MPD FOUNDATION
UPDATE

A PERIODIC NEWSLETTER FOR
THE MYELOPROLIFERATIVE DISORDERS COMMUNITY

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Stephanie Miltz (far left, back row) with Friends of ET Research tournament volunteers and participants at Branton Woods Golf Club, Hopewell Junction, New York, September 8, 2003.

BETTER TOGETHER

Alliance Between Friends of ET Research and MPD Foundation Will Increase the Number of Research Projects We Can Fund

By Celia Miltz
President, Friends of ET Research

Since we formed Friends of ET Research in 1999, we have hosted three consecutive and very successful annual golf tournaments to raise funds for MPD research. The organization's first grants supported Dr. Josef Prchal's research in locating the effective gene(s) for ET for two years, but by early 2003 it looked as if that research would be much more complicated than originally thought.

I began to speculate how our board could best identify other MPD researchers and place the money in the best possible circumstances.

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HOW ARE WE SPENDING YOUR MONEY?

We Ensure That Donations Go Where They Will Do Us All the Most Good, Because We're Members of the MPD Community Too

In the summer newsletter, we announced three new grants that were funded as a result of our joint solicitation for proposals with the Leukemia & Lymphoma Society. We are co-funding one of the grants and funding one on our own. The LLS is independently funding the other. Here's where the money is going:

A Search for New Targets to Attack …

Dr. Xiao-Feng Yang of Baylor College of Medicine, Houston, Texas, is studying novel antigen targets for immunotherapy in the myeloproliferative diseases. We are co-funding, with LLS, a three-year grant for $130,000 a year to Dr. Yang.

Dr. Yang hypothesizes that malignant MPD cells contain a set of specific protein molecules not found in healthy cells. By eliciting immune responses in those specific cells, he hopes to bring about a remission of the myeloproliferative disorder, without causing the side effects that force so many of us to end treatment with interferon, hydroxyurea or anagrelide.

Dr. Yang and his team have identified three new protein molecules of the type called tumor antigens. He now needs to confirm that they, or others like them, are present in MPDs. If they are, they can serve as targets for future antigen-specific immunotherapy that will be both more effective and less toxic than the medicines available today.

… for Novel Therapies for Myelofibrosis with Myeloid Metaplasia …

Dr. Ruben Mesa, of the Mayo Clinic and Foundation, Rochester, Minnesota, is investigating novel therapies for myelofibrosis with myeloid metaplasia (MMM). We are independently funding a three-year grant to him for $90,000 a year. Dr. Mesa is proposing a three-pronged approach to identify potential new therapies for myelofibrosis.

First, he will screen a spectrum of investigational drugs to identify agents that might be appropriate for future clinical trials.

Second, he will investigate the reason a novel drug with the imposing name of 17-allyamino-17-demethoxygeldanamycin (nicknamed 17-AAG) is effective in killing MMM-derived cells in the laboratory.

Finally, he will use the new techniques of proteomics (a method of studying all of the proteins in a cell at once) to identify proteins that are uniquely increased or decreased in MMM cells compared to normal cells.

Dr. Mesa recently provided this update: "We are currently using the funds from the MPD Foundation to evaluate Arsenic Trioxide, PS-341, Rapamycin, and Seocalcitol (a vitamin D analog.) The anti-angiogenesis pathway is an exciting avenue. These drugs have not yet been very useful in any disease except colon cancer, but time will tell. We are committed to making a difference. We will try our best!" Dr. Mesa's hope is that one or more of these investigations will lead directly to clinical trials of new, targeted therapies for MMM patients.

… and for the Molecular Trigger That Sets off Polycythemia Vera

The LLS is independently funding one of the proposals that we solicited jointly. Although your donations aren't going directly into this, we thought you'd be interested in the study because the LLS had never been interested in this type of research until they joined forces with the MPD Foundation.

Dr. Richard D'Andrea, of the Child Health Research Institute, North Adelaide, Australia, is trying to identify growth factor receptor mutations in polycythemia vera. In PV, blood precursor cells in the bone marrow are hypersensitive to several growth factors or hormones, and this is thought to be the source of the runaway proliferation of red and white blood cells.

Dr. D'Andrea has detected an abnormal sequence change in the DNA of a cell surface receptor associated with one of these growth factors. His team has already screened PV patients for this genetic alteration, and they will use the grant to screen larger numbers of PV patients and normal subjects to evaluate the importance of this altered sequence for the disease. Simultaneously, they will use novel cloning techniques to isolate genes from PV patients that cause normal cells to develop altered growth factor responses.

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NOTES ON THE NEW YORK MPD PATIENT SYMPOSIUM

By Celia Miltz and Robert Rosen

A number of our friends from the MPD community attended the MPD Patient Symposium organized by Dr. Richard Silver in New York City on October 15, 2003. Here are some personal impressions of the symposium from Celia Miltz and Robert Rosen.

CM: Each presentation was interesting and easy to understand with the assistance of accompanying slides, interspersed with good natured humor as well!

CM: Dr. Silver first acknowledged Harriet Gilbert's passing and asked for a moment of silence to honor her memory as well as the victims of 9/11. Then Dr. Silver spoke about CML and Gleevec vs. interferon. He said Gleevec has a much higher result than interferon with few side effects, so it has become the first line treatment for CML. Dr. Silver states that it is not considered to be a cure YET, as there are no long term statistics to prove this.

RR: Dr. Silver told me that he is having excellent success with Gleevec and PV patients. It appears to have a beneficial effect for many patients on blood counts, frequencies of phlebotomies, spleen size and bone marrow. More time is needed to study this drug.

When to Start Treating PV

CM: Dr. Tiziano Barbui of Italy said that it is prudent to begin treatment for ET once platelets go over 600,000. He also advocated the use of daily low-dose aspirin for ET patients, however NO aspirin if your platelets are over 1,500,000 as this can cause bleeding. He also stated that in ET, once thought to be a clonal disorder, about 50% of patients are polyclonal. Interesting.

Therapies for MF

CM: Dr. Ayalew Tefferi of Mayo Rochester presented on MF, but first recognized Dr Gilbert for her contributions to the MPD patient community. Dr. Tefferi stated that over 15 drugs for MF have been studied, but only thalidomide shows promise.

RR: Dr. Tefferi said Thalidomide alone was not tolerated by patients very well, but the addition of prednisone to thalidomide created 100% patient acceptance. Mayo feels that thalidomide and prednisone are their most effective drug combination for MF, although it does not seem to help reduce spleen size, so go figure that one out.

CM: Dr. Tefferi also thanked Robert Rosen of the MPD Foundation as well as my own Friends of ET Research for co-funding Dr. Mesa's work on MF at Mayo.

RR: At Mayo they have discovered an unusual inverse relationship of serotonin to PV and ET patients. Serotonin is higher in these patients. They are exploring the meaning of this. They are also working with a number of new drugs. Zarnestra has been largely ineffective, but good results are happening with Revamid, which will be officially used in its first trial soon.

On the Nature of PV

CM: Dr. Jerry Spivak of Johns Hopkins presented on PV. He believes that PV, MF and ET are all very closely related/intertwined. He recognized the lack of research funding and how little understood these diseases are. He mentioned the formation of the International Consortium (incorporating Drs. Hoffman - Chicago, Spivak - Hopkins, Fruchtman - Weill Cornell, Prchal - Baylor, et al) and the grant application at the NIH/NCI. Many studies are planned for PV, ET and MF if the grant is approved. All the doctors will share each other's tissue samples allowing for larger patient population studies (lack of large numbers of patients has stymied some studies in the past.)

CM: Dr. Spivak doesn't believe the old myths that using phlebotomy only equates to MF plus other complications later on. He believes that there is no natural progression of PV. The best we can do for PV therapy is HCT control. That's the key.

CM: When asked about the UK trial on anagrelide (AG) being halted, Dr. Barbui responded. The trial compared hydroxyurea (HU) and aspirin vs. anagrelide and aspirin. The AG+aspirin patients showed an excess of hemorrhagic events and an increase towards MF. Dr. Barbui spoke to the Chairman of that protocol (Tony Green) who said the results are not definitive. They

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AD SANGUINEM SANUM

A Tribute to Dr. Harriet Gilbert

The Latin means "toward healthy blood," and that was the way Dr. Harriet Gilbert signed her e-mails. It was also the goal she pursued all her life. Dr. Gilbert, one of the pioneers in MPD research and treatment, died October 8, 2003 at age 73.

Many of us remember her from her informative e-mails on MPD Net and her lively talks and delightful conversation at the MPD patient conferences in San Diego, California and Scottsdale, Arizona. Fewer know that Dr. Gilbert conceived and organized the first of all the MPD patient conferences, way back in 1998 when no one thought world-class specialists would ever be willing to discuss scientific matters with an audience of patients.

A quick check of PubMed easily leads you to conclude that Dr. Gilbert was a leading researcher in the field of myeloprolific disorders. The index cites 69 publications. Dr. Gilbert was one of the first doctors to explore the use of interferon for treatment of the myeloprolific disorders; now there are very few hematologist/oncologists who still resist using it.

Dr. Gilbert was also a caring clinician who treated many patients, and provided second opinions for even more, from her book-lined cubbyhole of an office on 72d Street in New York City. She loved to talk to patients and to give them the information they needed to better manage their own care. She was always full of energy, suggestions and opinions, and her enthusiasm could make you feel guilty for taking up so much of her valuable time. But she loved every minute of it and never considered retiring.

Dr. Gilbert saved some of our lives, and her work benefited every one of us. We thank her for her life and send our sympathies to her children, Laura, David and Daniel, and to her grandchildren.

Better Together *(Continued from page 1)*

Our board realized that we didn't have the medical knowledge or expertise to solicit or analyze new research proposals. The question was what to do with the $75,000 our organization raised in 2002.

I met Robert Rosen, President of the MPD Foundation, several years ago and maintained a friendly relationship with him, so we began discussions that eventually led to both our boards approving an informal alliance this past spring. The alliance allows Friends of ET Research to retain its non-profit organization status and work independently, raising funds through the annual golf tournament and mail campaign. However, it provides many benefits to both organizations. Friends of ET Research's funds are now leveraged with the MPD Foundation's funds, allowing for even more research projects to be funded.

The partnership also provides a greater, united voice within the patient community and the research community as Friends of ET Research and the MPD Foundation work in concert.

Finally, it allows for Friends of ET Research to take advantage of the MPD Foundation's highly accredited Medical Advisory Board, who review each research proposal and determine which ones have the highest potential. Since the Medical Advisory Board members are prominent MPD specialists, the alliance was a way to obtain their valuable expertise without placing additional demands on their time. As a result, the entire MPD patient community benefits from the Medical Advisory Board's help, ensuring that all money raised for MPD research by both organizations goes to the most qualified researchers, performing the most promising research in the highest qualified laboratories and facilities.

Your Money *(Continued from page 2)*

The interesting thing here is that a number of researchers – including Dr. Josef Prchal, whose three-year MPD Foundation grant ended earlier this year – are all focusing on the same area: the genetic abnormality or abnormalities that cause our illnesses. It's an elusive target, but when someone finds it, then science will be one giant step closer to developing an effective targeted therapy.

Don't be shy about praying for the success of all our grant recipients.

NYC Symposium *(Continued from page 3)*

must check and validate the results before finalizing the trial's outcome.
Dr. Tefferi stated that he believed this indicates a "red flag" for AG. He actually favors HU as it can decrease thrombosis. AG and INF lower platelets but he questions whether they really decrease thrombosis as well.

RR: There is still much disagreement over the use of hydroxyurea, anagrelide, and interferon. Barbui said that in his study over 10 years, only 2% of HU users converted to leukemia.

CM: Finally when asked if patients should store their stem cells for possible use later in life, Dr. Tefferi said yes, Dr. Bennet said no, Dr. Spivak said this issue needs studies, and Dr. Barbui said it "is an option." Two years ago, Dr. Gilbert said yes, by the way. There you have it.

In the end, we left with our heads spinning about all the differing opinions expressed by these doctors, but impressed with their interest and knowledge in our disorders.

A NOTE OF THANKS FROM DR. RONALD HOFFMAN

Dear Bob,

I just wanted to formally thank you and the MPD Foundation for supplying the MPD Research Consortium with a $25,000 planning grant, which enabled us to submit our program project grant to the NCI on October 1, 2003.

Without these funds this grant would never have been possible. I feel that this submission is an important step in making progress in the treatment of the MPDs. Thank you for your continued trust and support.

Hopefully we will get the grant!

Ron Hoffman

PLANNED GIVING THROUGH YOUR IRA, WILL OR TRUST

Each year The MPD Foundation receives gifts for support of the MPD Foundation programs from individuals who have made annual lifetime gifts and from individuals who have made testamentary gifts upon their death from their IRA, Will or Trust.

These gifts are generally 100 percent deductible for estate tax purposes and, if made by your IRA, may place your IRA account in a lower income bracket.*

The following are examples of how a gift by your IRA, Will or Trust may be worded:*

Specific Dollar Amount from IRA, Will or Trust:

"I give $_____ to the MPD Foundation, of Chicago, Illinois, or its successor by merger or consolidation, for use in such manner as it determines."

Percentage or Entire Residue of IRA, Will or Trust:

"I give (the entire balance) (or ____ percent) of (my IRA) [or the residue of my [(estate) (trust)] to the MPD Foundation, of Chicago, Illinois, or its successor by merger or consolidation, for use in such manner as it determines."

Gifts of Property Other Than Money:

If, during your lifetime or upon your death, you would like to give the MPD Foundation specific items or interests in personal or real property (such as shares of stock, an automobile or residence), please contact Robert Rosen, President of the Foundation, at dayrosen@aol.com. or call 312-683-7247.

The Foundation's Tax ID Number is 36-4330967.

*The MPD Foundation is not licensed to practice law and cannot give legal advice. Please consult your attorney.

PROGRESS REPORT

An Update on the First Research Project Jointly Funded by the MPD Foundation and The Leukemia & Lymphoma Society.

By Dr. Vahid Afshar-Khargan
Baylor College of Medicine, Houston, Texas

I am writing this letter to inform you about our progress in the project entitled as "The role of platelets in thrombo-hemorrhagic complications of myeloproliferative disorders". In this project, I have two main goals:

To understand the role that abnormal platelet functions play in the course of polycythemia vera and essential thrombocythemia.

To determine whether the genetic factors that influence platelet function also affect the frequency of thrombotic (excessive blood clot formation) complications in patients with PV and ET.

One of the key factors in the future success of this project is to be able to study platelet function accurately and precisely in each patient with PV or ET. In the past several months we have optimized platelet function studies in our laboratory and today we are capable of conducting 65 different tests studying platelet functions.

We are trying to determine whether platelets of PV and ET patients are already active without any stimulus, and, if so, whether this phenomenon is more common among patients with a history of thrombosis compared to those without a history of thrombosis. We also want to learn whether platelets of patients with PV and ET are more sensitive to different stimuli than those of the general population, and if so whether this phenomenon is more common among patients with a history of thrombosis compared to those without a history of thrombosis.

In order to determine the genetic factors that affect platelet function and the possibility of their contribution to the frequency of thrombotic complications in PV and ET patients, we are currently able to genotype each DNA sample obtained from patients for eight different polymorphisms (minor genetic variations present in the normal population). We hope that by participating in the MPD consortium we will be able to access about 1800 DNA samples available from European MPD patients.

We are also recruiting patients for our clinical trial. In addition to doing this at Baylor, I was able to establish a collaboration with Dr. Verstovsek at the Leukemia section of MD Anderson Cancer Center (MDACC). Their section sees about 20-30 new MPD patients each year. At MDACC, we also have access to the records of about 400 patients with an MPD. Dr. Verstovek is in the process of contacting these patients and calling them for further follow up visits.

At the national level, I am continuing my collaboration with Dr. Ayalew Tefferi from Mayo clinic in Rochester, Minnesota. At this time our effort is concentrated on obtaining DNA samples from MPD patients that are followed in the Mayo clinic. Platelet studies require access to fresh blood samples, and studying blood samples shipped overnight from Mayo clinic gives spurious results. I plan to expand our ability to perform at least some of the 65 platelet function tests (mainly the tests that are less operator dependent) on site at the Mayo clinic.

I want to thank LLS and the MPD Foundation for supporting my research activities, and I hope that our research effort can improve the medical care and treatment options currently available to MPD patients.

For more information or to make a donation, contact the MPD Foundation at:

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