



*Accelerating  
the  
Search  
for a  
Cure*

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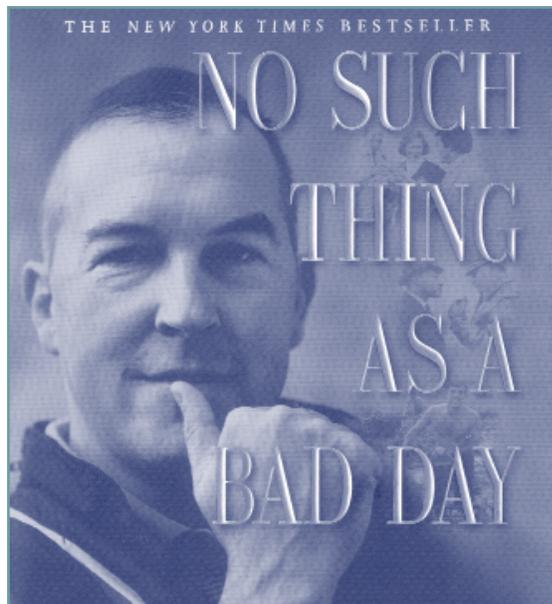
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# MYELOMA FOCUS

Newsletter of the Multiple Myeloma Research Foundation

## HAMILTON JORDAN AND JOAN RIVERS JOIN FORCES WITH MMRF

The MMRF is very proud to have Mr. Hamilton Jordan as our Honored Guest for this year's **Friends for Life** Fall Gala with Joan Rivers presiding as the Master of Ceremonies.



Hamilton Jordan will be the honored guest this year at the MMRF Friend's for Life Fall Gala. Mr. Jordan's best-selling memoir, *No Such Thing as a Bad Day*, is an American epic story.

Mr. Jordan, former White House Chief of Staff during the Carter administration, is a cancer advocate, best-selling author, and three-time cancer survivor. Among his many accomplishments, Mr. Jordan wrote the best-selling book, *Crisis*, which detailed the secret negotiations of the release of the American hostages in Iran. In 1982, Mr. Jordan and his wife

Dorothy, founded *Camp Sunshine*, the country's most successful camp and year-round program for children with cancer. In 1984, Mr. Jordan was diagnosed with the first of what would become three cancers that he would battle over the next 12 years. Of his battles with cancer, Mr. Jordan has remarked: "I tell people I have had one of 'each' - a lymphoma that led to my taking experimental, industrial-strength chemotherapy; a bout with prostate cancer which required major and delicate surgery; and an early skin cancer which was dealt with simply and swiftly with the flick of the surgeon's knife and a couple of stitches. **But, I don't feel cursed or put upon by my cancers, instead I feel very blessed and just plain lucky to be alive.**"



With the "irrepressible" and talented Joan Rivers as the Emcee at this year's Friends for Life Fall Gala, anything could happen!

# Welcome Letter

# Teeing-Off for a Cure

**D**ear Friends,

When we started the MMRF four years ago, there were few myeloma-specific drugs or recognized therapies. Because myeloma was not a common cancer, the NCI and pharmaceutical companies were not specifically directing their resources toward this disease. It is only recently, as a result of an increased awareness of myeloma brought about by organizations like the MMRF, that the NCI and pharmaceutical companies have become more committed to myeloma.

That's why it is such an honor and an amazing opportunity to be nominated to the NCI's Lymphoma Leukemia Myeloma Progress Review Group (LLM-PRG). It is a great privilege to work side-by-side with Dr. Barlogie, who will co-chair the Group, and Dr. Anderson -- both recognized as world leaders in the field of myeloma research, and with the other members of the lymphoma and leukemia communities.

On August 22<sup>nd</sup> and 23<sup>rd</sup>, the LLM-PRG met to provide input into the development of an upcoming Roundtable meeting scheduled to take place in December. The Roundtable will involve a broad group of scientists, clinicians, pharmaceutical industry representatives and advocates who will assist the NCI in establishing blood cancer research priorities. I look forward to this new and exciting opportunity for government, industry and advocates to collaborate together to cure myeloma. You have my promise to keep you informed of our progress.



Working together at the LLM-PRG Planning Meeting are: (L-R) Dr. Ken Anderson, Kathy Giusti and Dr. Bart Barlogie.

**W**hen Lou Malaquias' brother-in-law, Bruce Figurido, was diagnosed with multiple myeloma in the Spring of 1998 Lou decided to do something about it. He began researching myeloma on the Internet. Initially discouraged to find that there was little information available about this incurable disease, he then came across the MMRF website and learned of a foundation with a single purpose - to cure myeloma.

Through discussions with the MMRF, Mr. Malaquias and Mr. Figurido became aware that the only way to make a significant impact on myeloma was to fund scientific research. Both men became determined to raise as much money as possible to aid in these endeavors. They established the *Bruce Figurido/Multiple Myeloma Research Foundation Golf Fundraiser*. Mr. Malaquias said: "We selected the MMRF as beneficiary because the Foundation targets most of its funding toward directly funding research and maintains an exceptionally low overhead, which is important to potential donors."



L-R: Nancy and Louis Malaquias, Bruce and Joann Figurido working together golfing for a cure.

For the second year, friends, family, co-workers and business associates joined together for a day of golf and fun, raising

\$7,600 to aid in the fight against myeloma. Of that, \$2,000 alone was raised by raffling off two Jimmy Buffet concert tickets donated by Bill Ligas and Barton Beers. Mr. Malaquias said, "Last year we raised \$7,000, which may not sound like a lot of money, but if 500 people did what we did, then that becomes significant." Mr. Malaquias would like readers to know that "no matter how small you are, you should be able to do some kind of a fundraiser, it's not as difficult as it seems, and it's very rewarding." The MMRF would like to thank Mr. & Mrs. Malaquias and Mr. & Mrs. Figurido for their contributions to the Foundation and their continued support to the search for a cure.

# NBC'S "TODAY" SHOW TO FEATURE THE MMRF

The MMRF will be featured in an upcoming segment of "Today". The MMRF is excited about the national exposure that the Foundation, and more importantly the disease, will receive from this airing. "We hope the show will help people understand the devastation that cancer can bring to families and to help people understand that while we are making progress with many cancers, much still needs to be done. Also, that efforts to find a cure can come from many places -- including patients," said MMRF President Kathy Giusti.

For the upcoming segment, "Today" News Anchor, Ann Curry, along with "Today" Producer, Donna Zaccaro, who is familiar with the work of the MMRF as a Board Advisor, recently interviewed MMRF Founder Karen Andrews, MMRF President Kathy Giusti, and MMRF Scientific Advisory Board Chairman Dr. Ken Anderson. Ms. Giusti said: "The 'Today' show has a longstanding commitment to raising awareness of cancer issues, so we are very excited about this opportunity."

The MMRF will inform you of the actual air date as soon as it is announced, via our electronic

newsletter service MMRF SmartBrief -- so stay tuned! To receive MMRF SmartBrief, you must provide your email address. See the last page for details on our new and exciting free electronic newsletter service!



"Today" Producer Donna Zaccaro, MMRF Founder Karen Andrews, "Today" News Anchor Ann Curry and MMRF President, Kathy Giusti during taping for the upcoming "Today" segment.

## FALL GALA CONT.

In his new book, *No Such Thing as a Bad Day*, Mr. Jordan chronicles his fascinating life from his youth immersed in Deep South segregation to his tour as a civilian volunteer in Vietnam, to his tumultuous years in D.C serving under Democratic President Jimmy Carter, and to his overwhelming battles with cancer.

The MMRF is also very excited to announce that the irrepressible Joan Rivers will serve as Master of Ceremonies for the Gala. Ms. Rivers is a comedienne, author, actress, playwright, director, nightclub headliner and Emmy-Award winning television talk-show hostess - to name but a few of her roles in the world of entertainment! For all of her accomplishments in the industry she was honored with her own "Star" on the Hollywood "Walk of Fame" in 1989. The "queen of the barbed one-liners" however is also deeply

committed to helping others who are less fortunate. She is the National Spokesperson for the Cystic Fibrosis Foundation, an advocate for Suicide Prevention, and has been actively involved in the war against AIDS.

This year's **Friends for Life** Fall Gala will once again be a grand affair including cocktails, silent auction, dinner, and live auction, followed by dancing until midnight. The Gala will be held Saturday, October 21, 2000. The goal for the evening is to raise awareness of multiple myeloma and funds for myeloma research. The Gala will take place for the fourth year at the Hyatt Regency, in Greenwich, CT. All proceeds will be used to fund research for multiple myeloma. To purchase tickets, and to find out about volunteer and donation opportunities, contact Jenny McMahon at 203-801-5212.

# MMRF REPORTS

## INTERNATIONAL CONVERGENCE IMMUNE THERAPY RESEARCH ROUNDTABLE 2000

**T**he third experts' Research Roundtable in multiple myeloma, held June 9-10 in McLean, Virginia was a convergence of experts in immunotherapy with two objectives: (1) to deepen the participants' understanding of immune responses in order to identify the most effective attack on myeloma and (2) to learn more about vaccine strategies in other diseases, such as malignant melanoma, and how they might be applied to myeloma.

Organized and funded by the MMRF with the McCarty Cancer Foundation, the roundtable was sponsored by the Dana-Farber Cancer Institute. Co-chairs Dr. Kenneth Anderson and Dr. Freda Stevenson both agree that much progress has been made in the areas of adoptive immunotherapy and vaccines. Some of the key points of the Roundtable were that:

- ◆ Stem cell transplant research is demonstrating that immune cells from allogeneic donors can help attack the recipient's tumor cells, a process referred to as the "graft versus tumor" response.
- ◆ Advances in basic research in immunology are facilitating vaccine development for myeloma.
- ◆ A promising strategy to stimulate patients' immune response against their myeloma is the use of vaccines that utilize important immune cells known as dendritic cells.

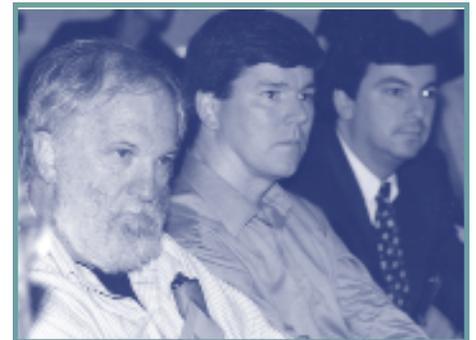
- ◆ New tumor antigens are being discovered and utilized as vaccines, including portions of a patient's own monoclonal protein.
- ◆ DNA vaccines for infectious diseases and vaccine strategies being developed against hematologic tumors and malignant melanoma provide an important framework for the development of myeloma vaccines.

These findings will influence the way myeloma patients will be immunized, including the specific kind of vaccine that is tested, how the antigen is delivered, and the schedule of vaccinations.

Perhaps the most exciting aspect of the Roundtable was the interchange between experts from around the world. "Not only do we broaden our horizons in terms of approaches that can be attempted, but we also foster new

collaborations between myeloma investigators and others who have expertise outside of the field," noted Dr. Anderson. "When we share information this way, progress is bound to occur at a more rapid pace."

Findings from the 2000 Immune Therapy Roundtable will be published in a future issue of "Cancer Research". Special thanks to the Palmer Foundation for supporting this publication.



Roundtable attendees: (L-R) Dr. Michael Kuehl, Dr. Keith Stewart and Dr. Hy Levitsky



Roundtable Sponsors and Chairpersons: (L-R) Dr. Ken Anderson of Dana-Farber Cancer Institute, Kathy Giusti of MMRF, Dr. Freda Stevenson of University of Southampton, Roberta McCarty of McCarty Foundation, and Dr. Larry Kwak of the NCI.

# MMRF REPORTS

## \$1.5 MILLION DISTRIBUTED TO FUND SENIOR RESEARCH AWARDS

The Multiple Myeloma Research Foundation, in partnership with the McCarty Cancer Foundation, is extremely proud to announce the 2000 Senior Research Awards winners. This unique collaboration combined to distribute nearly \$1.5 million toward Senior Research Awards this year, which represents the first step toward our \$2 million research commitment for 2000. Senior Research Awards target clinicians and researchers who have demonstrated for at least five years their ability to conduct original research bearing on blood cancers. Our careful selection of grant recipients supports the growth of myeloma research laboratories. These laboratories, staffed with exceptional scientists and state of the art equipment, will guarantee breakthrough developments in myeloma research.

The MMRF and the McCarty Cancer Foundation are also extremely pleased that **30% of the 2000 Senior**

**Research Award winners will receive second-year funding pending Scientific Advisory Board review of first-year progress reports.** The extraordinary growth experienced by the MMRF continues to allow unprecedented levels of funding for myeloma research. The high value (\$75,000-\$100,000 per year) of these grants is essential, as they continue to afford established senior researchers the unique opportunity to implement biological, or clinical, research projects that might not otherwise be possible.

In an effort to facilitate even more exciting and promising research, the MMRF also offers Fellows Awards of \$40,000 to researchers who are relatively new to the field of multiple myeloma. 2000 Fellows Award winners will be reviewed with the International Myeloma Foundation and announced in October. You can read about the Fellows Award winners in the next issue of Myeloma Focus.

### 2000 Senior Research Awards Funded by the MMRF and the McCarty Cancer Foundation

Senior Research Award Recipient	Affiliated Institution	Research Topics
Dharminder Chauhan, PhD	Dana-Farber Cancer Institute	Apoptotic and Survival Proteins as Novel Therapeutic Targets in Multiple Myeloma
Diane F. Jelinke, PhD	Mayo Clinic Foundation Immunology	Identification of Gene Expression Patterns Associated with Prognosis and Outcome in Multiple Myeloma
Alan Lichtenstein, MD	VAWest LAHospital - UCLA Medical School	AKT/p70S6K/4E-BPI Cascade in Multiple Myeloma
G. David Roodman, MD, PhD	University of Texas Health Science Center of San Antonio	Role of MIP-1a in Myeloma Bone Disease
Joachim L. Schultze, MD	Dana-Farber Cancer Institute	Determination of Antigen-Specific Immunity in Myeloma
Professor Freda Stevenson & Francesco F. Forconi, MD	University of Southampton	Development and Trial of DNA Vaccines Against Multiple Myeloma
Brian Van Ness, PhD	University of Minnesota	Profiling IL-6 and Stromal Induced Gene Expression and Signal Transduction in Myeloma Cell Lines
Helena Jernberg Wiklund, PhD, Assoc. Prof.	Ridbeck Laboratory, Uppsala University	The Control of Proliferation, Survival and Apoptosis in Multiple Myeloma
Qing Yi, MD, PhD	University of Arkansas for Medical Science	Optimization of Dendritic Cell-Based Immunotherapy in Multiple Myeloma

# MMRF INSTITUTIONAL INSIGHTS

## Learning About the Latest Research

In another exciting MMRF Institutional Insights (II) Program, the MMRF and Emory University joined forces to present *Novel Therapeutic Approaches in Treating Multiple Myeloma*. The program was held on June 1<sup>st</sup> and 2<sup>nd</sup> in Atlanta, Georgia, and included a physician symposium and a separate patient/family segment.

As with all MMRF Institutional Insights (II) Programs, this program sought to educate oncologists and hematologists, as well as nurses, researchers, patients and their families on the diagnosis and treatment of multiple myeloma; and raise awareness of the MMRF.

Guest speakers for this program included Dr. Leonard Heffner of the Emory Clinic, Dr. Bill Bensinger of the Fred Hutchinson Cancer Center,



Taking a lunch break together are: (L-R) Phil and Susan Goodsnyder speaking with Dr. Bensinger.



(L-R) Kathy Giusti, Dr. Bill Bensinger, Dr. Nikhil Munshi, Dr. L. Thompson Heffner and Ellen Kaplan at Emory II Program.

and Dr. Nikhil Munshi of the University of Arkansas. The Program addressed issues such as prognostic indicators, bisphosphonates, the role of high-dose chemotherapy and stem-cell transplantation, immune-based therapies, and new and supportive treatments in multiple myeloma. Patients were able to ask questions and speak to doctors one-on-one during dinner. The program was sponsored by Novartis and Celgene.

For information on future Institutional Insights programs, please visit the MMRF website [www.multiplemyeloma.org](http://www.multiplemyeloma.org) or contact Ellen Kaplan at 650-375-8852 or e-mail: [kaplane@themmrf.org](mailto:kaplane@themmrf.org).

## GAME DINNER SERVES UP \$30,000 TOWARD A CURE

The MMRF's third Annual Game Dinner raised more than \$30,000 toward funding myeloma research. The evening was a "mens night out" featuring a wild-game feast and a live auction. The addition of the live auction greatly added to the success of the evening this year. Salomon Smith Barney was a \$5,000 sponsor of the event, and once again the dinner was hosted by the team of Charlie Hinnant, President and CEO of Charkit Chemicals, John Andrews, President and CEO of American Natural Soda Ash Corporation (ANSAC), and David Lindsay, Vice President - Marketing of Rand Insurance.

The MMRF's Executive Director, Scott Santarella, said: "It's creative events like these that bring community members together to have fun while supporting a great cause." The MMRF greatly appreciates the efforts of all who contributed to this successful fundraiser.



Game Dinner participants: (L-R) Jim Mitchell, David Lindsay, Larry Langer, Charlie Hinnant, Scott Santarella, Bruce Sargent, Jack Mitchell, Andrew Mitchell and John Andrews.

# Ask the Expert

## MRI, Chromosome 13

This month's Ask the Expert features the MMRF's Scientific Advisor Sunder Jagannath MD, Chief of the Multiple Myeloma Service at St. Vincent's Comprehensive Cancer Center, New York City.



Dr. Sunder Jagannath

**1. Dr. Jagannath, my doctor would like me to undergo an MRI procedure to assess my bone involvement. I've already had a bone survey, which was negative. Why is MRI necessary?**

A bone survey, also referred to as a skeletal survey, is simply a series of x-rays of the skull, spine, arms, ribs, and legs. It is designed to assess changes in the bone structure as well as to determine the number and size of tumors in the bone. MRI (which stands for magnetic resonance imaging) is a procedure in which a magnet linked to a computer is used to create detailed pictures of areas inside the body. MRI of the spine and pelvis is often used in conjunction with x-rays to monitor myeloma disease.

Changes in the bone can be detected in a bone survey in the majority of patients with myeloma. However, about 10% of patients (including yourself) have a normal bone survey. This is largely due to the fact that at least 30% of the

calcium in the bone must be lost before the changes are detected on an x-ray. Bone x-rays do not visualize the plasma cell tumor in the marrow, the spongy tissue inside the bone where the tumor develops.

MRI is the best way to visualize tumor developing in the marrow. For example, in some patients with back pain, plain x-rays of the spine fail to reveal any lesion while MRI will show extensive replacement of the normal bone marrow by myeloma tumor. Also, tumors that come out of the bone in the spine and press on the nerve roots or spinal cord are best visualized by MRI.

**2. I've heard that chromosome analysis can provide important information about my disease. What can this test tell me? How is it performed?**

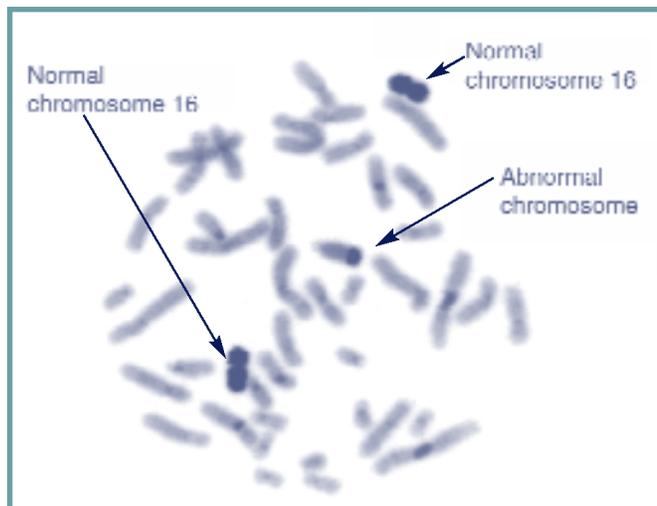
Chromosomes are thread-like structures in a living cell that contain the cell's genetic information. Human cells have

23 pairs of chromosomes and each chromosome contains thousands of genes. A variety of abnormalities in chromosome number or structure have been identified in myeloma cells. These abnormalities appear to promote the growth of the abnormal plasma cells and/or inhibit the process of normal cell death.

Almost all myeloma patients appear to have some type of chromosome abnormality, and certain abnormalities have been shown to have prognostic significance. For example, having an extra copy of certain chromosomes, such as 6, 9, or 17, is associated with longer survival. Conversely, the absence of chromosome 13 or having a particular abnormality in chromosome 1 is associated with a poor prognosis.

Therefore, analysis of a patient's chromosomes at the time of diagnosis can be useful in determining a treatment plan. For example, if the absence of chromosome 13 is

identified, more aggressive therapy might be given. Chromosome analysis, also known as cytogenetic testing, measures the number and normalcy of chromosomes. To perform a chromosome analysis, a sample of bone marrow is collected from the hip bone (pelvis) or the breast bone (sternum). The bone marrow is then sent to a laboratory where the chromosomes are



Chromosome map from a myeloma patient showing an abnormal chromosome containing a translocation (a joining of parts of two different chromosomes). Such translocations are thought to be of importance in how

Visual courtesy of Rafael Fonseca, MD, Mayo Clinic

# Medical Corner

## Cell Signaling

**M**uch research is being conducted in the area of cell signaling, the process by which a cell responds to information received from its environment. In this month's Medical Corner we describe the research being conducted by four MMRF Senior Research Award recipients in the area of cell signaling in myeloma.

### What is Cell Signaling?

Cell signaling, sometimes referred to as signal transduction, refers to the means by which information from a cell's environment is relayed (transduced) inside the cell such that the cell can respond to it.

Normally, a cell is somewhat dormant until it receives an external signal, such as a hormone or growth factor, or direct contact with another cell. The signaling process begins at the cell surface where the signal molecule binds to a specific receptor. (See figure page 9.) This binding sets off a cascade of enzymes and other proteins that act in a step-by-step fashion. The end result of the cascade is usually the turning on of a specific gene and production of a specific protein. These events cause some response by the cell, such as cell growth.

Cell signaling is vital to normal cell function. In myeloma, it appears that defects in cell signaling cause the tumor cells to grow unrestrained and/or prevent them from dying as normal cells do. Thus, many myeloma researchers are investigating the various mechanisms by which cell signaling occurs, with the hope that a deeper understanding of this process will help identify new treatments.

As an example of how cell signaling

research can lead to new therapies, one has only to look at the remarkable results with the agent STI-157 in chronic myelogenous leukemia (CML). This drug inhibits a specific protein in the cell signaling pathway that causes unrestrained growth of CML cells.



Alan Lichtenstein, MD

Alan  
Lichtenstein,  
MD  
UCLA  
Medical  
School

Dr. Lichtenstein is investigating various cell signaling

pathways involved in cell growth. In normal cells, these pathways are stimulated by growth factors such as interleukin-6 (IL-6). In one pathway being studied, an enzyme known as AKT kinase plays an important function in cell growth. This enzyme, in turn, acts on a variety of proteins within the cell, continuing the chain of events in several directions. All of these pathways help the cell to divide and grow.

In normal cells, there is a mechanism that turns off the cascade and cell growth. In myeloma, however, there are defects in one or more of these signaling pathways such that they are constantly activated and never turned off. In particular, the AKT kinase appears to be active all the time in myeloma cell lines, which might account for their uncontrolled growth.

With MMRF funding, Dr. Lichtenstein is working to identify the pathways that are important in myeloma cell growth

and to see if signaling abnormalities are present in myeloma cells from patients. The hope is that inhibitors that act specifically in certain signaling pathways can be used therapeutically against myeloma.

Helena Jernberg-Wiklund, PhD  
Rudbeck Laboratory, Uppsala,  
Sweden

Normal cells undergo a process of programmed cell death referred to as apoptosis. However, in many diseases there is a defect that prevents apoptosis from occurring. Although a hallmark of tumor development is the turning off of apoptosis, the mechanisms by which myeloma cells shut down this process are largely unknown.



Helena Jernberg-  
Wiklund, PhD

With MMRF funding, Dr. Jernberg-Wiklund is investigating the various molecular mechanisms by which myeloma cells are able to avoid apoptosis, particularly those involved in

cell signaling. First, she is looking at the growth factors that are known to act as signals for myeloma cells, such as IL-6 and insulin-like growth factor (IGF)-1. These growth factors act as "survival factors," enabling the cells to continue to grow and divide. Next, there are a number of intracellular components activated by these growth factors that transfer the signal to the nucleus of the cell via a cascade of reactions. Several specific enzymes responsible for this cascade have been identified that may

# Medical Corner

## Cell Signaling

account for the survival of myeloma cells. Lastly, several genes specific to tumor cells have been shown to be turned on as an end result of this signaling cascade. These genes appear to be important in controlling myeloma cell survival. It is the hope that by identifying and characterizing these components, new therapies can be developed that can re-establish normal programmed cell death of myeloma cells.

**Dharminder Chauhan, PhD**  
Dana-Farber Cancer Institute



Dharminder Chauhan, PhD

Dr. Chauhan's research is also centered on the mechanisms of abnormal growth and survival of myeloma cells. He is investigating

how various drugs might be used to turn on apoptosis in myeloma cells. It is the hope that these types of targeted drugs can be used to enhance direct death of myeloma cells or to complement current therapies.

With MMRF funding, Dr. Chauhan is characterizing the various cell surface molecules and cell proteins that are involved in the process of apoptosis. In particular, he has been studying the process of myeloma cell death that is triggered by the drug dexamethasone. A number of molecules have been identified in this cell signaling cascade, as well as proteins that can either trigger apoptosis or prevent it.

It has been found that the myeloma growth factor IL-6, which is secreted by cells in the bone marrow, helps myeloma cells survive by blocking the effect of cytotoxic drugs. Dr. Chauhan is also investigating signaling molecules that

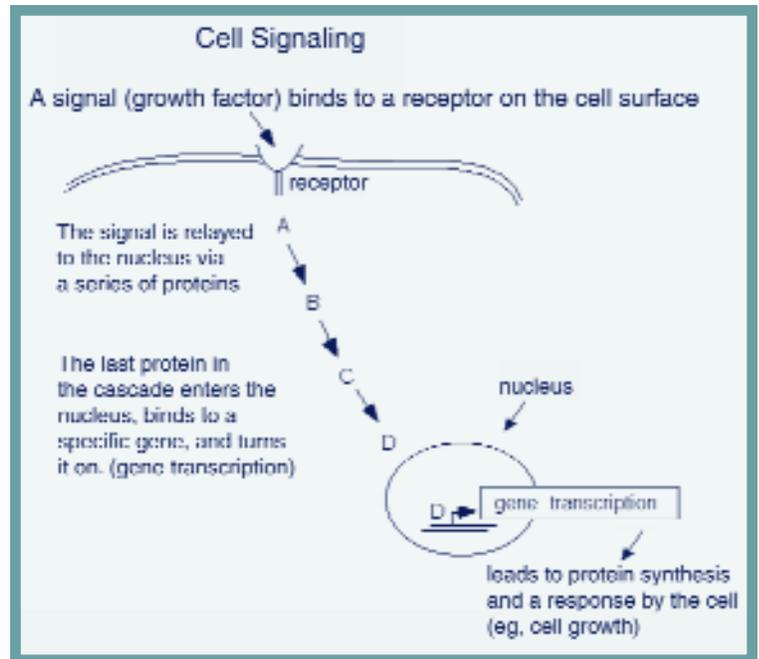
are involved in this process, with the hope of identifying compounds that can block the IL-6 signaling pathway and thus enhance the effect of cytotoxic drugs.

**Brian G. Van Ness, PhD**  
University of Minnesota



Brian G. Van Ness, PhD

One of the goals of Dr. Van Ness' research is to understand why myeloma disease can be so different from patient to patient. Although patients may appear the same clinically, it appears there are genetic and cell signaling differences that can significantly impact disease progression and response to therapy. With MMRF funding, Dr. Van Ness will look at differences in the



specific genes that can affect the disease, as well as the various signaling pathways initiated within the bone marrow microenvironment. The long term goal is to provide a comprehensive genetic and protein profile of myeloma cells to better classify disease progression and therapeutic response. These profiles will aid in developing new targeted therapies and tailoring these therapies to the patient.

One important difference in how myeloma cells behave compared with normal blood cells appears to be the way they respond to the growth factor IL-6. Whereas blood cells respond to IL-6 by continuing their normal development in the bone marrow, migrating to the bloodstream, and eventually dying, myeloma cells increase in number in response to IL-6 and use it to alter their response to therapeutic agents. The difference boils down to different signaling responses, with signaling being intermittent in normal cells and sustained in myeloma cells.

# YOU NEED TO KNOW CLINICAL TRIALS

**A**s a patient with myeloma, you may be interested in or asked to participate in a clinical trial, a research study conducted to determine the safety and efficacy of new drugs and treatments. Clinical trials are required by the Food and Drug Administration (FDA) before a new treatment can be made widely available for use.

Before a new therapy can be tested in humans, it must be thoroughly tested in the laboratory and in animal studies. At this point, a sponsor submits the data to the FDA in the form of an Investigational New Drug (IND) application, which is a request to begin testing the treatment in humans.

## PHASES OF A CLINICAL TRIAL

Clinical trials are carried out in a series of steps, or phases. Each new phase builds on information from an earlier phase and a treatment will only proceed to the next phase if it passes the previous one. The table shown describes the phases of a clinical trial.

When Phase III trials are complete, the sponsor submits the data to the FDA in the form of a New Drug Application (NDA), which is a request for marketing the treatment. The time required by the FDA to review an NDA varies, but may be as little as 6 months. In 1999, new drugs were approved in an average of 13 months.

## WHY PARTICIPATE IN A CLINICAL TRIAL?

You can take a more active role in your own health care by participating in a clinical trial. The potential benefits of

participation include close medical monitoring and access to new treatments before they are widely available. In addition, you have an opportunity to make a valuable contribution to myeloma research. Rest assured that

PHASES OF A CLINICAL TRIAL		
Phase	Characteristic	Length
I	* Involves a small number of patients * Determines safety and dosage, as well as what happens to a drug in the body	~ 1 year
II	* Involves a greater number of patients * Evaluates efficacy and safety * May be conducted at several institutions at once	~1 - 2 years
III	* Involves an even greater number of patients * Patients receive the new treatment or a standard treatment and the efficacies are compared * May be conducted at several institutions at once	~ 2 - 4 years

patients in cancer trials always receive treatment, whether it is the new treatment being investigated or a standard treatment, *not a placebo*.

Any medical treatment, particularly that used for cancer, can have side effects. Patients who are considering participating in a clinical trial are given detailed information so that they can understand what is involved in a trial, including the potential risks and benefits (and costs, if any). The choice is then up to you to take part in the study. In addition, clinical trials have built-in safeguards to protect patients, including safety reviews by institutional review boards (IRBs) and government agencies. A patient may withdraw from a clinical trial at any time. Also, if a patient is not benefiting by a treatment, a physician is ethically bound to remove him or her from the trial and to use an alternate therapy.

Clinical trials are funded by the federal

government and/or the pharmaceutical industry. In many cases there is no cost to the patient for participating in a trial, particularly those sponsored by pharmaceutical companies. Some insurers cover trial medication costs and several organizations also offer financial aid for participants' medical and travel expenses.

The government's Health Care and Financing Administration has proposed a National Coverage Decision to allow Medicare coverage of routine costs in clinical trials. Although the decision intends to include coverage of both federally and privately funded trials, the wording has led to

some confusion in the press regarding coverage of privately sponsored trials. The decision should be made final by the end of September. Sign up for SmartBrief (see the last page) to receive updated information on this topic.

## WHERE CAN I FIND MORE INFORMATION?

First, ask your oncologist whether any trials are being conducted in your area. Second, visit the websites that are listed below.

FOR MORE INFORMATION:  
 CenterWatch Clinical Trials Listing Service  
 Myeloma trials:  
[www.centerwatch.com/studies/cat212.htm](http://www.centerwatch.com/studies/cat212.htm)  
 National Cancer Institute:  
[www.Cancertrials.nci.nih.gov](http://www.Cancertrials.nci.nih.gov)  
 MMRF Hotlinks:  
[www.multiplemyeloma.org/aboutmyeloma/hotlinks.html](http://www.multiplemyeloma.org/aboutmyeloma/hotlinks.html)  
 Coming soon -- clinical trials listing and automated matching referrals:  
[www.emergingmed.com](http://www.emergingmed.com)

# NCI Holds First LLM-PRG Meeting MMRF IS THERE

The National Cancer Institute (NCI) announced the formation of the Leukemia, Lymphoma and Myeloma Progress Review Group (LLM-PRG). The goal of the LLM-PRG is to create a national research agenda for blood cancers.



LLM-PRG Advocates Ilene Penn Miller (Cure for Lymphoma), Kathy Giusti (MMRF) and George Dahlman (Leukemia and Lymphoma Society) collaborate prior to the PRG Planning Meeting.

The PRG Planning Meeting was held on August 22-23 to set the agenda for the larger Roundtable that will be held in December. The Roundtable Meeting solicits input from a broad base of scientists, clinicians, industry representatives and advocates regarding key scientific questions that must be

addressed to advance medical progress against the blood cancers. Breakout sessions for the December meeting will include topics such as Epidemiology; Diagnosis, Prognosis and Disease Monitoring; Biology of Normal and Neoplastic Tissue Targets; Clinical Trial Methods and Infrastructure; Therapeutics: Development and Discovery; Specific Targets and Education, Communication and Behavioral Research. Input provided at the Roundtable ultimately forms the basis for NCI research priorities. The MMRF looks forward to keeping you informed about this exciting, collaborative effort.

## LLM- PRG Schedule

December 2000	Roundtable and first draft of report
May 2001	Final report released to public
October 2001	Director discusses implementation plans
November 2001	NCI communicates its plans to the community (Broad PA, print media ads, website...)
Continuous	Updating PA, tracking/monitoring of progress
June 2003	Formal report of progress to the community

## The MMRF Thanks the following corporations for their support of Myeloma Focus

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## MEDICARE NEWS FLASH

The Healthcare Financing Administration (HCFA) recently announced that Medicare will begin covering stem cell transplants for myeloma as of October 1<sup>st</sup>, 2000. HCFA initially indicated that this coverage would not occur until January 1<sup>st</sup>, so this is great news for myeloma patients waiting for this procedure.

For the latest information on Medicare coverage of stem cell transplants for myeloma patients, visit the website [www.hcfa.gov/quality/8b3-c1.htm](http://www.hcfa.gov/quality/8b3-c1.htm)

# SUPPORTING THE MMRF HAS NEVER BEEN EASIER

**A**s the holiday season approaches and you begin to think about your year-end donations, please consider the MMRF as one of your charities of choice. Below are some simple, but effective, methods by which the MMRF and you can benefit from your charitable contributions of monetary support.

**Cash Donations** - This is the most common of all charitable giving, often in the form of a personal check. Checks can be made out to: **The MMRF** and mailed to The MMRF, 11 Forest Street, New Canaan, CT 06840. Those interested in making Credit Card donations can contact the MMRF Office Manager, Terry Banks at 203-972-1250.

**Stock Donations** - This form of donation is becoming more common as individuals reap the rewards of smart investment

strategies and a strong economy. Individuals interested in making stock donations can do so by contacting the MMRF via the address or phone number mentioned earlier.

**Estate Planning** - Remember the MMRF in your will by making a charitable bequest to the MMRF.

In planning your donations for the year, The MMRF advises all donors to consult with a qualified legal and/or accounting professional when making donations and monetary gifts of any kind. We hope these donation methods will help you identify the options that best suit your needs. Thanks for all of your support and please contact the Foundation regarding any of your charitable gifts and ideas.



## GIFTS OF MEANING

**H**onor someone close to you with a beautiful piece of sterling silver jewelry! MMRF acorn jewelry is the perfect gift to honor someone special who has played a role in the battle against multiple myeloma - a patient, doctor, nurse, friend, or family member. Give MMRF acorn jewelry as a gift and ask recipients to wear it knowing they have been honored for their courage and kindness. Wear the jewelry yourself to help build awareness of multiple myeloma and the MMRF. Every dollar you spend on acorn jewelry supports a MMRF research grant. MMRF acorn jewelry is available in the Acorn Pin, Cufflinks, and Earrings. Enclose your check with this form in the attached envelope. You will receive your order within two weeks, so order early.

Photo by Stephanie Tracy



Jewelry designed by Susan Barkann

THE "WEAR THE PIN" PROGRAM WAS DEVELOPED, ORGANIZED AND UNDERWRITTEN BY ELIZABETH DONALD AND JEWELRY DESIGNER SUSAN BARKANN. THE MMRF IS VERY GRATEFUL TO BOTH WOMEN FOR THEIR EXTRAORDINARY GENEROSITY.

### Acorn Jewelry Order Form

I have enclosed a check for \$\_\_\_\_\_ to purchase the following items at \$100.00 each:

- \_\_\_\_ Acorn Pin(s)
- \_\_\_\_ Acorn Cufflink Set(s)
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### MMRF Acorn Jewelry makes the perfect gift for:

Thanksgiving 11/23  
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Birthdays, Anniversaries, to say Thank You,  
and just because...

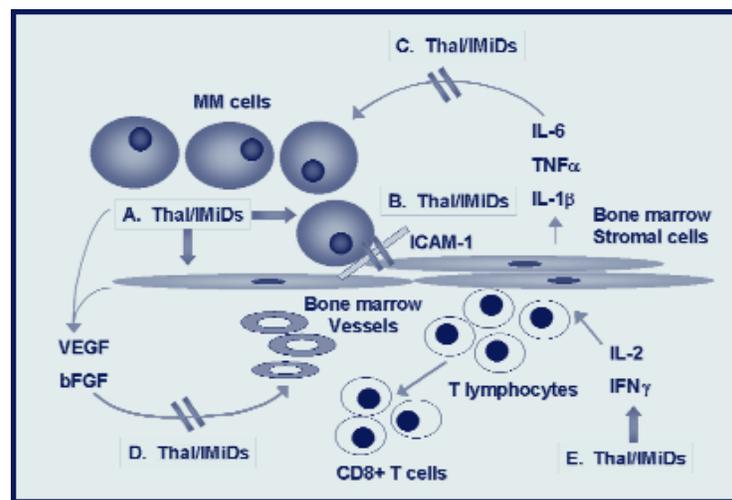
# Thalidomide and its Analogs Overcome Drug Resistance of Human Myeloma Cells to Conventional Therapy

CONTRIBUTED BY DR. KEN ANDERSON

**R**ecent reports of increased new blood vessel formation or angiogenesis in myeloma bone marrow, coupled with the known anti-angiogenic activity of thalidomide, provided the rationale for the use of thalidomide to treat patients with multiple myeloma. Investigators at the University of Arkansas were the first to show that thalidomide can achieve responses even in patients whose myeloma has returned after conventional therapy including high dose therapy and stem cell transplantation. Although thalidomide was initially used due to its anti-angiogenic effects, both thalidomide and its potent analogs, the immuno-modulatory drugs (IMiDs), appear to act in many ways against myeloma cells.

First, these drugs act directly on myeloma cells to either induce tumor cell death or dormancy. This is true even for myeloma cells which are resistant to conventional myeloma chemotherapy. Second, myeloma cells grow and survive in the bone marrow where they adhere to the normal bone marrow cells and proteins. This binding of tumor cells assures their localization in an environment where they can grow and survive, and furthermore makes them resistant to

chemotherapy. Thalidomide and the IMiDs inhibit the ability of myeloma cells to bind to bone marrow cells, thereby removing these growth and survival advantages. The adherence of myeloma cells to the bone marrow also induces the production of interleukin-6 (IL-6), a tumor cell growth and survival factor, as well as vascular endothelial growth factor (VEGF), which stimulates new blood vessel formation or angiogenesis. Thalidomide and the IMiDs also block this increased production of both IL-6 and VEGF in the marrow milieu triggered by tumor cell binding, thereby mediating both anti-myeloma and anti-angiogenic activity.



patient's own T cell and natural killer cell immune response against myeloma cells. These agents therefore offer great potential to improve the outcome of treatment, since they both directly kill myeloma cells and, in addition, act to change the bone marrow in ways which further inhibit the ability of the myeloma cell to grow and survive. They offer great potential to improve the quality of life and survival of patients with myeloma.

## Announcing: MMRF Teleconference

The Multiple Myeloma Research Foundation and Cancer Care Present:

### Perspectives on Stem Cell Transplantation in the Treatment of Multiple Myeloma

This is a free teleconference workshop for people living with multiple myeloma, their friends and families, and healthcare professionals. The conference features two world leaders in the field of myeloma: Bart Barlogie, MD, PhD, of the University of Arkansas for Medical Sciences, and Phil Greipp, MD, from the The Mayo Clinic. **The conference will take place on November 14<sup>th</sup>, 2000, at 1:00 EST. Pre-registration is required. To register call 1-800-813-HOPE, or register online at: [www.cancercare.org](http://www.cancercare.org).** Sponsored by Nexell Therapeutics

# MEET OUR BOARD

**K**aren Andrews, Associate General Council for Time Inc., is the founder of the MMRF. Ms. Andrews, twin sister of MMRF President Kathy Giusti, said of the Foundation: "It was born of a vision that both Kathy and I shared." Ms. Andrews indicated that the impetus for establishing the Foundation was that, at the time of Kathy's diagnosis, there was very little research being conducted on myeloma. She said further that "once we came to the realization that raising money to fund research was the best way to fill this void, it was then just a matter of how to put the process in place, and set up the Foundation."



MMRF Founder Karen Andrews  
Associate General Council, Time Inc.

Ms. Andrews commented: "What makes the Foundation unique is that it's run like a Fortune 500 Company with a professional Board of Directors, an expert Scientific Advisory Board and a strong planning process in place. The MMRF focuses on curing myeloma." Ms. Andrews further explained that of key importance to the Foundation is that "we continue to become an international foundation, fostering collaboration among myeloma researchers worldwide while continuing our advocacy efforts in Washington to gain higher levels of funding for myeloma research."

As a member of the Board of Directors, Ms. Andrews volunteers her time providing legal and business affairs support, but also strives to expand her role based on the needs of the MMRF. For example, Ms. Andrews serves as Chairman of the MMRF's Fall Gala. In that capacity she recruits celebrities to support the MMRF's fundraising events, and solicits financial support.

Ms. Andrews wanted to emphasize the importance of all of the people who volunteer their services to the success of the Foundation. Consistently the people of Time Inc., including those at *In Style* and *Sports Illustrated* magazines, have donated their vast skills and energies toward aiding the MMRF in the search for a cure. It is with the help of individuals and organizations like Time Inc. that a cure for myeloma will be found.



# DATES TO REMEMBER

## October 5, 2000 BOSTON, MA

**INSTITUTIONAL INSIGHTS:** One symposium for clinicians and another free program for patients and family members. Presented by the MMRF and Dana-Farber Cancer Institute. Speakers: Dr. Ken Anderson, Dr. James Berenson, Dr. Joan Blade, Dr. Bob Kyle, and Dr. Nikhil Munshi.

## October 7, 2000 NEW YORK, NY

**INSTITUTIONAL INSIGHTS:** One symposium for clinicians and another free program for patients and family members. Presented by the MMRF and Weill Medical College of Cornell University. Speakers: Dr. Ken Anderson, Dr. Bart Barlogie, Dr. Leif Bergsagel and Dr. Joseph Michaeli.

## October 21, 2000 GREENWICH, CT

"Friends for Life" Fall Gala. For more information contact Jenny McMahon at 203-801-5212.

## November 3-5, 2000 CHARLOTTE, NC

Oncology Nursing Society (ONS) Meeting.

## November 9-10 CHICAGO, IL

**INSTITUTIONAL INSIGHTS:** One symposium for clinicians and another free program for patients and family members. Presented by the MMRF, the Cure for Lymphoma Foundation and Northwestern University. Speakers: Dr. Ken Anderson, Dr. Leif Bergsagel, Dr. Phil Greipp, Dr. Martin Oken and Dr. Steve Rosen.

## November 14, 2000 1:00 EST

Teleconference: Perspectives on Stem Cell Transplantation in the Treatment of Multiple Myeloma. (See page 13 for details.)

## December 1 - 4, 2000 SAN FRANCISCO, CA

American Society of Hematology (ASH) meeting.

For more information on INSTITUTIONAL INSIGHTS events, contact Ellen Kaplan at 650-375-8852.

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The information herein is not intended to replace the services of trained health professionals (or to be a substitute for medical advice.) You are advised to consult with your healthcare professional with regard to matters relating to your health, and in particular, regarding matters which may require diagnosis or medical attention.

# INDUSTRY PARTNERS

## Arsenic TriOxide Designated As Orphan Drug

The U.S. Food and Drug Administration (FDA) has recently granted Cell Therapeutics Inc., Seattle-based company, orphan drug designation for the use of Arsenic TriOxide (ATO) in the treatment of multiple myeloma.

ATO is a novel cancer drug that exhibits activity against various blood cell cancers and solid tumors. At low doses, ATO induces programmed cell death (a process known as apoptosis) through a pathway that is different than that seen with other drugs. ATO is currently in Phase I/II studies for the treatment of myeloma; some of these trials are being funded by the National Cancer Institute. (See You Need to Know for more information on clinical trials.)

The FDA designates a product as an orphan drug when it will be used against diseases that affect fewer than 200,000 people in the U.S. (Multiple myeloma affects approximately 50,000 Americans.) The FDA established the orphan drug designation in 1983 to encourage sponsors to develop drugs for patients with rare diseases. The FDA also works with the sponsors to help develop and market these orphan drugs.

Cell Therapeutics Inc. submitted a New Drug Application (NDA) in March to the FDA for ATO in the treatment of patients with relapsed or refractory acute promyelocytic leukemia. The company does not expect to file an NDA for the use of ATO in myeloma for another 2 years.

## Zometa™ Launch

Novartis Pharmaceuticals Corporation recently launched a new cancer drug called Zometa™ (zoledronic acid for injection), available to patients the week of October 9<sup>th</sup>, 2000.

At an internal product launch meeting, MMRF Scientific Advisor James Berenson and MMRF President Kathy Giusti spoke with Novartis representatives about the new drug and its potential impact on patients. Zometa is now available for the treatment of hypercalcemia of malignancy (HCM), a common and potentially life-threatening disorder characterized by elevated serum calcium levels in patients with cancer. HCM, also referred to as tumor-induced hypercalcemia (TIH), is found most often in patients with breast cancer, multiple myeloma and non-small cell lung cancer, and often occurs as a complication of bone metastases and may be associated with cancer in general. HCM usually occurs late in malignancy with limited survival, and is the most common

life-threatening metabolic complication associated with cancer affecting upwards of 10 percent of all cancer patients.

Clinical findings presented at the 2000 American Society of Clinical Oncology (ASCO) meeting in New Orleans this spring strongly suggest that Zometa is more effective than pamidronate -- the current treatment of choice for managing HCM. Findings presented were from two multi-center trials involving some 275 patients, which compared patients receiving a single dose of Zometa 4mg or Zometa 8mg infused over five minutes, to patients receiving a single dose of pamidronate 90 mg infused over two hours. By the tenth day of the treatment, corrected serum calcium concentrations were normalized in 88.4 percent of the patients treated with Zometa 4 mg, and 86.7 percent treated with Zometa 8 mg. In comparison, only 69.7 percent of patients treated with pamidronate 90 mg achieved normalized serum calcium concentrations.

# RECEIVE FREE WEEKLY UPDATES ON MYELOMA -- REGISTER NOW FOR MMRF SMARTBRIEF!

The MMRF has partnered with SmartBrief.com to bring you the most current, accurate, comprehensive and timely information available on multiple myeloma, for free!

Always on the cutting edge, and constantly striving to keep its audience well informed, the MMRF is the first foundation to offer a SmartBrief on myeloma. MMRF SmartBrief seeks out the most important and relevant myeloma information and provides you with quick, well-organized, and easy-to-read summaries on research updates, legislative news, Medicare updates, pharmaceutical industry news directly affecting the community, as well as general lifestyle and wellness tips.

The amount of information available

today can be somewhat intimidating, that's why MMRF SmartBrief is such a valuable tool. Houston Multiple Myeloma Support Group member Robert Tyburec said of MMRF Smartbrief: "I forwarded the SmartBrief to members of the Houston MM support group in case they did not receive it directly. This is a great development, and I hope it will evolve and help accelerate cures for all myeloma patients. Thank you."

Subscribe to MMRF SmartBrief today! Visit the MMRF website at [www.multiplemyeloma.org](http://www.multiplemyeloma.org) and click on "register now". Once you register with the MMRF, hit the REGISTER button on

the bottom of the page and you will be launched to sign up for MMRF's SmartBrief.

You may also register by using the form below, by filling in your name and e-mail address, and sending it back to the MMRF at the address provided.

## MMRF SmartBrief

### Registration

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