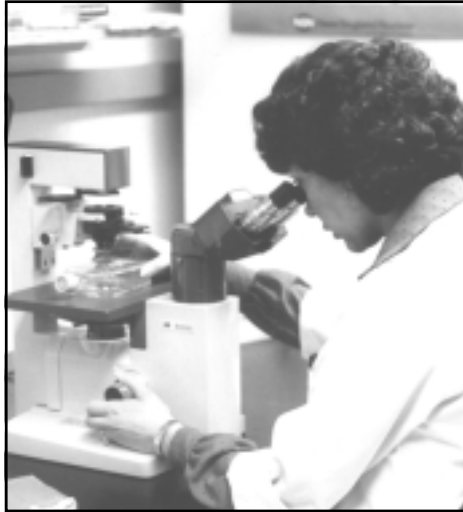
**Bottom Line — This targeted therapy linking radioactive isotopes with drugs should lead to earlier diagnosis as well as destroying tumor cells.**

## ■ Diagnosis and Treatment of Cancers

*Dr. Kattish Katti, CRC award recipient*

Although a number of modalities are available for diagnosis of cancer, there is a need for the development of more selective diagnostic agents which can detect primary sites, identify sites where it has spread (metastatic sites), guide surgical interventions, and monitor efficacy of therapeutic agents to improve patient outcomes. In this context, receptor based site-specific <sup>99m</sup>Tc-labeled radiopharmaceuticals provide emerging diagnostic tools which can fulfill these needs.

Receptor based site-specific radiopharmaceuticals, when prepared with a suitable radioisotope (incl., <sup>188</sup>Re), are also useful in the treatment of cancer. They can localize with high specificity at primary as well as secondary cancer sites, even when their location in the body is unknown. Therapeutic radiopharmaceuticals that specifically target tumors will deliver high radiation doses to the tumor while producing minimal radiation damage to the normal tissue. This would make them more effective than existing external beam radiotherapy.



Hence, site-specific radiopharmaceuticals could be called “magic bullets” due to their potential efficacy in selective eradication of cancer.

**Bottom Line — This targeted therapy linking radioactive isotopes with drugs should lead to earlier diagnosis as well as destroying tumor cells.**

2. Basic understanding of what triggers chromosome damage and the repair of that damage. Although there are dozens of different kinds of cancer, all of them have one thing in common. All tumors are initiated by damage to DNA. Fortunately, cells have repair mechanisms for repair of this damage. However, in some cases, damage is too great or repair is inadequate and cancer develops. These are the investigators who study DNA damage and repair, and their description of their research.

## ■ Study of Cytoskeletal Targets for Prevention of Cell Division During Cancer

*Dr. Heide Schatten, CRC award recipient*

While some progress had been achieved in recent years to inhibit cell division with taxol, this treatment is not ideal because of the unwanted side effects associated with taxol. The goal of our research is to inhibit very specifically cell division in cancer cells which will destroy only cancer cells without interfering with cell metabolism in healthy tissue. For this approach we have undertaken studies in a transgenic mouse (TRAMP) model and in the prostate cancer cell lines LNCaP and DU145 to investigate the molecular mechanisms during cell division that specifically distinguish cancer cells from normal cells. For technical reasons, our investigations specialize in prostate cancer but will also benefit cancers of the breast, lung, liver, and other affected organs.

We have focused on the cell organelles which are crucial for cell division. Centrosomes are composed of highly specific proteins which are responsible for precisely organizing the distribution of cellular material to the two daughter cells after cell division. One of the problems during cell division in cancer is that centrosome proteins are imbalanced which results in imbalanced and unequal cell divisions. This sets up cycles of no return into the resting stage of the cell cycle. In order to control, cancer it is crucial to assure a precise regulation of centrosome proteins.

**Bottom Line — These approaches are preferable over unspecific arrest of cell division with current anti-mitotic drugs such as taxol.**

## ■ Cancer: A Balance Between DNA Damage and Repair

*Professor Stephen Alexander, CRC award recipient*

DNA, the genetic material of all living organisms is constantly subjected to damage from ultraviolet light and chemicals. In animal cells,



“There are no such things as incurables; there are only things for which man has not found a cure.”

-Bernard M. Baruch



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unrepaired damage can result in mutations and ultimately cancer. Indeed, skin cancer due to overexposure to sunlight is one of the most prevalent forms of cancer in the world. Fortunately, cells of all organisms have mechanisms for repairing damaged DNA. Several repair mechanisms have been identified in animal cells and they seem to be biased towards the type of DNA damage. However, little is known about how the cell senses the type of DNA damage and how it elicits the correct response to the damage. Solving this problem remains one of the most important challenges in cancer biology today because the solution will provide clues to novel detection methods and therapies.

In addition to mutants that are hypersensitive to DNA damage, we also expect to obtain mutants that repair DNA damage better than normal cells. These mutants may define another class of genes and have great potential for investigating the response to other DNA damaging agents including chemicals and other types of radiation.

We expect to identify several genes involved in the response to UV light induced DNA damage. We can immediately determine how these genes are regulated and whether they are involved in the response to other DNA damaging agents or are specific to UV damage. Virtually nothing is known about the mechanisms that animal cells use to protect themselves from cancer by repairing damaged DNA. The identification of these protective mechanisms will allow many possibilities for developing new diagnostic protocols, as well as novel therapeutic drugs that intervene at specific steps of the pathway.

**Bottom Line — By identifying the chemical and immunological structure of critical cell components, superior drugs can be developed to specifically destroy those cell components that lead to runaway growth of tumors.**

■ **Genes that Regulate Synthesis of Anti-Oxidant Enzymes that Avoid or Repair Cancer-Causing Damages**

*Professor Abraham Eisenstark (in collaboration with Associate Professor Miriam Golomb and Research Assistant Professor Michael Calcutt)*

Oxidants are like molecular bullets that can damage chromosomes, thus capable of initiating tumors. These oxidants are present in certain

foods, present in ultraviolet rays of the sun, and also are produced in cells as a result of normal metabolism. Fortunately, cells also produce anti-oxidants and anti-oxidant enzymes that can both destroy oxidants and repair damaged chromosomes. In addition, foods that contain anti-oxidants such as vitamin C, vitamin E, and selenium are important in countering damaging effects of oxidants.

Our research has focussed on understanding how regulatory genes are involved in the synthesis of anti-oxidant enzymes and DNA repair enzymes. One of our earlier discoveries [with Professor John McCormick] was that ultra-violet B radiation from the sun produced oxidants that can cause skin cancer. Because of the recognition of the oxidative effects of sunlight, sunscreens now contain anti-oxidants to combat these harmful effects.

**Bottom Line — Basic knowledge of the damaging effects of oxidants and the role of anti-oxidant enzymes should lead to the reduction of cancer incidents.**

■ **Finding Essential Proteins that Regulate Cell Growth and Death**

*Dr. Mark Hannink, CRC award recipient*

This research involves the understanding how the activity of proteins implicated in cancer is controlled. Many genes and their encoded proteins have been implicated in cancer, and our laboratory works on one group of these proteins, termed the Nuclear Factor *kappa B* transcription factor. This group of proteins, also known as NF- $\kappa$ B for short, is an important regulator of both cell division and programmed cell death. As cancer cells arise when cell division is inappropriately stimulated and programmed cell death pathways are shut off, the NF- $\kappa$ B proteins are important modulators of cancer development.

We will characterize two mechanisms that control the activity of NF- $\kappa$ B proteins. One mechanism is through inhibition of nuclear import of NF- $\kappa$ B. In normal cells, NF- $\kappa$ B is retained in the cytoplasm through association with an inhibitor protein, known as I $\kappa$ B. However, in various types of cancer, I $\kappa$ B is no longer able to inhibit nuclear import of NF- $\kappa$ B, with the result that NF- $\kappa$ B is able to enter the nucleus and activate expression of growth-stimulatory and anti-cell death genes. This research will enable us to understand how association of NF- $\kappa$ B with I $\kappa$ B leads to a block

in nuclear import of NF- $\kappa$ B.

Our laboratory has recently discovered a second regulatory mechanism whereby I $\kappa$ B controls NF- $\kappa$ B. In particular, we have shown that I $\kappa$ B is able to export NF- $\kappa$ B from the nucleus. This nuclear export function of I $\kappa$ B is part of a feedback inhibitory loop that keeps NF- $\kappa$ B activity under control. A second focus of this research will be to dissect the molecular mechanism(s) that are responsible for I $\kappa$ B mediated nuclear export of NF- $\kappa$ B.

What is the potential impact of this research for reducing cancer incidence and deaths? As NF- $\kappa$ B activation occurs in response to a large number of cancer-causing agents, including DNA-damaging agents such as UV irradiation.

**Bottom Line — We anticipate that this research will lead to a better understanding of how regulation of NF- $\kappa$ B activity can be restored and thereby interfere with the development and growth of cancer cells.**

■ **Role of Estrogens in Cancer Control**  
Professor Dennis Lubahn, CRC award recipient

Breast cancer is one of the leading causes of death among women with approximately one in nine contracting some form of this disease within her lifetime. It has been known for some time that certain types of breast cancers require estrogens for proliferation. This observation has led to a therapy

based upon the administration of an estrogen antagonist such as tamoxifen over time, rendering such treatment ineffective. This leads to the development of a tumor that is no longer estrogen responsive. The development of estrogen resistance leads to two central questions. First, what makes some cancers halt cell division in response to estrogen? Second, how do the cancerous cells develop a resistance to this treatment? The answers to these questions are key to developing an effective therapy for many types of breast cancer.

We use specific approaches to identify proteins involved in estrogenic responses in an attempt to isolate a putative estrogen receptor (ER- $\gamma$ ). The first approach will use the lactoferrin gene promoter that responds to methoxychlor, and estrogenic compound, in an unusual manner.

Identification of all of the receptor proteins involved in the estrogen response of cells is the fundamental first step to understanding how interactions can occur to affect the tumor progression. Such understanding will lead to positive treatments for hormone-responsive cancers through use of selective estrogenic agonists and antagonists to specific receptors. This type of targeted therapy would be a more effective alternative to currently available therapies in the fight to control breast cancer and other estrogen responsive tumors.

**Bottom Line — This targeted therapy would be a more effective alternative to currently available therapies in the fight to control breast cancer and other estrogen responsive tumors.**

3. Destruction of tumor cells with novel drugs and toxins. The search is still on for much better therapeutic agents to destroy cancer cells.

■ **Novel Ways to Inhibit the Growth of Cancer Cells**  
Dr. Gary Weisman, CRC award recipient

A major emphasis in the development of new cancer treatments is to devise novel ways to inhibit the growth of cancer cells, thereby preventing tumor formation. Another effective approach is to employ cancer treatments that increase the rate of tumor cell death. We are studying a family of proteins called nucleotide receptors that are present in a wide variety of tissues. Evidence suggests that a specific nucleotide receptor called P2X, functions to promote tumor cell death. We are investigating this protein at the molecular level to understand how it kills cancer cells. Another nucleotide receptor called P27, functions to increase the growth of blood vessels that accelerate tumor formation. By studying P2Y receptors, we hope to learn how to pre-

Continued on page 12

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## 10th Annual Jim Kidwell Memorial Gala

Saturday, April 29, 2000  
Knights of Columbus Hall  
2525 North Stadium Blvd.  
Columbia, Missouri

Social Hour and Silent Auction begin at 6:00 p.m.  
Dinner will be served at 7:00 p.m.  
Live Auction will follow.

Tickets only \$50 each

A table of eight is available for \$400

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- **BROOKFIELD, MO**  
Walter & Marilyn Carr  
John & Clarita Casey  
Rhodes Funderal Home
- **BRUNSWICK, MO**  
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Bill & Roberta Hardwick  
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Bill & Jean Cox  
Billy & Margie Kamp
- **CAMDENTON, MO**  
Russell & Louise Elsberry  
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- **CAMERON, MO**  
Raymond & Billie Goll
- **CANTON, MO**  
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Cleta Mae Van Tress
- **CARROLLTON, MO**  
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Mr. & Mrs. Skip White
- **CARTHAGE, MO**  
Vernie & Mary Ayres  
Class of 1949
- **CENTRALIA, MO**  
Chance Foundation  
Arlen & Fay Dailing  
First Christian Church  
K-4th Grades  
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Harrison Farm Women Club  
The Holiday Luncheon Club  
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George & Pauline Jennings  
Matt & Phyllis Lewis  
Helen March  
W.D. & Evadine Overfelt  
Emma Palmer  
Alma Remley  
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Eugene & Charlene Shores  
Nancy Sweezer  
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Mrs. R.F. Willett  
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Edyth Wood
- **CHESTERFIELD, MO**  
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Harber  
Mr. & Mrs. Sam G. Johns  
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- **CHILLICOTHE, MO**  
Erma Lee Pryor
- **CLARK, MO**  
O.E.S. Clark Chapter No. 396  
Louis & Evelyn Owings  
K.R. & Billie Ridgway  
Virginia Frances Truesdell  
Wanda Truesdell
- **CLARKSVILLE, MO**  
Jim Thurmond Cooper
- **CLINTON, MO**  
Anonymous  
Bud & Jeanie Boehler  
Jean Booth  
Fred & Susan Braun  
Gladys Doan  
First National Bank of Clinton  
Bruce Hord  
David & Joyce Kelsay  
Henry Wurzer
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Helen K. McClary
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Baumgartner  
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J.E. & Mathilde Berkley  
Bill Bower  
Clifford & Agnes Boyd  
Don Ray Brady  
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Joe K. Crews  
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Sue Dalton  
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Heriberto & Alda Del Porto  
Joan DuBose  
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Charles & Mary Dysart  
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- Fabulous Fifties Plus  
Mr. & Mrs. John Falloon  
Nancy Toedebusch Fay  
The Feintuch Family  
First National Bank -  
Employees Charitable Fund  
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Virginia Higdon Forsberg  
Bob Franke  
Vera Franke  
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Debra Glover  
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Harlan & Jane Hackett  
Doris & Ed Hampton  
Everett & Virginia Hancock  
Logan & Mary Heathman  
Katherine Anne Himberger  
Dorothy Hitzeroth  
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Christopher Hueser  
Garrell Iddings  
Dorothy M. Jacob  
Everett & Lucille Jacobs  
Martha B. John  
R.D. & Marguerite Johnson  
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Elmer Kiehl  
Susan Klockow & girls  
Margaret Klug  
Leona & Virgil Koch  
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Randall & Marian March  
Shirley Marshall  
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Shawna & Calvin McGee  
Susie McGee  
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Terri Ogden & Gary Parham  
Owen & Gertrude Oliver  
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Ben & Madge Riley  
Katie Rodgers  
Mr. & Mrs. Schermer  
Raymond Schooler  
Evelyn Scott  
Bob & Eva Scott  
David & Claire Self  
Ronald & Doris Shannon  
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Beatrice Smith & Family  
Richard & Mary Smith  
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- LaVerne Strom  
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Terry & Herb Taylor  
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Sherman & Merline Tennyson  
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Toastmaster, Inc. MIS Dept.  
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Nelson & Lorene Trickey  
James Turk  
Wayne & Linda Walker  
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Lawrence Wasson  
Grace West  
Loretta Wilkinson  
Dorothy Williams  
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- **EL DORADO SPRINGS, MO**  
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Jim & Donna Harrison
- **ELSBERRY, MO**  
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David & Elizabeth Pruett  
Patsy & John Schaefer  
Beverly Williams
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Joe & Loretta Gallatin  
A.P. Green Refractories -  
Employee Recreation Fund  
Georgia & Darrel Haymart  
Toni & Jim Klick  
Robert & Dorothy Pasley  
Gregory & Tammy Sellmeyer  
Richard & Marnie Tutt  
Anna Walker
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Mr. & Mrs. Mark Freese  
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Gertrude Johanning Family  
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Louise Niekamp  
Bernadine Renne  
Eldred & Marie Speiser  
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- **GORIN, MO**  
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- **GREEN CITY, MO**  
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- **GREENVILLE, MO**  
James (Boss) Clark  
Esther Frazier
- **HALE, MO**  
Clara Guilford
- **HALLSVILLE, MO**  
Marvin R. Sims  
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- Leonard & Carol Stegeman &  
Family
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Harwood Royal Neighbors  
of America
- **HIGGINSVILLE, MO**  
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Eglentyne B. Russell  
W. Dale & Ethel Sherman  
Max E. Tyler
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Mildred Menefee
- **HOLTS SUMMIT, MO**  
Mary June & Ray Bonnett  
W.R. "Pete" Petrus
- **HOUSTON, MO**  
Bucyrus Community Club  
Daisy Gilley
- **HUGHESVILLE, MO**  
John & Kay Tevis
- **HUMPHREYS, MO**  
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- **HUNTSVILLE, MO**  
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- **INDEPENDENCE, MO**  
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- **JEFFERSON CITY, MO**  
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Frank & Jean Crooks  
Alice Hahn  
Fern Mayes  
Alberta Meyer  
Missouri State Employees  
Charitable Campaign  
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Mary Jones Eime  
Mrs. Carl Hildebrandt
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- **KAHOKA, MO**  
Jewel Glasscock
- **KANSAS CITY, MO**  
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- **KEARNEY, MO**  
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- **KINGDOM CITY, MO**  
Clifford Borgelt
- **KIRKSVILLE, MO**  
Lou Jean Simmons
- **KNOB NOSTER, MO**  
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- **LA BELLE, MO**  
O.E.S. LaBelle Chapter No.  
316
- **LA GRANGE, MO**  
St. Peters Lutheran Social  
Club
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Treva Moyer  
Lola M. Waddell  
Frankie Woody
- **LAREDO, MO**  
Pauline Baldwin
- **LEBANON, MO**  
Melvin & Verna Anglin
- **LEWISTOWN, MO**  
Richard & Janet Porter
- **LICKING, MO**  
Delmar & Patsy Kissiar  
Coy L. Rodgers
- **LINCOLN, MO**  
Ethel White
- **LINN, MO**  
Linn State Bank
- **LOHMAN, MO**  
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Dick & Cindy Asquith
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Wanda Lewellen  
Agnes Lindsey  
Doc & Mickey Madison  
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Mr. & Mrs. Hubert W. Moehle  
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- **MALTA BEND, MO**  
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Joyce J. McRoberts
- **MARSHALL, MO**  
Freddie & Lauretta Adams  
Norm & Mary Clark & Family  
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Becky Gieringer  
Gene Heinzer  
James R. Johnson  
Josephine V. Keyton  
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Charlotte & Brian Sidwell  
Eunice Stallings  
Mr. & Mrs. Frank Swisher-Biz  
Luetta D. Vardimann  
John & Elizabeth Ann Wright  
Kaye Wright
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Don & Leona Cope  
Mary B. Fennewald
- **MEADVILLE, MO**  
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Clarence & Thelma Buttman  
Wendell Holcer
- **MEXICO, MO**  
A & B Prescription Shop  
Rexene P. Boren  
Jerry & Shirley Brauer  
Margaret Cole  
Mary Lou Crockett  
Mr. & Mrs. John Hagan  
Gary & Sue Ann Keith  
Mike & Joy Keith  
Stanley & Artelia Kelley  
Don & Vicki Mason  
Nancy Miller  
Anna M. Payton  
Marshall & Reba Penn  
Bill, Betty & Jennifer Potts  
Lorrest & Leda Sears Trust  
Jerry Sudbrock  
Clay & Marilyn Taliaferro  
Martha E. Vanskike  
Betty P. Whalen
- **MIAMI, MO**  
Mrs. Carlisle Morrison
- **MIDDLETOWN, MO**  
Dora Wells Harness  
Mr. & Mrs. Lowell Harness  
Claudia Wells  
Mr. & Mrs. Homer Wille
- **MOBERLY, MO**  
Charles & Roberta Crutcher  
Bill Hagedorn
- **MOSCOW MILLS, MO**  
Peggy Powelson
- **NEW FLORENCE, MO**  
Jewel E. Rickhoff
- **NEW FRANKLIN, MO**  
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Auxiliary  
Turley Fenical  
Mr. & Mrs. Cary Lang
- **NEW HARTFORD, MO**  
Hopke Christian Church  
Elaine & Marcine Niemeyer  
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Mr. & Mrs. Bill Painter

■ **O'FALLON, MO**  
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Ronald & Barbara Pohlman

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Alton & Thelma Carnell  
Raymond & Betty Thompson

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Wilma Johnson

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Baxter Club

■ **SALISBURY, MO**  
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Patty Farnham  
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Anna Mae Hillsman  
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Waterloo Industries, Inc.

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Rey Eilers  
Christopher & Arlene Farrar  
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Donald, Ricky & Barbara  
Green  
Ben & Dorothy Lamb  
Mrs. Vernon Milne  
O.E.S. Home Chapter No. 313  
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Janet & Lou Wright  
Yellow Rockers Square Dance  
Club

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Pulaski County Sewer District  
#1

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■ **STOVER, MO**  
Bessie E. Wilson

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Marion & Shirley Self  
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Cathy Gould  
Debra A. Jones  
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Polk Township Charity Drive

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Geraldine Gore  
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Bessye Ambler  
Everett Asquith, Sr.

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Dean Baldwin  
Donal Baldwin  
Wayne Baldwin  
Brenda J. Bannister  
Wayne Barfield  
Melvin Barks  
Archie Clay Barton  
Andrew Bass  
Susan Bauer  
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Ruth C. Bertels  
Harold D. Bidwell  
Charles Fielder  
Bigelow  
Dewayne Black  
Charles Boley  
Don Bolli  
Lorna June Bone  
H.T. "Buddy"  
Borchers  
Ronald Bormann  
Fred & Wenonah  
Brady  
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William Bramble  
Betty Bramblett  
Howell "Pete"  
Brandenburg  
Lester Bratcher  
Charles Brigham  
Larry Brown Brooker  
Richard Brown  
Shirley Kay Brown  
Tillie Brown  
Verne Brownlee  
Ruby Bruzaitis  
Alvin Buchmeier  
Imogene Buttman

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Patsy Sue Carey  
Gwen Watters  
Carlberg  
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Dorothy Jane Casey  
Lawson Chadwick  
Pauline Charles  
Billie Jean Charlton  
William L. Chick  
Celia Clark  
Elizabeth Black  
Clarke  
Kenneth Clavin  
Allyn-Joy Colborn  
Donnie Cole  
Dorothy Collins  
Mary Connell  
Howard Cooper  
Mrs. James Cornell's  
mother  
Evelyn Corum  
Edna Mae Coss  
Ernest & Ruby  
Cottle  
Louise Crews  
Mary Crews  
Edna Mae Cross  
Walter Crow  
Claudine Crowley  
Gene Cullom

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Bob Decker  
Laura DeClue  
Virginia Louise Dehn  
Mary Devier  
Myra B. Donovan  
Dorothy Dorner  
Alice Douglas  
Dennis Dowell  
Mona Connors Downey  
Billy Joe Duren  
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Virginia F. Edwards  
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Mac H. Elzea  
Marion B. England  
Roger Dale England  
Lloyd & Larron  
Engleman  
Shirley Evans

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Homer Feit  
Annie Feldman  
Newton P. Ferguson  
Albert E. Fischer  
Coleman B. Fite  
Betty Flowers  
Clayton "Red"  
Follensbee  
Doris Forsee  
Janet Fountain  
Nadine Fowler  
Raymond W. Freese  
A.M. "Nick" Frising  
Bertha Fritz  
Jim Fulkerson

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Barbara Kay Gallatin  
Lois Gardner  
Terry Dwayne Gargus  
Robertz Saltzman  
Gasaway  
Mrs. Robert Ghio  
Mrs. Victor Gierke  
Horace E. Gill  
Celeta Gillespie  
Charles Godager  
Richard Mark Golden  
Victor W. Gooch  
Richard Gordon  
Janice Goss  
Max Gossick  
Grace Gowing  
Bruce Roy Graham  
Milton Green  
Corrine Gregory  
Margie Griffith  
Carol Griswold  
Charles Groomes  
William Gross  
John W. Guilford

■ **H**  
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Mavis Hagan  
Mary Hager  
Arthur Lee Hampton  
Marie Hanley  
Ruth Lorenzen Hansen  
Frances Hanstein  
Raymond Harlow  
Cora Harrison  
Harold & Jewell  
Harrison  
Robert Hartman  
Amy Evelyn Harvey  
Saleem Hassein  
Hazel Hawkins  
Geneva Henderson  
Francis James  
Henrietta  
Mary Hibbs  
Carl F. Hildebrandt  
Joseph Himberger

Blanche Hobbs  
Richard Hogue  
Glenn H. Holman  
E.J. "Bud" Hotop  
Joseph Houston  
Mary Ann Howard  
Irvin B. Hurt

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Robert D. Ince  
Donald Ingram  
Donald Isgrig

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Martha James  
Ray Janke  
Carl Jants  
Cecil Jennings  
Lloyd J. Jennings  
Mary Margaret  
Johanning  
Allie Johnson  
Billy Jo Johnson  
Florence Johnson  
Hilary Ashby Johnson  
Bud Jones  
Frances Jones  
Tullie Ben Jones  
Olga Jungbluth

■ **K**  
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Ronald Karis  
Eros Lee Keith  
Jeanetta Keller  
Roland Kellerman  
Annie Kelly  
James Keplinger III  
Marion Keplinger  
Lillie Kimmel  
Buddy P. Kirby  
Jerry Kizzort  
Kenneth Knipp  
Henry Koester  
Margert Kuipers

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## MEMORIALS

# Pamela Dunn Legacy of Hope

Many fine minds have contributed to cancer research. At CRC, we honor the memory of one of our own — Dr. Pamela Dunn. Dr. Dunn died in 1983 from the very disease she sought to conquer through her work in microbiology. She had participated in several important breakthroughs in cancer research. Her work was both scientific and humanitarian, with a genuine concern for the cancer patient and the trauma he or she experienced.

In 1981, Pamela Dunn was diagnosed as having a rare form of breast cancer. For many months, she was both research subject and

scientist, adding to our knowledge of the disease which had perversely selected one of its prime opponents.

Despite all possible measures, she lost her personal battle against cancer. However, her work continues through the Pamela Dunn Legacy of Hope. The Pamela Dunn Legacy of Hope was established to honor her commitment in the fight against cancer. This special fund provides the financial backing necessary to ensure that her work can be completed. The gifts to the fund remember and honor not only Dr. Dunn, but the thousands of Missourians who die each year of cancer.

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List as of December 31, 1999



*Nutrition is one of the most positive messages related to cancer. What you eat may reduce your risk for cancer. You have the ability to take control of areas of your health by eating more fruits, vegetables, beans and grains — and eating lighter and leaner.*

**A few helpful hints:**

- ✓ Eat 3 of your grain servings a day from whole grains .
- ✓ Look at the label to make sure you're getting 100% juice.
- ✓ Fill a jar with a variety of dried fruit and keep it handy. The natural sweetness satisfies candy cravings.
- ✓ Reduce the amount of oil in a recipe by replacing it with an equal amount of milk, water, chicken broth or fruit juice.
- ✓ Search out recipes that combine beans and grains.
- ✓ Reap the benefits of soy products. Studies show they may reduce the risk of breast cancer in women.
- ✓ Frozen vegetables are easy to keep on hand and easy to add to any meal.

*You don't have to say no to everything. If you're craving something decadent, don't deny yourself, give in to a small portion.*

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vent them from stimulating blood vessel growth, so that we can promote tumor regression. Thus, the nucleotide receptor family offers promising new targets for cancer therapy that require further investigation.

**Bottom Line — This strategy of blocking blood vessel growth increases the probability of destroying tumor development.**

■ **Exploration of Bacterial Toxins for Use as Chemotherapeutic Agents**  
*C.W. Caldwell and Kelly Edwards, Postdoctoral Fellow, CRC Laboratory Associate*

Bacteria are capable of producing toxins that can be used in beneficial therapeutic applications in both human and animal medicine. Specifically, certain strains of *Escherichia coli* have been shown to express Shiga toxins that have demonstrated anti-cancer properties. Subsequent investigation has shown that Shiga toxin type I is the agent responsible for the anti-cancer activity. Ovarian carcinoma cell lines were found to be highly susceptible to the killing effects of the toxin in laboratory experiments. The toxin also has the ability to cross the blood-brain barrier in humans, which facilitates the ability to attack certain types of brain tumors. Cancerous cells are specifically targeted for killing through the expression of a unique receptor molecule on the cell surface which is not typically found on normal healthy cells except in the kidney.

The specific aim of this project is to survey various tumor types for expression of the toxin receptor and therefore sensitivity to the killing effects of the toxin. This objective will be accomplished with an interdisciplinary approach. Molecular biology will be utilized for analysis of the purified toxin and the mechanisms involved in targeting the toxin to cancerous tissues. Electron microscopy will facilitate the survey of various cell types for the expression of the toxin receptor using antibodies for detection. Finally, cell culture systems will allow the study of the specific interaction of the toxin with susceptible cells. The exploration of this phenomenon will allow a potent bacterial toxin to be used in a beneficial way as an alternative to other methods of chemotherapy which have potentially devastating effects for cancer patients.

**Bottom Line — Some drugs in current use are not particularly effective in penetrating certain tissue barriers. This bacterial toxin would not only penetrate tissue surfaces, but may also destroy certain types of tumor cells more effectively than today's drugs.**

■ **Development of New Approaches to Cancer Therapies: Closing Doors on Cancer Spreading**  
*Dr. Vladislav V. Glinskii, CRC Senior Scientist*

Metastasis is the process by which cancer cells spread from the primary tumor site to form secondary tumors in distant tissues and organs. While the initial disease is often curable, there is little if any hope once the primary tumor has metastasized and a many of organs become diseased.

In the metastatic process, some of the cancer cells (metastatic cells) dissociate from the primary tumor and enter a blood circulatory system. Before a secondary tumor growth site is initiated, the metastatic cells need to land in the capillaries of the lymph nodes or distant organs.

Recent studies demonstrate that only those circulating cancer cells that became specifically attached to the capillary endothelium, lining the wall of the blood vessels, are capable of giving rise to metastasis. Thus, if one could prevent the adhesion of the metastatic cells to the vasculature endothelium, it will close the doors on cancer metastasis.

For the past four years, in collaboration with Dr. Thomas P. Quinn of MU's Department of Biochemistry, we have been working on the identification and development of the new compounds capable of efficiently interfering with cancer-endothelial cell interaction. The utilization of innovative technologies such as phage display libraries, developed by Dr. George Smith of MU's Biological Sciences, allowed us to identify several most promising peptides (small protein-like molecules). Our recent experiments demonstrate that blocking cancer-endothelial cell interaction with these compounds can reduce adhesion of the metastatic breast and prostate cancer cells to the endothelium up to 80%.

**Bottom Line — This research will lead to development of novel interventive anti-cancer therapies for breast and prostate cancer victims.**

4. Development of synthetic vaccines and antibodies.

**Development of Effective Immunological Diagnostic Peptides**  
*Professor George Smith, CRC award recipient and associates*

This research represents an altogether different approach. In brief, we plan to identify small peptides that specifically bind to antigens and antibodies associated with cancer. We call these "diagnostic" peptides because they should serve as diagnostic tests for cancer. Equally important, however, they might in the future provide a network of research paths for discovering unknown antigens. Such antigens could not only help to illuminate the disease process, but also serve as anti-cancer vaccine components.

The underlying supposition of the present research is that even diseases like cancer, which are neither infectious nor conspicuously autoimmune, may nevertheless be marked by the appearance, or a change in form or distribution, of disease-specific substances that we will call generically "neoantigens" (NeoAg's).

Tests for infectious diseases detect the infected subject's antibodies (Ab's) to pathogen antigens. Some autoimmune diseases are similarly diagnosed in part by detecting immunogenic. In using the term in this sense, we are abstracting somewhat from its original meaning; for we mean to include any disease-marking substance that can be specifically detected by a binding ligand, even if that detector molecule is not an antibody.

**Bottom Line — The use of small peptides as antigen-antibody components, in place of large, natural, immunological components should lead to earlier diagnosis and more effective treatment of disease.**

5. Scholarships. With your donations, CRC also provides scholarships to outstanding students to work with scientists. Recent scholars include Christopher Hueser (Hofheins Scholar), Sharyn Parks, Susanne Curran (Director's Scholarship Fund), Samantha Potter, and Raphael Buencamino.

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