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MYELOMA FOCUS

Newsletter of the
MMRF

Today Show's ANN CURRY HONORED \$1.1 MILLION RAISED FOR MYELOMA RESEARCH

Through the leadership of this year's Honorary Chair, Mr. John Costas, President and COO of UBS Warburg, the 2001 Friends for Life Fall Gala raised \$1.1 million. Mr. Costas opened the evening by saying, "I am privileged to be associated with this event. The MMRF is nothing less than the highest quality organization, with tremendous leadership and a singular focus -- to find a cure." Mr. Costas also thanked his business associate and MMRF Board Member, Mr. Robert Wolf, for having introduced him to the MMRF.



"I am honored to accept this award" said Ann Curry at the MMRF's Friends for Life Fall Gala



(L-R) Ann Curry, Geraldine Ferraro, Kathy Giusti and Deborah Norville

The engaging Mistress of Ceremonies, Deborah Norville of *Inside Edition*, captivated the more than 800 guests with her warmth and belief in the MMRF. Ms. Norville opened the evening by saying, "In life, when it is all said and done, you need to ask yourself if you matter. Well, everyone here tonight matters. Your support matters and you make a difference. Your being here tonight, gives great cause for hope to so many people."



(L-R) Robert Wolf, Barb and John Costas

Ann Curry, *Today Show* Anchor, graciously accepted the 2001 MMRF Public Awareness Award for her feature segment on the MMRF on NBC *Today*. Ms. Curry stated in her acceptance speech, "I understand the tragedy of cancer. I lost my mother to gall bladder cancer and my

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Welcome Letter

Families Funding Research

Dear Friends,

Progress. It can happen a few steps at a time, or in giant leaps. When the Multiple Myeloma Research Foundation (MMRF) began in 1998, we were making up for lost time and progress came an inch at a time. Today, our progress is measured in miles.

This year the MMRF has:

• funded **\$4 million** of the most promising myeloma research. We are now supporting 30 myeloma labs worldwide.

• kept you informed of every new drug, every new trial and every new hope through our educational programs, all free of charge.

• spearheaded the first Congressional Hearing on blood cancers with the support of Geraldine Ferraro and Senator Kay Bailey Hutchinson.

• brought awareness of myeloma to millions of people through media programming on *Today*, CNN, Fox News, and CNBC, and coverage in the *New York Times* and *USA Today*.

We can only continue this rapid progress with the help of every patient, family member, friend, and healthcare worker. This year, we are hoping to double the participation rate. Please make your year-end donation now, so we can continue in our mission to accelerate the search for a cure.

There is real hope today, and you can be part of this progress. Help make a difference and support the MMRF. Your donation is an investment in a cure. Think of yourself as a partner in our efforts. Please give whatever you can. Together, we will achieve the goal of finding a cure.

Thank You.



Tom Corbett had been a vigorously active outdoorsman, playing polo for the last 25 years and spending summer vacations fly fishing in the heart of the Colorado Rockies. Although recently retired from the decorative lighting firm he founded in Dallas in the 60s, he was filling in full-time while a new CEO was being sought. It was a polo injury that led to a disturbing discovery. "I had a herniated disc in my neck that required surgery in April of '99," says Tom. "The surgeon found that my bone was abnormally soft and didn't heal properly; he said I had better check into it." By October, and after several false starts, Tom finally learned he had multiple myeloma. A course of conventional VAD chemotherapy at the University of Texas Southwestern Medical Center had limited success and Tom decided to turn elsewhere.

Fortunately, a little serendipity came into play. "For years, I had participated in a charity event, called *Polo on the Prairie*, out in the middle of West Texas," Tom explains. "Tommy Lee Jones plays in it, too. It's to raise money for the MD Anderson Cancer Center in Houston. As it turned out, they have a multiple myeloma department." At MD Anderson, Tom came under the care of MMRF Scientific Advisory Board member Dr. Raymond Alexanian and Dr. Thomas Martin. After a bone marrow transplant and a long recovery, he is in complete remission.



Tom Corbett

Early on, Tom learned of the MMRF. "After my diagnosis, my wife Roberta got on the Internet and found the MMRF immediately," he says. "They were just terrific. Their web site has a tremendous amount of information, and on the phone they were very helpful and encouraging. As I surveyed what was going on in research with an eye towards my future treatment, I became familiar with the work of Dr. Ken Anderson and the unique position he occupies both in the MMRF and in the worldwide myeloma community."

With the generous assistance of his mother, Patricia A. Corbett, Tom is funding a MMRF Senior Research Grant. "The MMRF is in the forefront of so much cutting edge research that we felt we had to do whatever we could to support what they are doing. Someday it may save my life."



FRIENDS FOR LIFE

Continued from page 1.

sister has breast cancer. My mother, who was Japanese, taught me the Japanese word *gambaru*, which means persistence and determination in the face of overwhelming adversity. The MMRF signifies *gambaru* and I am honored to receive this award."

Dr. Richard Klausner, former Director of the National Cancer Institute, was unable to attend the event but was honored for his leadership work and support of funding research for all blood cancers. In a written statement, read by Deborah Norville from Dr. Klausner, he stated that if he had one message to deliver it would be this: "We will find a cure for multiple myeloma."

Geraldine Ferraro closed the evening eloquently expressing that "My family and I believe Kathy Giusti has literally been a lifesaver in creating and leading what we consider to be the best vehicle for pushing research into the cure and treatment of this disease. We need to continue to fund research, to get new drugs to market, to help myeloma and all cancer patients and that's what the MMRF is all about."



(L-R) John Zaccaro, Cindy Anderson, Dr. Ken Anderson, and Geraldine Ferraro



(L-R) Jenny McMahon, Barbara Wright, Auction Chair - Lori Ward, and Bonnie Arrix



Above (L-R): Karen Andrews and Deborah Norville



(L-R): Scott Santarella and Donna Zaccaro



Left: Deborah Norville signing her children's book *I Can Fly!*

Competitive bidding fueled by charitable intentions, created a spirited atmosphere as event-goers bid on unique items and travel packages:

Guests of **Sports Illustrated** at the XIX Olympic Winter Games; VIP passes to the Grammy Awards and its VIP pre- and post-event parties; Getaways to world class spas and resorts, i.e. **Lapa Palace** in Lisbon, Madeira's **Reids Palace** and **The Fairmont Banff Springs** in Canada; A 12-day Mediterranean Cruise on **Silversea Cruises**; an evening at **Casa Blanca** and dining at the **French Culinary Institute**.. were among the many exciting donations for the auction made by: **Jetson Direct Mail**, **Robin Rotenier**, **Jet Blue Airways**, **Four Seasons Hotel**, **The National Academy of Recording Arts and Sciences**, **Sports Illustrated for Kids**, **Grand Hyatt** and **United Envelope**.

MMRF RESEARCH ROUNDTABLE

MICROARRAY TECHNOLOGY SHOWING POTENTIAL IN DIAGNOSIS AND STAGING

The seventh MMRF Research Roundtable session brought together internationally recognized research scientists and clinicians involved in myeloma and the evolving field of genomics -- the study of gene expression. Several key technology companies provided a broad overview of the state-of-the-art technologies available for myeloma research. A focused discussion followed on the progress being made by the myeloma community and an exploration of ways to foster collaborative research efforts.

understanding of the molecular basis of how myeloma develops." Comparison of these genetic profiles with those of normal cells can help pinpoint genes that are abnormal in myeloma. These abnormal genes can then be potential targets for directed myeloma therapy. In early studies, the information provided by these genetic profiles is already showing its potential for use in the diagnosis and staging of myeloma disease and may provide important prognostic information, including how a patient might respond to treatment.



Dr. Shaughnessey and Dr. Stewart

Another aspect of the roundtable focused on the need for a collaborative effort that would move myeloma research forward at a more rapid pace. Dr. Stewart commented, "we quickly realized that our focus on these technologies was too narrow; what we really need is myeloma researchers working together in many different areas beyond microarray technology."

Dr. Thomas Kipps, head of the Special Hematology Department at the University of California at San Diego, provided an important perspective on collaborative efforts based on his experience with a group of researchers in chronic lymphocytic leukemia (CLL) who have formed a CLL Consortium across several academic centers. Such a collaboration would help shift individual laboratory-based efforts to a collective pooling of resources, allowing important biologic questions to be answered in a more timely and coordinated fashion, bringing us closer to a cure.

This informative session took place October 10-11 in Boston, Massachusetts, and was co-chaired by Diane Jelinek, PhD (Mayo Clinic), Keith Stewart, MD (Princess Margaret Hospital), and Brian Van Ness, PhD (University of Minnesota). The roundtable was funded by the MMRF with support from Celgene and Millennium Pharmaceuticals.

How is Microarray Technology Used in Myeloma?

Microarray technology is a method of analyzing the expression patterns of thousands of genes at one time. This technology allows the creation of individual genetic profiles for each patient's myeloma cells. According to John Shaughnessey, Jr., PhD, of the University of Arkansas, these genetic profiles have led to a "quantum leap in our



(L-R) Jeffrey Brown, PhD (Millennium); Thomas Theriault, PhD (Incyte); Douglas Robinson, PhD (Affymetrix); G. Reid Asbury, PhD (Amersham Pharmacia Biotech); Craig Gelfrand, PhD (Orchid BioSciences); George Mulligan, PhD (Millennium); Scott Patterson, PhD (Celera Genomics); Gustave Stolovitsky, PhD (IBM T.J. Watson Research Center)

Ask the Expert

This month's Ask the Expert features the MMRF's Scientific Advisor, Mohamad A. Hussein, MD, Director of the Cleveland Clinic Myeloma Research Program in Cleveland Ohio.



Mohamad A. Hussein, MD
Cleveland Clinic

1. I have been troubled with bone complications of my myeloma disease. However, a friend with myeloma has had no bone problems, but has suffered kidney damage. Why the difference if we have the same disease?

Although weakened bones and kidney damage are both complications of multiple myeloma, one may affect a patient more so than another. Part of the reason behind this is the fact that myeloma has both direct and indirect effects on various organs in the body. During the disease process, a variety of cytokines (chemicals that have biologic activities) are released that support the growth and survival of myeloma cells. These cytokines also stimulate bone destruction (see figure below), which is why bone disease is seen in the majority (70% to 100%) of patients with myeloma. Some of these cytokines -- the growth factor IL-6 (interleukin 6) in particular -- are also associated with kidney damage, which is

seen in about 30% of patients. In addition, myeloma cells produce large quantities of dysfunctional antibodies (M protein) that have a direct toxic effect on the kidneys, and patients who produce light chain proteins of the λ (lambda) type, tend to have more kidney complications. Moreover, the combination of bony destruction and the increased activity of the myeloma cells produce excess chemicals, such as calcium and uric acid, further damaging the kidneys. Both the stage of the disease and the extent of the chemical abnormalities occurring are responsible for the differences in symptoms and complications from one patient to the other, and also within the same patient at different time points in the course of the disease.

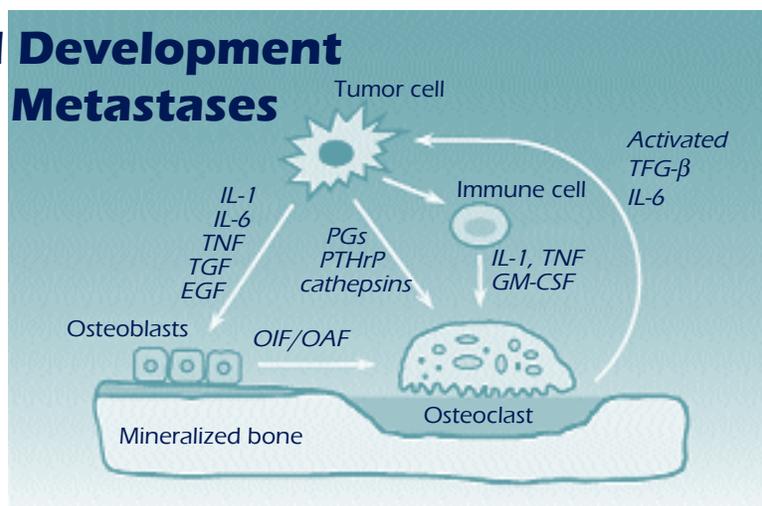
2. Why is thalidomide used together with dexamethasone?

Dexamethasone, a type of steroid, is probably the most active drug we have against myeloma. However, the response rates to dexamethasone are not very durable and patients quickly become resistant to the drug. Dexamethasone's effectiveness can be enhanced by using it in combination with other chemotherapeutic agents. Dexamethasone and thalidomide have a synergistic effect when used together -- the combination is more effective than either agent alone. Moreover, 40% of patients who don't respond, or stop responding, to either drug alone, will respond to the combination. This enhanced effect is thought to be due in part to the ability of thalidomide to inhibit

the interaction between myeloma cells and stroma cells (cells lining the bone marrow). One of the ways myeloma cells become resistant to steroids and chemotherapy is by attaching themselves to the bone marrow stroma. Therefore the interruption of this interaction by thalidomide results in the myeloma cell being more vulnerable to these therapeutic agents, leading to greater efficacy.

Origin and Development of Skeletal Metastases

Myeloma cells produce a variety of cytokines (shown in italics) that directly and indirectly stimulate the activity of bone-destroying osteoclasts and lead to bone complications.



Medical Corner

NEW THERAPIES FOR MYELOMA ...

There is much excitement in the myeloma field with the identification of several new therapies, including agents such as the IMiDs™ (immunomodulatory drugs), the proteasome inhibitor PS-341, and arsenic trioxide (ATO). Each is being evaluated in Phase II clinical trials in myeloma, results of which will be presented in our upcoming special edition newsletter reporting on the American Society of Hematology (ASH) meeting.

Here we review how these new therapies work against myeloma. Although each of these agents is unique, they share many similarities (see the box at right for more information).

Different from Chemotherapy

Standard therapy for myeloma includes conventional or high-dose chemotherapy. Chemotherapy drugs act directly on myeloma cells (as well as other rapidly dividing cells), damaging their internal machinery so that they cannot grow and divide. Although myeloma cells are initially sensitive to chemotherapy, they eventually develop resistance to it so that it is no longer effective.

The mode of action of the newer therapies is different from that of chemotherapy and these new agents have several advantages. Unlike chemotherapy, the newer therapies appear to act on multiple targets within the myeloma cell. In addition, these new agents act not only on myeloma cells, but also affect other neighboring cells in the bone microenvironment that enhance myeloma cell growth and survival. The result is a multi-pronged attack on the disease. Additionally,

NEWER THERAPIES FOR MYELOMA

IMiDs™

IMiDs™ (Celgene Corporation) are derivatives of thalidomide designed to be more potent and potentially safer. These agents display significantly greater immunomodulatory activity than thalidomide against myeloma cells in the laboratory. IMiDs have direct anti-myeloma effects, including induction of apoptosis and inhibition of cell growth, and indirect effects on the cells in the bone marrow. Revimid™ (CC-5013) is the first agent of this class of drugs being tested in myeloma trials.

PS-341 (proteasome inhibitor)

PS-341 (also known as LDP-341, Millennium Pharmaceuticals, Inc.) inhibits the activity of proteasomes, which are complexes of enzymes found in cells. Proteasomes serve as housekeepers, breaking down and clearing out proteins after they've done their job and are no longer needed. Not surprisingly, proteasomes are necessary for a normal cell to function and grow. However, no major harm occurs in a normal cell if the activity of proteasomes is temporarily blocked. In contrast, some cancer cells, including myeloma cells, appear to be particularly dependent on proteasomes to grow and survive. If proteasome activity is blocked, they rapidly die off. This selective activity against cancer cells is one reason why proteasome inhibitors such as PS-341 are promising therapies for myeloma.

Arsenic Trioxide (ATO)

Arsenic trioxide (Trisenox™, Cell Therapeutics, Inc.) is a novel drug that exhibits activity against various blood cancer cells and solid tumors. It is a formulation of arsenic, a compound used as a medicinal for centuries. Approved for use in treating acute promyelocytic leukemia, arsenic trioxide has been shown to inhibit myeloma cell growth, induce apoptosis, and inhibit angiogenesis.

See Industry Update and Clinical Trials on page 8 for more information on these agents.

because they appear to have a more focused activity against cancer cells, the newer agents do not exhibit some of the toxic side effects associated with chemotherapy.

One of the greatest features of these new agents is that they appear to be effective against cells that are resistant to conventional chemotherapy. Thus, these agents may provide a treatment option when other agents have failed. In addition, these agents act synergistically with other anti-myeloma agents, such as dexamethasone, and may be highly effective as part of combination chemotherapy.

Key Anti-Myeloma Effects

All of these agents have similar actions that make them effective against myeloma. These actions are detailed in the diagram on the next page and are explained below. They:

A induce apoptosis (programmed cell death) of myeloma cells. Because they are cancer cells, myeloma cells do not follow a normal life cycle of growth followed by death. These new agents help "reprogram" the cell to die.

B interfere with the interaction of myeloma cells with other cells in the bone marrow, which leads to decreased production of growth and survival factors by the bone marrow stromal cells and makes the environment less hospitable to myeloma cells.

C inhibit the growth and multiplication of myeloma cells.

D inhibit angiogenesis (blood vessel formation) in the bone marrow, which also

Medical Corner

...and How They Work

makes the environment less hospitable to myeloma cells.

E modulate the immune system to induce an anti-myeloma response.

NF-κB: A Key Target

Researchers are beginning to understand how these agents work in myeloma. It appears that all three drugs (IMiDs, PS-341 and ATO) exert some of their anti-myeloma effects by blocking a key protein known as NF-κB. NF-κB in the cell acts as a messenger and for that reason it is also referred to as a signaling protein. When a cell receives an external signal, such as a growth factor, proteins such as NF-κB transfer the message to the nucleus of the cell, causing a response, such as cell growth.

NF-κB also sends a message for cells to increase the expression of various molecules on their cell surface. In the case of myeloma, these surface molecules (adhesion molecules) allow myeloma cells to stick to cells in the bone marrow. This interaction stimulates the bone marrow cells to produce factors such as IL-6 and vascular endothelial growth factor (VEGF) that promote the growth and survival of myeloma cells and promote angiogenesis.

Therefore, by blocking NF-κB, these agents inhibit myeloma cell growth and induce cell death. They also inhibit the production of growth and survival factors by blocking the production of adhesion molecules on the myeloma cell surface and the interaction between myeloma and bone marrow cells. Angiogenesis is also inhibited as a result.

Other Anti-Myeloma Effects

These newer agents have additional anti-myeloma effects in addition to their inhibition of NF-κB, that are distinct to each agent. Arsenic trioxide for example, has been shown to inhibit a signaling protein known as STAT3, which is also important in cell growth. PS-341 inhibits the activity of bcl-2, a protein that enables cells to become resistant to conventional chemotherapy.

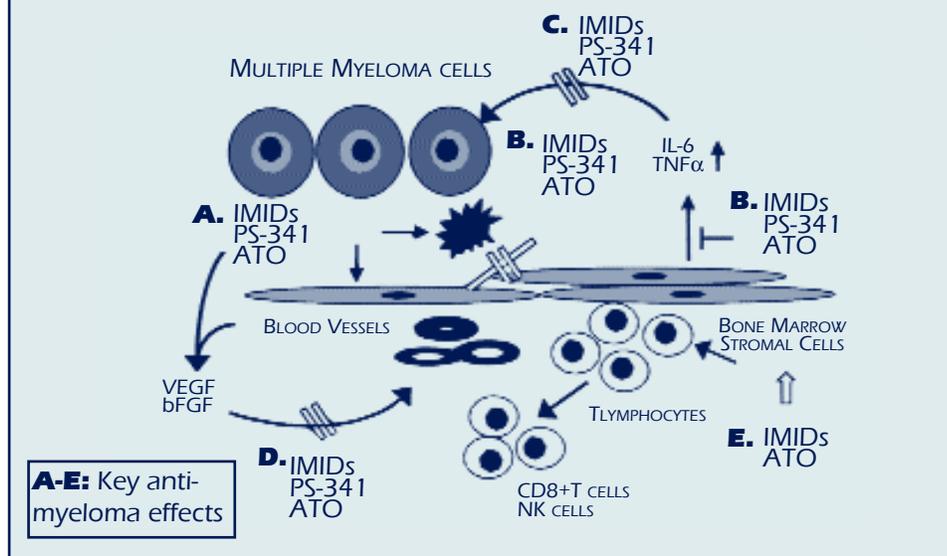
In addition to their effects on myeloma cells and the bone marrow, these agents have effects on the immune system that may be beneficial in myeloma. For example, IMiDs increase the number and activity of natural killer cells, immune cells that play an important role in tumor cell killing. Arsenic trioxide also appears to boost the immune system against myeloma.

Finding the Right Combination

The results of early clinical trials of these agents are just being reported and are very encouraging, particularly in light of the fact that the patients in these trials have often failed all available therapies.

As more information becomes available, we'll be better able to determine the best way to utilize these new agents as part of myeloma therapy. These agents act on different signaling pathways, therefore it may be beneficial to use some of these agents together to exert a stronger response and a broader anti-myeloma effect. Because of their synergistic effects with conventional chemotherapy, they may be highly effective as part of combination therapy. Thus, they will offer greater options for the treatment of myeloma.

Mechanisms of Action of Novel Biologically - Based Therapies



INDUSTRY UPDATE

Amgen's Aranesp™ Approved for Anemia Associated with Chronic Renal Failure

Aranesp (darbepoetin alpha), a long-acting anemia treatment, was recently approved for use in the treatment of anemia associated with chronic renal failure. It is administered every one or two weeks. Amgen is currently seeking approval for use of Aranesp in the treatment of anemia associated with chemotherapy.

Genasense™ Receives Fast Track Designation for Myeloma

Genasense™ (Genta Incorporated), an agent currently in Phase III clinical trials in myeloma, was granted fast track designation by the FDA. This status, granted to drugs intended to treat serious or life-threatening conditions for which current therapies are not optimal, facilitates rapid review of clinical data submitted for approval of the drug.

Millennium Completes Enrollment of PS-341 Trial in Myeloma

Enrollment of a multicenter Phase II trial of the proteasome inhibitor PS-341 (also known as LDP-341) in myeloma was recently completed. Patient accrual into the trial was completed ahead of schedule and the trial has been extended to capture additional data. An additional Phase II trial in patients who have failed to respond to or relapsed following first-line therapy is ongoing.

FDA Grants Revimid™ Orphan Drug Status for Myeloma

Revimid™, Celgene's lead immunomodulatory drug (IMiD™), was granted orphan drug designation by the FDA for myeloma. Granted to products used against diseases affecting fewer than 200,000 people in the U.S., this status entitles Celgene to seven years of market exclusivity in myeloma following FDA approval. Revimid is currently being evaluated in two Phase I/II trials in myeloma.

FDA Grants Priority Review for Zometa® in the Treatment of Bone Metastases

Novartis' Zometa (zoledronic acid) has been granted a priority review by the FDA for use in the treatment of bone metastases in patients with myeloma, breast cancer, and other tumor types. Priority review is granted for therapies that may offer a significant improvement over available treatments.

Zometa is already approved for the treatment of hypercalcemia of malignancy. A recent Phase III study showed that Zometa reduced the occurrence of cancer-related bone complications (such as fractures, spinal cord compression, or the need for surgery or radiation) in patients with myeloma or breast cancer and delayed their onset.



Ongoing CLINICAL TRIALS in Myeloma

Trial & Contact Information

Phase II study of arsenic trioxide and dexamethasone in patients with recurrent or refractory stage II or III multiple myeloma.

Raymond Comenzo - 212-639-8086
Memorial Sloan Kettering Cancer Center
New York, NY USA

Phase III study of dexamethasone with or without Genasense™ in patients with relapsed or refractory myeloma.

Recruitment Coordinator - 908-286-5994

Phase II study of Thalidomide, high-dose dexamethasone and Zometa for patients with newly diagnosed multiple myeloma.

Olcay Bautman - 718-270-2785
SUNY Health Science Center
Brooklyn, NY USA

Phase III study of Novel Erythropoiesis Stimulating Protein (NESP) for the treatment of anemia in patients with lymphoproliferative disease receiving chemotherapy.

Ellen Church - 416-946-2317
Princess Margaret Hospital
Toronto, Ontario Canada

Phase II study of Panzem™ for relapsed or plateau myeloma.

S. Vincent Rajkumar - 507-284-2511
(pager 46000)
Mayo Clinic
Rochester, MN USA

MMRF

INSTITUTIONAL INSIGHTS



INSTITUTIONAL
INSIGHTS
ON MYELOMA

The MMRF partnered with Scientific Advisor Dr. Keith Stewart, the McCarty Cancer Foundation and the University of Toronto to host an MMRF Institutional Insights program in Toronto, Canada. Both the patient and professional programs were filled with eager participants who wanted to learn more about the most recent progress in myeloma research.

Special thanks to Daniel Bergsagel, MD for being this program's honored course director. We also want to thank Ms. Marion State, Toronto's support group leader, for all of her help with promotions, volunteering, and more. We also would like to acknowledge Celgene, Novartis, and Ortho Biotech for their generous support of this program.

The MMRF Institutional Insights program will be expanding to ten institutions in the upcoming 2002 schedule. Our hope is that everyone has an opportunity to attend a program close to home. Each program is updated to incorporate the latest research and clinical trial information available. Refer to the calendar in each issue of Myeloma Focus for a program near you. You can also sign up for MMRF Smartbrief for the latest news and reminders about upcoming programs.



(L-R) Scott Santarella, Roberta McCarty and Loren Feingold

Below (L-R) Loren Feingold, Dr. Leif Bergsagel, Dr. Nikhil Munshi, Dr. Daniel Bergsagel, Dr. Keith Stewart, Dr. Kevin Imrie and Scott Santarella



Kathy Giusti

KATHY GIUSTI APPOINTED

TO NCI DIRECTOR'S CONSUMER LIAISON GROUP

Kathy Giusti, President of the MMRF, has been appointed to the National Cancer Institute's, Director's Consumer Liaison Group (DCLG). The appointment followed a stringent nomination and evaluation process that spanned several months.

"It's an incredible honor to serve on the DCLG," said Kathy. "It's a chance to make a tremendous difference for all cancer patients."

The DCLG was founded in 1997 as the NCI's first all-consumer advisory body. Members work to ensure that those who experience the burden of cancer also help shape the course of the NCI's efforts to eradicate the disease. Each of the 15 mem-

bers is appointed for a three-year term. They must have demonstrated an exceptional effectiveness in cancer advocacy that has grown out of a direct involvement with the disease -- as a survivor, as one affected by the consequences of the disease, or as one who works with survivors. The DCLG issues recommendations directly to the Director of the NCI and is structured to represent the full demographic range of the cancer advocacy community and the diversity of cancer types.

Dr. Alan Rabson, Acting Director of the NCI, sums up what Kathy brings to the DCLG; "Kathy Giusti is a leader in the cancer research advocacy community," he said. "She brings her great understanding and skills as a manager, combined with her remarkable understanding of the problems of cancer patients, to the DCLG where I look forward to the opportunity to work closely with her."



MEET OUR BOARD

DATES TO REMEMBER



Jean Kovacs
President and CEO
Comergent Technologies

Sun Microsystems, Cisco, Dupont -- these are just a few of the major corporations using the e-business software of Comergent Technologies, the company founded by President and CEO Jean Kovacs some three years ago. As a Harvard Business School graduate, Jean had worked hard to prepare for her success. While studying there, she made two very good friends -- Kathy and Paul Giusti. "The Harvard program is very intense, and you develop close ties with certain people," said Jean. "I have tremendous respect for both of them. They're very ethical and hardworking, and they're the kind of people who stay in touch."

Jean and Kathy did stay in touch, following their parallel paths to success, she in technology, Kathy in the pharmaceutical world. Then, some six years ago, came Paul's phone call. "I was in shock," she said. "To have someone so young and vibrant as Kathy stricken by something like myeloma is a horrible tragedy." But her friend showed her true spirit. "In a very short time, Kathy picked herself up and said, 'I'm going to fight this' -- and not just on a personal level. She took a skills inventory and saw that she could do something for all myeloma patients."

The MMRF has been enormously successful by any measure. "They've been extraordinarily effective in attracting research funding and promoting a cure," said Jean. "Kathy has touched thousands of people's lives; she's given them hope."

Last year, when Kathy was looking to expand activities on the West Coast, Jean was a natural choice. "It was a huge honor," she said. "Coming from a business background, I was particularly happy to become involved in an organization so well focused, so well managed, and with such clear objectives."

Jean was instrumental in staging the November 2000 Fundraiser in San Mateo, California. "It was a great location," she said. "We were able to draw Silicon Valley people from San Francisco down to the southern part of the peninsula and raise their awareness about our cause."

Jean surveys the future with unmixed optimism. "Kathy's energy and vision have gotten some of the most brilliant minds in medical science to look at multiple myeloma," she said. "People invest in people; it's not that different from the business world, and when you get the brightest minds looking at a problem, they will find the answer, regardless of conditions. There is not a doubt in my mind that we will find a cure."



March 14-15, 2002 Little Rock, AR

*Institutional Insights on Myeloma
University of Arkansas

April 3, 2002 Cleveland, OH

*Institutional Insights on Myeloma
Cleveland Clinic Cancer Center

April 18-21, 2002 Washington, DC

Oncology Nursing Society (ONS) Mtg.

May 18-21, 2002 Orlando, FL

American Society of Clinical Oncology (ASCO) Meeting.

May 29, 2002 Houston, TX

*Institutional Insights on Myeloma
MD Anderson Cancer Center

May 2002

Teleconference with Ken Anderson, MD
Dana-Farber Cancer Institute

June 2002 New York, NY

*Institutional Insights on Myeloma

June 21 & 22, 2002 Stanford, CA

*Institutional Insights on Myeloma
Stanford University Medical Center

Continual Programs:

MMRF Webcast, visit <http://multiplemyeloma.org>. Past Myeloma Teleconferences, visit www.multiplemyeloma.org/events/teleconference.html

***Institutional Insights on Myeloma**

programs consist of two symposia sessions -- one for patients and their families and one for healthcare professionals. For more information on Institutional Insights Programs call (203) 972-1250 or visit: www.multiplemyeloma.org/events/seminars.html

FUNDRAISING

MMRF Race for Research Raises \$50,000



On October 13, 2001, myeloma patients, family members, and MMRF staff and board members participated in

the **MMRF Race for Research** held in Chicago, Illinois.



Special thanks to our sponsors, Allegiance, Baxter, Celgene, Genta, Neopharm, Silver Creek Natural

Spring Water, Fleet Feet Sports of Chicago, Kraft Foods, Lifesavers, the new 94.7, the Zone, and the top fundraising family, the Stevensons.

Miles Conquer Myeloma



Goshen, Connecticut was host to the first **Miles Conquer Myeloma** road race. Eighty runners raised nearly \$7,000 for multiple myeloma. Special thanks to Nancy Wadhams for organizing this event to honor her husband and to her children Andree and Gene Stone to honor their father, John Wadhams.

The holiday season is a time for reflection and for giving thanks. As we prepare for the end of our fiscal year, we are truly thankful for all of the support we have received. As you reflect on your year and prepare year-end charitable gifts, we hope you will consider the MMRF as one of your top choices. Think of your donation as an investment toward a cure. Think of yourself as a partner in our efforts. Below are a few of the ways that you can help.

Cash Donations Usually in the form of a check or credit card transaction, cash donations are the most popular and most convenient form of support.

Matching Gifts You can multiply your dollars given to the MMRF for myeloma research by contributing through your company's "Matching Gifts" plan. Many companies contribute to non-profits on behalf of their employees through "Matching Gifts" programs. Contact your personnel or human resources office. They generally handle the process of matching gifts. Please let your employer know you support the MMRF and encourage your company to become a corporate donor.

Donations of Securities Appreciated securities can be gifted to the MMRF. This form of giving often provides the donor with a tax deduction on the current value of the securities without any capital gain implications.

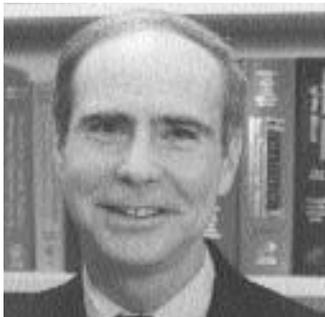
Planned and Deferred Gifts The MMRF receives financial support from many friends who choose to make planned and deferred gifts to the foundation. Each year, we learn of supporters who have made provisions for us in their wills, and some donors make contributions through charitable gift annuities. Planned giving is a form of donating to the MMRF that benefits you and your family while ensuring that the MMRF will have the resources to carry out its mission in the years to come.

When considering a donation to an organization, make sure it is a fiscally responsible charity that maximizes donations by minimizing administrative and overhead costs. The MMRF has traditionally maintained its operating expenses at 5% or less. Therefore, 95% of all funds raised are applied directly to funding research and mission-related programming. We are committed to holding ourselves to the highest standards of fiscal responsibility, ensuring that your investment continually returns progress toward our goal of accelerating the search for a cure.



\$1.5 MILLION FOR RESEARCH

The Collaborative Program Grant from the MMRF provides **\$1.5 million** for research over a 3-year period. Never before has there been such a collaborative approach to myeloma research. The MMRF's goal is to foster unique collaborations among researchers and institutions to help bring new therapies to the clinic quickly. The investigators that submitted the winning grant entitled "Development of Novel Target-based Therapies for Multiple Myeloma," represent three centers of excellence in Myeloma Research: Dana-Farber Cancer Institute, H. Lee Moffitt Cancer Center, and Mayo Clinic.



Kenneth C. Anderson, MD,
Dana-Farber Cancer Institute



William Dalton, MD, PhD,
H. Lee Moffitt Cancer Center



Robert Kyle, MD,
Mayo Clinic

The grant applications underwent rigorous review by a panel of experts in myeloma and hematology/oncology leaders with expertise in the grant application topic areas of immunotherapy, novel compounds and genetics. A stringent annual review process will evaluate the program's progress.

Three Interrelated Projects

The winning grant encompasses three interrelated projects. The focus will be to identify new therapies and to rapidly move promising leads from the bench to the bedside for evaluation in clinical trials at all three institutions. Therefore, this innovative program couples basic science and clinical research expertise with a large patient base allowing for rapid identification and evaluation.

According to Dr. Dalton, a common theme of the grant is

to investigate how the bone marrow microenvironment influences the development and progression of myeloma. "All the projects examine a unique aspect of how the environment can influence myeloma, he noted. "These efforts will be highly coordinated between projects and the results from one project will influence the design and interpretation of experiments in other projects."

THE FIRST PROJECT involves characterizing the cell pathways involved in myeloma cell growth, survival, and migration in the bone marrow environment. This will identify novel molecular targets for therapy. This project is centered at Dana-Farber Cancer Institute. Dr. Anderson will head this project and will also serve as the Principal Investigator for the entire program, directing and coordinating all preclinical and clinical studies.

THE SECOND PROJECT is centered at the H. Lee Moffitt Cancer Center, where Dr. Dalton will head the project, investigating how myeloma cells become resistant to therapy. The goal is to design strategies to prevent or overcome drug resistance. There is a particular emphasis on the role of myeloma cell interaction with the environment in the development of resistance.

THE THIRD PROJECT will evaluate the role of angiogenesis in disease progression. This project, centered at the Mayo Clinic, will involve the work of Drs. Kyle, Rajkumar, and



Nikhil C. Munshi, MD,
Dana-Farber Cancer Institute



Vincent Rajkumar, MD,
Mayo Clinic

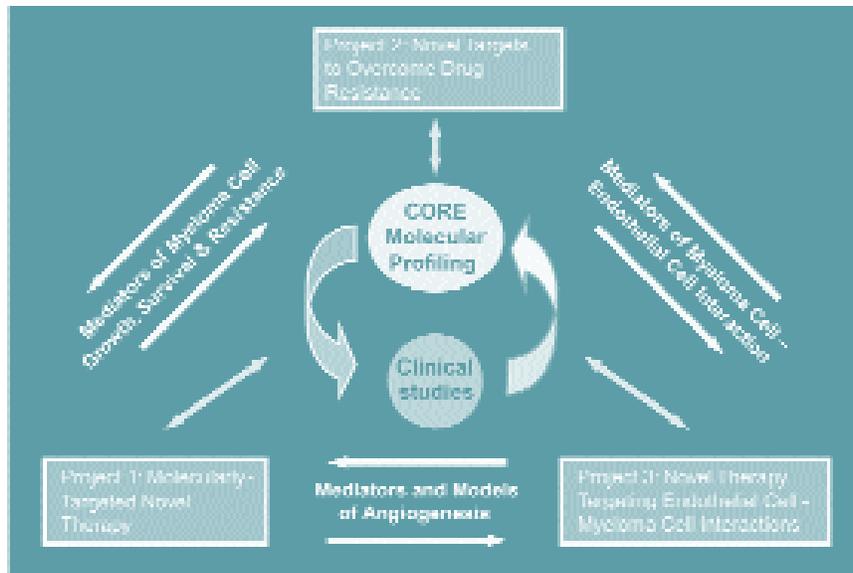


Stephen Russell, MD, PhD,
Mayo Clinic

continued next page

COLLABORATIVE PROGRAM GRANT

Russell. According to Dr. Rajkumar, the goal is to identify targets that are involved with increased angiogenesis in myeloma, as well as targets that are related to angiogenesis but which promote myeloma cell growth more directly. Then, they will use these targets to develop new therapeutics. As an example, Dr. Russell has developed a therapy that involves the use of a modified measles virus to target myeloma cells and the blood vessels critical for myeloma cell growth.



clinical testing of new therapeutics. "While each of the centers is dedicated and focused on developing new treatments for myeloma, each has unique strengths," noted Dr. Anderson. "By combining our efforts, we will be able to rapidly identify novel targets for myeloma therapies." Dr. Kyle, who has been involved in myeloma research for over 40 years, noted that the collaborative approach will result

The Core Lab: A Fourth Component

In addition to funding the three individual research projects, this unique grant will also support a central core laboratory to perform gene analysis for the entire program. Dr. Munshi, will head the core laboratory, and he explained how the lab will be central to the new research being conducted. The lab will first look at the genetic and molecular mechanism of action of the new drugs in the laboratory. Then when the drugs are tested in clinical trials, they will determine whether their anti-myeloma effect in patients is the same as what was seen in the lab. Ultimately, this will allow the identification of specific targets for new treatments that will be more efficacious and better tolerated. The figure above shows how all components of the program work together.

Collaboration: Key to Rapid Movement from Bench to Bedside

All the investigators involved in the program agree that the collaborative effort is innovative and will be key to rapid identification and

in more rapid accrual of patients in clinical trials, enabling promising agents to be evaluated more quickly.

Grant Application Review Criteria

1. The synergy and collaboration to be derived from the interdisciplinary and interactive projects and cores.
2. The importance of the research to the treatment of myeloma.
3. The clarity of thought and presentation.
4. The likelihood that the research findings will find eventual clinical application.
5. Experience, background, and qualifications of investigators.
6. Quality of the resources and environment.
7. Adequacy of provisions for protection of human subjects, lab animals, and staff.

There is much excitement and optimism among the grant recipients that their collaborative efforts will be fruitful. Dr. Anderson noted the ideal timing of the grant. "We have so many promising avenues of research for translating new treatments to the clinic that it is critical to combine our efforts," he commented. "Working together, we have the opportunity to really make a difference for our patients." Dr. Kyle echoed Dr. Anderson's sentiment, and added, "the support from the MMRF is of major benefit to all of us, and ultimately, to the patient with myeloma."

"This collaboration has been catalyzed by the existence of this grant. I'm very optimistic that we're really going to make a difference."

– Dr. Russell

\$400,000 FOR 2ND YEAR RESEARCH AWARDS

The MMRF proudly announces the 2000 MMRF Senior Research Award winners receiving \$400,000 toward a second year of research funding. We make our Senior Awards competitively renewable each year by funding the top 30% of grant recipients. The renewal program adds incentive for researchers to meet their objectives and excel in their work. The recipients will each receive an additional \$100,000 for this new grant cycle.

Dharminder Chauhan, PhD

Dana-Farber Cancer Institute



Apoptotic and Survival Signaling Proteins in Multiple Myeloma: Therapeutic Implication

These MMRF supported studies are focused on improving therapeutic uses of dexamethasone, based upon targeting genes and proteins that regulate myeloma cell growth and survival. In particular, identification of cell

death and survival signaling proteins will allow targeting these proteins for therapies to either enhance dexamethasone-induced cell death or inhibit interleukin-6-mediated survival of myeloma cells. DNA microarray analysis will further provide insights into the basic mechanisms of dexamethasone activity against myeloma, as well as mechanisms of dexamethasone resistance in myeloma cells.

G. David Roodman, MD, PhD

University of Pittsburgh



Role of MIP-1 α in Myeloma Bone Disease

MIP-1 α is made by myeloma cells and induces bone destruction in a mouse model of human myeloma. Previous research found that blocking MIP-1 α activity decreased myeloma cell growth and capacity to go to the bone marrow. The current proposal strives to identify the adhesion molecules regulated by

MIP-1 α to see if blocking these adhesion molecules has a similar effect, and continue characterizing antagonists to the MIP-1 α receptor for their capacity to block development of myeloma in the mouse model. A goal is to determine the utility of these antagonists for future studies in myeloma patients.

Professor Freda Stevenson, DPhil, FRCPath

University of Southampton, United Kingdom

Genetic Vaccination Against Multiple Myeloma.

This group is developing novel vaccines made of DNA that codes for harmless but specific tumor proteins to treat patients with myeloma. Upon injection, the protein is made by the patient's muscle cells, which leads to an immune response to kill the myeloma target cells. The

strategy is to add an extra gene from tetanus toxin to the tumor gene, tricking the immune system into responding to the attached tumor protein. Vaccines are being tested directly in patients, and in donors of allogeneic transplants so that immune cells can be transferred to the recipient in order to suppress their myeloma.



Brian Van Ness, PhD

University of Minnesota

Profiling IL-6 and Stromal Induced Gene Expression and Signal Transduction in Myeloma Cell Lines.

This group is examining gene and protein profiles that will define myeloma growth and response to therapeutic agents using model myeloma cell lines.

The goal is to develop gene and protein arrays that will characterize therapy-sensitive and therapy-resistant patient samples and provide novel approaches in therapeutic design.



MYELOMA FOCUS

Newsletter of the Multiple Myeloma Research Foundation

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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.

YOU NEED To KNOW

Medical Meeting Updates Now Available

The MMRF realizes the importance of providing the myeloma community with the most current information presented on myeloma as quickly as possible. That is why we are dedicated to being your official Major Medical Meeting Update Resource for Myeloma.

We received such wonderful feedback on our programs following the VIIIth International Myeloma Workshop, that we continue to remain dedicated to providing you with the same coverage for other major myeloma meetings. The most current meeting highlights are available now.

MMRF Webcast Available On-line Now

The MMRF, in collaboration with CancerEducation.com, is pleased to present this cutting-edge program. Hear directly from world-renowned myeloma experts who will summarize the latest information on myeloma staging and profiling, current

therapies, transplants, and novel therapies. Access this webcast from our website to hear audio interviews with the experts who have summarized everything you need to know. You can also view and print interview transcriptions, key slides, and abstracts.

Log on to: www.multiplemyeloma.org.

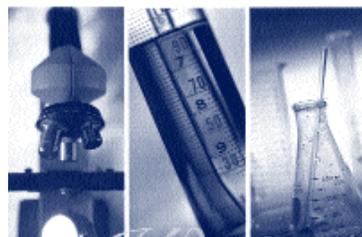
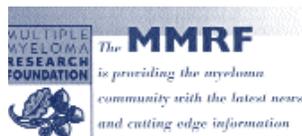
Special Upcoming Edition of Myeloma Focus

Arriving in your mailbox soon will be a special edition of **Myeloma Focus** dedicated to the latest myeloma information. The MMRF, in collaboration with our scientific advisors, is committed to keeping you up to date with the latest myeloma information along with details on new compounds and clinical trials.

Teleconference:

"Myeloma Update: Emerging Treatments and Clinical Trials Update"

In a continual partnership with CancerCare, the MMRF is holding a teleconference featuring Myeloma Expert: William Dalton, MD, PhD. If you missed this teleconference, a replay will be available soon via our website at <http://multiplemyeloma.org/events/teleconference.html>



MMRF Webcast

- TOPICS
- Myeloma Staging and Profiling
 - Current Therapies
 - Transplants
 - Novel Therapies

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