



*Accelerating
the
Search
for a
Cure*

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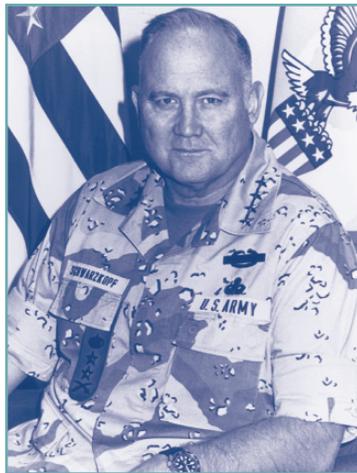
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MYELOMA FOCUS

Newsletter of The Multiple Myeloma Research Foundation

Schwarzkopf Storms 1999 Fall Gala as MMRF Honoree

The MMRF is proud to announce General H. Norman Schwarzkopf as our 1999 Leadership Award Honoree at this year's "Friends for Life" Fall Gala. He is being honored for his outstanding efforts toward raising cancer awareness. General Schwarzkopf, a cancer survivor, served as honorary chairman for "The March: Coming Together To Conquer Cancer" a major event in Washington, DC, last fall to demonstrate the need to increase funding for cancer research and treatment.



Two-time Emmy Award winner, Deborah Norville, of *Inside Edition*, will once again M.C. the Fall Gala. The Gala will be held November 13, 1999 in Greenwich, CT. All proceeds will fund research for multiple myeloma. Contact Jenny McMahon at 203-801-5212.

New York City Symposia

The MMRF and St. Vincent's Comprehensive Cancer Center will present a physician symposium and a patient symposium on October 1st and 2nd, respectively, in New York. Both sessions

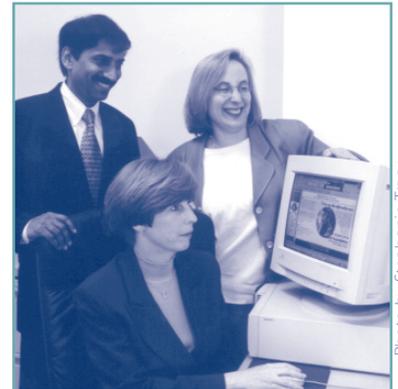


Photo by Stephanie Tracy

(l-r) Dr. Sundar Jagannath, Jill Anderson and Shara Sokol evaluate internet program

will feature key speakers from the Myeloma World Congress in Sweden and provide the latest information on myeloma treatment. The speakers and their respective topics include:

Phillip Greipp, M.D.: Prognostic Indicators and Risk Categories.
Robert Vescio, M.D.: Events in the Bone Marrow
Bisphosphonates and Viruses
Hakan Mellstedt, M.D.: Stem Cell Transplantation
Larry Kwak, M.D., Ph.D.: Vaccines and Idiotype Immunity
Sundar Jagannath, M.D.: New and Supportive Treatments
including Thalidomide

The entire symposium, including slides and complete audio, will be broadcast over the Internet. For information on accessing the Internet broadcast, go to the MMRF web site at:
www.multiplemyeloma.org

Research on **Chromosomal Abnormalities** in Multiple Myeloma

The MMRF and the McCarty Cancer Foundation are funding research into the chromosomal abnormalities associated with multiple myeloma (MM) and its early stages including the premalignant monoclonal gammopathy of uncertain significance (MGUS) and smoldering multiple myeloma (SMM). Understanding when in the disease process these chromosomal abnormalities occur could provide reasons for disease progression and the possible cause of MM.

(Story details in Medical Corner, pages 4-5)

Welcome Letter

MMRF and IMF to Co-Sponsor ASH Symposium

Dear Friends,

When my sister, Karen Andrews, and I founded the Multiple Myeloma Research Foundation (MMRF), our vision was to run it professionally and efficiently. A key priority to us then, as now, was to raise significant funds for myeloma research while keeping overhead as low as possible.

I am pleased that our 1998 audit reports that we are indeed succeeding: the MMRF now ranks in the top fifteen percent of cancer-related non-profit organizations in the United States; approximately 97% of our funds were dedicated to research grants, symposia and patient information; and less than 3% of our funds supported overhead.

How do we achieve such amazing results? Volunteer support! I volunteer as full-time president of the organization. Over 100 other individuals volunteer, helping with administrative work and fundraising. Their talent, energy, and support are building a world-class organization at a minimal cost. Thanks to all the individuals and organizations that have so generously given their time and resources, enabling the MMRF to continue its aggressive search for a cure.



A Continuing Medical Education symposium titled "*Multiple Myeloma: New Advances in Biology and Treatment*" will be presented as part of the American Society of Hematology's (ASH) 41st Annual Meeting. The symposium, sponsored by The International Myeloma Foundation (IMF) and The Multiple Myeloma Research Foundation (MMRF). The event will be held from 6:00 to 9:00 pm, on Friday, December 3, 1999, in New Orleans, LA. The program, chaired by Dr. Ken Anderson and Dr. Brian Durie, will include the following topics: molecular biology, mechanisms and treatment of bone disease, appropriate testing for diagnosis and monitoring, standard approaches to treatment, the role of immunological therapies and the current role of High Dose Therapy. ASH pre-registrants will receive their invitations by mail in October. Others interested in attending should contact the MMRF (203-972-1250) or IMF (800-452-CURE).

Update From Sweden Special Newsletter

Our fall issue of *Myeloma Focus* will be fully dedicated to reporting the results of The VIIth International Workshop on Multiple Myeloma held September 1-5, 1999, in Stockholm, Sweden. The MMRF team will be on-site in Sweden, including our medical writer, to report on critical presentations made by the world's most renowned researchers and physicians. Register now on our website if you are not currently on our mailing list, or add someone you think would like to receive a free copy.

Save The Date The MMRF Chicago Gala March 2000.

Join the Gala Committee today.
Call Jenny McMahon at 203-801-5212.

You Can Help Accelerate the search for a cure.

- Provide a donation in the enclosed envelope.
- Ask your company to sponsor our Fall Gala.
- Call us if you have an item for our Gala auctions (e.g. jewelry and vacation packages).
- Provide names of friends or family to receive *Myeloma Focus*.
- Call us if you have a specific skill that could support our efforts (e.g. printing).

A Special Thank You

to the following corporations for helping support
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Expert Planning Launches The MMRF into the New Millennium

The MMRF has experienced rapid growth since its inception. To ensure our continued success, the MMRF sought the assistance of talented and knowledgeable professionals to develop a long-term business plan. The MMRF took a three-step approach:

1. The MMRF contacted Community Partners, an organization which partners experienced Harvard Business School alumni with non-profits seeking business planning expertise - all on a volunteer basis! A five-member team assigned to the MMRF project was comprised of Program Manager, Jay Misra; Team Leader, Colleen Riley; Doreen Collins, Susan Callaghan and Jeff Brodlieb. The team met over a five-month period and drafted a business plan that clearly defines the MMRF's objectives and strategies based on the needs of the myeloma community.



Community Partners: (l-r) Colleen Riley, Doreen Collins, Susan Callaghan and Jeff Brodlieb (Not pictured) Jay Misra

2. The MMRF Board Advisors reviewed the Community Partner's plan during the month of June. Board Advisors were selected based on their business experience and professional achievement. Several members are patients, or patient family members, ensuring that the perspective of the myeloma community is properly addressed. Board Advisors, working entirely on a volunteer basis, reviewed the plan, provided insights and made further recommendations on fundraising, patient programs, physician programs, and staffing.

Board Advisors

Dean Assink
Barbara Blasso
Dorry Bless
Ellen Coleman
Peter Freeman
Adella Krall
Mark Krueger
Ralph Manganiello
Craig McCarty
Elaine Snyderman
Donna Zaccaro



Board of Directors: (l-r) Lynn O'Connor Vos, Al Heller, Karen Andrews and Anthony Kesman. (Not pictured) Robert Grusky

3. The final plan was then presented to the Board of Directors on June 23rd. The Board, also working on a volunteer basis, reviewed the plan, evaluated its comprehensiveness and feasibility, provided final comments and addressed Board expansion, to meet the Foundation's long-term needs. The plan leads us into the new millennium with: (A) a strong mix of fundraising support from individuals, foundations, and corporations; (B) continued focus on funding research grants, supporting physician roundtables and informing patients and (C) a well-thought out staffing and board development plan, which continues to maximize volunteer support.



A Unified Voice For Myeloma

An important goal of the MMRF is to elevate multiple myeloma on the national research agenda. Kathy Giusti, President of the MMRF, recently met with Craig McCarty, President of the McCarty Cancer Foundation and Jean Ard, Vice President of Government and Legislative Affairs for the Leukemia Society of America, to form a unified strategy to raise awareness and support for multiple myeloma. These organizational leaders agreed that one strong voice for myeloma would help to increase awareness and funding levels at the National Cancer Institute (NCI).



Teaming up for myeloma
(l-r) Kathy Giusti, Craig McCarty and Jean Ard.

The team reviewed myeloma statistics, analyzed current funding levels, and discussed strategies for working with the NCI. All three organizations are working together to set research priorities for multiple myeloma, and look forward to presenting them to the NCI next month.



Medical Corner

Chromosomal Abnormalities

In Multiple Myeloma

How might understanding disease progression change treatment?

Knowing which patients with MGUS will progress to multiple myeloma might mean that these patients would be treated, even though they are asymptomatic. Knowing the cause of disease progression may make possible elimination or even avoidance of that cause. Understanding the cause could indicate a method for interrupting or altering the biological mechanisms involved, thus slowing or even stopping the disease progression. Additionally, the existence of some chromosomal abnormalities are associated with less favorable response to therapies such as transplantation. Knowing when these abnormalities occur could indicate a timing for therapy that would result in more favorable outcomes.

What causes disease progression in individuals with MGUS or SMM?

The cause of disease progression is not known. However, current research is investigating the possible role of several factors including:

- Cytokines: An increase in production of specific cytokines (growth factors)

correlates with progression of multiple myeloma.

- Adhesion Molecules: Located on the tumor cell surface, changes in these molecules correlate with the progression of multiple myeloma.

- Human Herpesvirus-8 (HHV-8): This virus is detected in bone marrow dendritic cells in approximately 25% of patients with MGUS, and in 83% of patients at diagnosis of multiple myeloma.

- Chromosomal Abnormalities: Specific changes in particular chromosomes that are often associated with certain types of cancer include:

- Gain or loss of chromosomes
- Deletion (loss of a segment of a chromosome)
- Inversion ("flip-flop" of two segments of a chromosome)
- Translocation (rearrangement of segments between two chromosomes)
- Selective amplification of certain regions of chromosomes

What chromosomal abnormalities are associated with multiple myeloma?

- Results of a recent study demonstrated a

deviation from the standard number of chromosomes in about 70% of multiple myeloma cases.

- The most frequent abnormalities involve chromosomes 13 (13q-) and 14 (14q+). These abnormalities may result in an impairment of natural cell death and subsequent resistance to therapy.

- Certain chromosomal abnormalities are identified in patients who experience multiple myeloma relapse.

- The most frequent chromosomal translocation in patients with multiple myeloma (14q32) appears to involve the long arm (q) of chromosome 14 in the area (32) related to immunoglobulin. This chromosomal translocation, which is thought to occur in nearly all patients with myeloma, is an important abnormality in disease development.

What causes these chromosomal abnormalities?

Knowledge of the causes of chromosomal abnormalities in multiple myeloma is limited. Evidence has implicated ionizing radiation, autoimmunity, viral infections, and chemical toxins.

MGUS (or monoclonal gammopathy of uncertain significance) is considered to be premalignant because the monoclonal does not grow progressively; it is stable and asymptomatic. Approximately 16% of individuals with MGUS eventually progress to multiple myeloma. The table here shows the clinical features of MGUS; smoldering multiple myeloma (SMM); and multiple myeloma (MM).

No laboratory studies exist that can predict which patients with MGUS will progress to multiple myeloma. In the future, prediction of disease progression may be helped by the use of other markers such as: plasma cell labeling index; cytogenetic abnormalities; and serum levels of IL-6.

| Clinical Features of MGUS, SMM, and MM | | | |
|--|-----------|----------------|-----------------|
| Characteristic | MGUS | SMM | MM |
| Marrow Plasma Cells | <10% | ≥10% | ≥10% |
| Serum M-spike | <3 g/dL | ≥3g/dL | ≥3g/dL |
| Bence-Jones protein | <1 g/24 h | <1 g/24 h | ≥1 g/24 h |
| Anemia | absent | may be present | usually present |
| Hypercalcemia, renal insufficiency | absent | absent | may be present |
| Lytic bone lesions | absent | absent | usually present |

Medical Corner

MMRF Research is Providing Answers

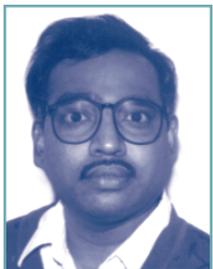
Does the chromosomal 14 translocation also exist in patients with MGUS?



At the Mayo Clinic, Dr. Rafael Fonseca's research is determining whether the translocation 14q32, so frequent in patients with multiple myeloma, occurs as often in patients with MGUS. Also, the chromosome exchanging segments with chromosome 14 to produce this abnormality is being identified.

Rafael Fonseca, MD Dr. Fonseca points out, that although their early findings are in a small number of patients, they are exciting. Data from chromosome analysis of 15 patients with MGUS strongly suggest that MGUS plasma cells do have translocations at 14q32, the same as in patients with multiple myeloma. Additional findings potentially identify the chromosomes that are exchanging segments with chromosome 14 as chromosome 11 and 16.

Are certain genetic changes associated with multiple myeloma development and progression?



Two new technologies, comparative genomic hybridization (CGH) and spectral karyotyping (SKY), are being used in combination, by Dr. Pulivarthi Rao at Sloan Kettering Cancer Center, to identify recurrent genetic changes in patients with MGUS and those with SMM. Using these new technologies and traditional methods,

Dr. Rao has been able to identify a dozen common recurrent chromosomal changes and several new chromosomal translocations in patients with multiple myeloma.

Dr. Rao's results indicate that these new technologies are very promising tools for identifying patients at risk for developing multiple myeloma. Also these technologies will help in the identification of genes that contribute to or cause multiple myeloma.

Do chromosomal abnormalities produce proteins that contribute to the progression of multiple myeloma?

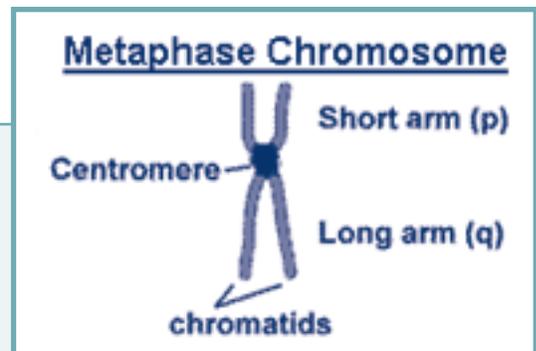
Ku86 is an important protein that helps in the repair of DNA and is required for normal B cell development. Normally, Ku86 occurs inside the nucleus of the cell. However, in myeloma cells, Ku86 is abnormal and is on the cell surface rather than inside the cell nucleus.

Conducting her research at Dana-Farber Cancer Institute, Dr. Yu-Tzu Tai's results show that the abnormal Ku86 is common in patients with multiple myeloma. Results also strongly support the idea that this multiple myeloma Ku86 may contribute to abnormalities in DNA repair.



Yu-Tzu Tai, MD

Currently, Dr. Tai is determining the chromosomal mechanism responsible for production of the abnormal Ku86 protein. A copy of the gene that produces this multiple myeloma form of Ku86 protein will be tested to see if it causes normal B cells to become myeloma cells. This information will not only increase the understanding of multiple myeloma causes, but could provide new targets for future immunotherapy and gene therapy for patients with multiple myeloma.



Chromosomes

Chromosomes are long threads of DNA located within the cell nucleus that are made up of sections known as genes. Genes, which serve as blueprints for proteins in the body, influence all aspects of body structure and function. Human cells are either gametes (sperm and egg cells) or somatic cells. Each somatic cell has 23 pairs or a total of 46 chromosomes.

Examining Chromosomes

New somatic cells are formed through mitosis (division of the nucleus) and cytokinesis (cytoplasmic division). Although some cells in the adult do not replicate and divide, many other cells such as those of the skin divide continuously and rapidly. As cells replicate and divide during mitosis, they go through several phases.

Typically, chromosomes are chemically fixed for examination while they are dividing and in the phase of division known as metaphase. During metaphase, two chromosomes exist and are held together at a structure called the centromere,

which is usually in the same position on a specific dividing chromosome; the lengths of the two arms are constant for each chromosome. Therefore, the fixed chromosomes have a short arm (called p) and a long arm (called q). An increase in the length of the arm is indicated by (+), a deletion in length by (-).

Identifying specific chromosomes

Specific chromosomes can be identified by using dyes that produce reproducible patterns of bands on the chromosomes. Each chromosome displays a unique banding pattern similar to a "bar code," which makes possible identification of an individual chromosome.

MYELOMA FOCUS

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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

Ortho Biotech Empowers Cancer Caregivers

Having a loved one diagnosed with cancer is probably the most difficult challenge any family will face. Increasingly, family members are taking on more responsibility for the care of loved ones. Recognizing this trend, Ortho Biotech has developed a comprehensive education and support program for cancer caregivers called Strength for Caring.

Strength for Caring was modeled closely after a successful caregiver program developed by the University of Pennsylvania School of Nursing. Conducted by a nurse or social worker, the six-hour program presents information using slides, videotapes, group discussions and handout material. Issues such as understanding cancer, talking to physicians, managing pain, fatigue and other

symptoms, caring for yourself, and dealing with relationship changes are addressed. For more information about the program, and for times and locations near you, talk to your physician. You can also find information on the Internet:

www.oncolink.upenn.edu/psychosocial/caregivers/sfc/

FACTS ABOUT FAMILY CAREGIVERS:

36% reported caregiving 40 hours per week.
77% reported a significant increase in stress.
39% reported that their own health had suffered as a result of caregiving.
25% reported having physical limitations of their own.
74% reported significant concerns about their ability to handle the patient's care in the future.

Thalidomide Update

In December, S.Singhal, J.Mehta, P. Eddlemon, et al. reported on 89 patients with advanced multiple myeloma who had received thalidomide, and concluded that this drug had "remarkable anti-tumor activity."

Investigation of thalidomide continues in numerous clinical trials in many types of cancer. Among these is a Phase II trial in patients with indolent and relapsed multiple myeloma, which recently began at the Mayo Clinic. At MD Anderson, approximately 30 patients with multiple myeloma resistant to standard therapies have received thalidomide. According to Dr. Raymond Alexanian, Dir. of Myeloma Studies at that center "approximately one-third of the patients have derived meaningful benefit from thalidomide. ...but the specific role - either alone or in combination, in remission, or as part of initial therapy, needs to be defined more clearly by further study."

Further study of thalidomide is scheduled to begin before the end of the year in the U.S. with a multi-center Phase III trial to test the efficacy and toxicity of thalidomide in patients with multiple myeloma. Additionally scheduled are seven pilot studies to determine appropriate dosing and thalidomide's potential in combination

chemotherapy for multiple myeloma.

Myeloma Focus spoke with Dr. Mehta, previously with the Univ.of Arkansas and now at the South Carolina Cancer Center.

Dr. Mehta, in December you and your colleagues at the Univ. of Arkansas reported on 89 patients, what is the update on that study?

We have now treated more than 170 patients with thalidomide and the response rate continues to be 30 to 40%.

How does thalidomide work?

Thalidomide's mechanism of action is unknown, but inhibition of blood vessel development to the tumor appears to be a possible mechanism. Additionally, the drug alters several immune system components including: tumor necrosis factor, interleukin-2, interleukin-10, adhesion molecules, and lymphocyte subsets.

What is the time to response with thalidomide?

Some patients respond within a few weeks, but average time to response is six weeks. Some patients have taken more than three

(continued on page 7)

You Need To Know

What is Your Blood Count and what does it mean?

If you have cancer, and especially if you are receiving chemotherapy, knowing and understanding your complete blood count (CBC) is important. Your CBC measures red cells, white cells, and platelets.

Red Blood Cells:

The CBC gives three measurements for red cells.

- Hemoglobin (how much hemoglobin is available)
- Hematocrit (what percentage of your blood is red cells)
- Erythrocytes (the number of red cells)

Red cells contain hemoglobin that carries oxygen throughout your body. When red cell measurements are low, anemia can result. Anemia can make you physically and mentally tired.

White Blood Cells:

• Leukocytes (white blood cells) gives the count for all types of white blood cells. This is followed by the count for each type-neutrophils, monocytes, lymphocytes, basophils, and eosinophils. White cells help fight infection and a low count can increase the possibility of infection.

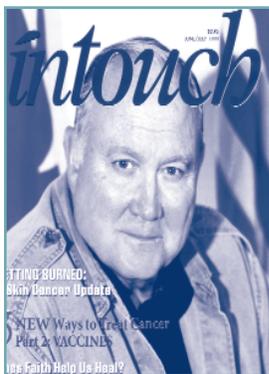
Platelets:

• Platelets help blood clot; a low count can cause excessive bleeding.

Cancer and cancer therapy can cause blood counts to decline, but there is therapy. Remember, when you have a CBC, *ask for your results and keep a CBC diary.*

| CBC w/ Differential | Normal Range † | Results |
|--------------------------------------|--|---------|
| Hemoglobin | Female 12.0 - 16.0 g/dL Male 13.0 - 18.0 g/dL | *11.0 |
| Hematocrit | Female 36.0 - 46.0% Male 37.0 - 49.0% | *31.3 |
| Erythrocytes (red blood cells) | Female 4.1 - 5.10 x 10(12)L Male 4.5 - 5.30 x 10(12)L | * 3.36 |
| Leukocytes (total white blood cells) | 3.5 - 10.5 x 10(9)L | 5.0 |
| Neutrophils | 1.7 - 7.0 x 10(9)L | * 1.69 |
| Monocytes | 0.3 - 0.9 x 10(9)L | * 0.28 |
| Lymphocytes | 0.9 - 2.9 x 10(9)L | 2.90 |
| Basophils | 0 - 0.3 x 10(9)L | 0.00 |
| Eosinophils | 0.05 - 0.50 x 10(9)L | 0.13 |
| Platelet Count | 150 - 450 x 10(9)L | 182 |

*results outside the normal range
†normal ranges may vary



Get In Touch and support Myeloma Research

InTouch, The Good Health Guide to Cancer Prevention and Treatment, is a new magazine providing up-to-date and authoritative information on cancer. Kathy Giusti, President of the MMRF is on the *InTouch* editorial board. Best of all, a portion of your subscription payment will be donated to the MMRF to help fund myeloma research. Just tell them you heard about *InTouch* from the MMRF.

To order a subscription, send an e-mail to intouch@cancernetwork.com, call toll-free 1-877-2INTOUCH (1-877-246-8682), or write *InTouch* at 48 South Service Road, Melville, NY 11747.

Multiple Myeloma to be featured on ITV

Multiple Myeloma will be featured on an upcoming episode of **The Cutting Edge Medical Report**. A segment of the TV special will include discussions with physicians and patients who are coping with this devastating disease, and will also explain the role of the Multiple Myeloma Research Foundation.

The program is produced by Information Television Network (ITV) in association with the MMRF, and is made possible by an educational grant from the Celgene Corporation. Tentative airtime is 9 am, Monday, September 13, on the PAX TV Network, and will also be available on the Internet at www.broadcast.com. For details, or to order a video, call 1-888-380-6500.

Thalidomide Update continued from page 6.

months. Therefore, an adequate trial of at least three months is very important.

What about side effects?

Compared with side effects for most chemotherapy agents, thalidomide side effects are mild. Usually, constipation with thalidomide can be managed with aggressive use of agents such as dulcolax, lactulose, stool softeners, etc. (often in combination). Drowsiness may be overcome by dividing the thalidomide dose. Frequently, we give vitamin B6 (25 to 50 mg) daily to prevent tingling/numbness that may occur.



Escada and Neiman Marcus Join Cancer Fight

\$18,000 Raised for Myeloma Research

Photographer: Diane Reilly



(l-r) Lori Ward, Diana Maguire and Vicki Nolan

Fashion and fundraising worked together to fight multiple myeloma with the success of the Neiman Marcus White Plains fashion show premiering Escada's 1999 Fall/Winter Collection. The event netted over \$18,000 toward accelerating the search for a cure.

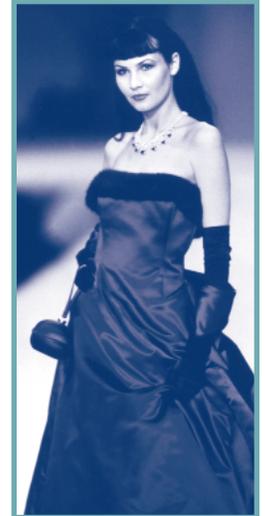
Over 200 friends of the MMRF attended this evening of excitement, featuring a spectacular cocktail reception, dazzling runway models, and cutting-

edge fashion. Guests were treated to the unveiling of Escada's new collection which "defines a new reality of dressing...it's about modernism, what really works, what's really essential, and what's exciting."

The MMRF extends a special thanks to Dru Pyne, Manager Public Relations, Neiman Marcus; Bob Devlin, Vice President, General Manager, Neiman Marcus; Carol Wolf, Fashion Show Chair; Escada, our guests and to all those who participated in this special event.



Photos courtesy of Escada



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