MPD FOUNDATION®
UPDATE

A PERIODIC NEWSLETTER FOR
THE MYELOPROLIFERATIVE DISORDERS COMMUNITY

VOLUME VIII, NO. 1 FALL, 2009
WWW.MPDFOUNDATION.ORG

PATIENTS AS PLAYERS

by Robert Rosen

As I write this it is August and still high summer here in Chicago. This year we feel a rare seasonal hopefulness. Both our baseball teams are still roughly in contention for their division pennant races, and the angst normally associated with the Cubs swoon has not yet set in. My wife and I took two neighbor boys, young men actually, to see the Cubs last week. We had good seats and ample time to enjoy the slow elegance of the game in our role as spectators.

As MPD patients we sometimes feel like spectators, ineffective in our hopeful waiting for the next scientific victory, observing but not influencing the pace of progress. We may feel this way, but the truth is more encouraging. The difference is this: fans at a baseball game cannot affect the outcome, but you as a patient can make a difference. You can be the game changer, a vector of force that pushes us closer to success.

As patients, we're helping the scientists make progress.

Patients, their friends and families make the MPD Foundation. Without your support, there would be no MPD Foundation. We could not have funded the best scientists in the world to investigate our disease and advance the field of knowledge. You enable the foundation to function, to fund medical research and to support patients in other ways as they wrestle with issues related to an MPD diagnosis.

Since the decoding of the human genome, our knowledge of the biology of MPDs continues forward in leaps and bounds.

(continued on page 7)

MYELOPROLIFERATIVE DISORDERS RESEARCH CONSORTIUM UPDATE

by Prof. Dr. Heike Pahl, Center for Clinical Research, University of Freiburg

From April 1st to 3rd, 2009 the principal investigators of the Myeloproliferative Disorders Research Consortium (MPD-RC) held their annual meeting in New York.

The MPD-RC, which is funded by the National Institutes of Health with $19.6 million over a four year period, brings together clinicians and scientists from the US and Europe. It is chaired by Dr. Ron Hoffman of the Mount Sinai School of Medicine and consists of five basic science research projects and a clinical consortium.

The MPD Foundation provided early seed money for the MPD-RC, which helped cover start-up and operating costs during the lengthy process of pursuing the NIH grant.

The MPD-RC's research projects are dedicated to furthering the understanding of the molecular and genetic processes underlying the development of MPDs, as well as to the development of novel therapies. The clinical consortium currently consists of over 20 centers in the US as well as six centers in Italy and is rapidly expanding in order to manage two new trials to be initiated in the fall of 2009.

At the annual meeting, principal investigators shared their newest results and discussed their implications. Within the MPD-RC, researchers benefit from the close collaboration, which has grown over the six years since inception of the consortium. There is a strong spirit of kinship and camaraderie, and a sense of working toward a common goal.

One of the five basic science projects, chaired by Dr. Prchal from the University of Utah Medical School in Salt Lake City, is collecting families in which MPDs occur in more than one member. Such families are very helpful in searching for genes that contribute to the development of MPDs. Since familial MPDs are rare, the participation of many clinicians within the consortium, who may each take care of only one or two MPD families, is vital to this effort. Only through such a common initiative can the large number of families required for genetic studies be collected.

Dr. Migliaccio from the Mount Sinai School of Medicine in New York reported results from animal studies, in which a new drug, Aplidin (Plitidepsin), which is isolated from marine organisms, was used in a mouse model of myelofibrosis. The results are encouraging and a Phase I trial of Aplidin in myelofibrosis, chaired by Dr. Vannucchi from Florence, has been initiated in Italy.

Important clinical trials coming up

The MPD-RC is currently recruiting patients to three different clinical trials in the US. The trials are open to patients with myelofibrosis and include a bone marrow transplantation trial, a trial of Avastin (Bevacizumab) and a trial of CEP-701, a JAK2 inhibitor. In addition, two large trials are planned to open by the end of 2009. (See related article on page 3.)

One Phase III study will compare Hydrea (hydroxyurea) to Pegasys (pegylated interferon alpha) in ET and PV patients. The second trial will study the use of Pegasys in patients intolerant of or refractory to Hydrea. Both trials will be conducted by the MPD-RC at participating institutions in the US and in Europe and are expected to enroll over 600 patients in total.

The realization of two large clinical trials within the first three years of receiving NIH funding is a major success for the MPD-RC.

Given the substantial amount of progress presented, the meeting concluded on a very positive note, the investigators expressing optimism that despite the uncertain economic environment, renewal of the MPD-RCs NIH grant in 2010 will be successful.

LARGE SCALE PEGASYS TRIALS TO OPEN THIS YEAR

By Ruben A. Mesa, M.D., Professor of Medicine, Mayo Clinic, Scottsdale, Arizona

MPD Research Consortium will launch two international trials to help define best-practice treatment for high-risk PV and ET

Pegasys (pegylated interferon - alpha 2a) has shown promise in early pilot studies. The goal of these large-scale international clinical trials is to help establish a current true standard of care for high risk PV and ET, and to determine the full impact of treatment on MPD symptoms, disease control, and perhaps disease progression.

The current therapy of essential thrombocythemia (ET) and polycythemia vera (PV) consists of decreasing short-term risks of "vascular events" (i.e. blood clots or bleeding) with a long-term eye on potential progression of these diseases to either myelofibrosis or acute leukemia. Treatments to control those short-term risks include low-dose aspirin (for both ET and PV patients) and phlebotomy (mainly for PV). Patients at higher risk of blood clots or bleeding (age over 60, or prior "vascular event") usually also take hydroxyurea (or anagrelide) to lower their hematocrit (or platelet count) to further decrease risk.

Interferon-alpha has been used (primarily in PV) to control counts, and according to non-randomized trials (by Dr. Richard Silver and others) might slow down progression of the disease to MF.

Pegylated interferon alpha - 2a (Pegasys: Roche Pharmaceuticals) lasts longer than regular interferon, and generally needs to be injected only once a week. This is obviously more convenient for patients, and it also seems to lead to fewer side effects.

Two recent and important studies, one by Dr. Jean-Jacques Kiladjian from France and the other by Dr. Srdan Verstovsek from M.D. Anderson, have shown that this form of interferon in PV and ET a) was tolerable, b) helped control counts well c) seemed to decrease risk of blood clots and bleeding and d) decreased the relative amount of the mutant JAK2 burden in patients.

In order to determine whether Pegasys is indeed as beneficial as these initial pilot studies suggest, the MPD Research Consortium is undertaking two parallel studies on the use of Pegasys in patients with high-risk ET and PV.

These trials will be available at 35 medical centers around the world, 12 in the United States and 23 in Europe (representing 11 separate European countries).

Two parallel studies

The first trial is a randomized study between the use of Pegasys versus hydroxyurea therapy in patients with high risk PV and ET. This large study measures the impact of therapy on MPD associated symptoms (i.e. fatigue, itching, night sweats), blood count control (i.e. phlebotomy or platelet count), side effects of treatment, and the JAK2 allele burden.

The second parallel study is also for patients with high risk PV and ET, but who have "failed" hydroxyurea due to either intolerance of the side effects or lack of response. This latter study is for patients who likely have had an MPD for a longer time than patients in the randomized trial.

These trials highlight the role of international cooperation for rapidly and successfully conducting important clinical trials to help patients with MPDs. Results will likely decide which current therapy should be considered the current "gold standard" for comparison to future therapies (such as JAK2 inhibitors).

Further information about these clinical trials (including participating centers and dates of opening) will be available this winter on the MPD Consortium website at **www.mpd-re.org** or the MPD Foundation website at **www.mpdfoundation.org**.

OF MICE AND MPDS

by Ann Mullally, MD

Ann Mullally is a Clinical Fellow in Medicine at Dana-Farber Cancer Institute at Harvard. She joined Dr. Gary Gilliland's laboratory there to work on the JAK2 mutation. When Dr. Gilliland left, she remained at the lab to work with Dr. Ben Ebert, who has replaced Dr. Gilliland as a member of the MPD Foundation's MPD Research Alliance.

The discovery of the JAK2V617F mutation has produced a promising candidate for molecularly targeted therapy in the majority of patients with myeloproliferative diseases. But … it's not that simple.

Researchers have also discovered a mutation in the TET2 gene in some MPD patients; it also occurs in MDS and AML. But we know very little about the function of the TET2 gene or how it interacts with JAK2. In fact, we don't even know how either of these mutations causes MPDs. In short, we're looking for something far more complex than a simple biochemical on/off switch to disable the JAK2 mutation.

A unique analytical tool: the conditional knock-in mouse

For a number of reasons, we can't find what we're looking for by simply testing one potential JAK2 inhibitor after another in clinical trials on humans. It would be unacceptably risky and prohibitively expensive; it would take decades to run through all the possibilities; and it would ultimately delay the introduction of the more effective treatments that MPD patients need now.

What we need is a fast way to test large numbers of compounds in a way that accurately replicates what happens with MPDs in humans. And the exciting news is that at Harvard we have developed an effective analytical tool that does just that: a conditional knock-in mouse model.

That's a strain of mice with the JAK2 gene activated. (A knock-out model has the gene deactivated.) These mice have the JAK2 mutation present in their stem cells, and they express the mutation exactly as it is expressed in MPD patients.

This gives us a superlative way to understand what's happening in the stem cells. We can also study combinations of mutations using other mice, and can recapitulate in mice what happens in patients. We can also create either disease-free or "in remission" mice.

We are also developing TET2 conditional knock-out mice that can be crossed into the JAK2V617F knock-in mice, to better understand the role of TET2 in MPDs in humans, and how it might impact the therapeutic activity of JAK2 inhibitors.

This is the most sophisticated model available today. Some labs, for example, inject human MPD cells into immunocompromised mice. This is a less precise model because of both the human cells and the immunocompromised mice.

What we can learn from our mice

By studying our conditional knock-in mice, we can develop an extremely accurate model of what will happen in MPD patients in various circumstances. We're looking at basic questions such as, "How does the JAK2 burden influence disease development?"

"What is the relationship between JAK2 and TET2?"

"What are the consequences of these mutations in the context of the hematopoietic stem cell, which is the ultimate therapeutic target?"

But we never forget that patients want a cure, not a lesson in genetics. So we're also looking for answers to the questions patients care about most:

"Which cells can self-renew and create the disease?" and "How can we stop them?"

"What are the effects of various therapeutic agents on JAK2? On stem cells? And, most important, on the disease itself?"

There's a long way to go before we discover a cure, but we can proudly say that we're making progress far faster than would have been conceivable even a few years ago.

"FEEL THE NEED. FEED THE CURE."

MPD Foundation launches new program to help supporters become active fundraisers

by Ann Brazeau, VP of Development

With a little help from our friends, we can all do more to help the MPD Foundation make a difference and accelerate the development of a cure for MPDs!

The MPD Foundation is very excited to launch, for the first time, an annual fundraising initiative, "Feel the Need. Feed the Cure." Food will be the central theme. During the entire month of February, we're encouraging supporters to host an event in your home, at a restaurant or wherever you choose, to help the Foundation raise money.

The event can be big or small, plain or fancy. There are endless possibilities. For example:

- Formal dinners (100 and more)/intimate dinners (10-20)/progressive dinners
- Wine and cheese gatherings/wine tastings
- Julia Childs "Recipes for a Cure"
- Ethnic appetizers and drinks
- Tailgate parties/BBQs/picnics/ice cream socials
- French breakfasts/brunches
- Hot air balloon rides with champagne and appetizers
- Your favorite restaurant can participate by offering a percentage of their gross for a day, week or the entire month

How it works

All events will be promoted under the name

MPD Foundation's
"Feel the Need. Feed the Cure."

We'll post event guidelines on our website and send out an event agreement letter for each host's signature. We'll also send out event packets filled with tips to help make your fundraiser a success.

Within our broad guidelines, you choose the kind of event you want to host in terms of type, size, location and budget.

FEEL THE NEED
FEED THE CURE

You'll be responsible for out-of-pocket costs, although you may be entitled to deduct them from your income taxes as charitable expenses. We aren't qualified to give tax advice, so please consult with your own tax advisor.

If you think you'll need help, by all means designate a co-host or hosts.

You can ask your guests to donate a fixed amount or anything above a minimum you suggest. Or just sell tickets or charge an entry fee at the door. Your guests' tax deductible contributions should be in the form of a check made payable to the MPD Foundation. We'll need their names and mailing addresses as well, so we can acknowledge each individual gift with a thank you letter that can also be used for income tax purposes. In order for us to acknowledge gifts promptly, we ask you to send all proceeds to the Foundation within five days after the event.

Start planning your own special February 2010 event now!

The Foundation will highlight the most creative event and the one that raises the most money on our website and in the spring 2010 newsletter. We'll regularly post fundraising goals and outcomes on our website. If you would like assistance in planning your event, or would like to learn more, please contact Ann Brazeau at abrazeau@mpdfoundation.org or Celia Miltz at cmiltz@comcast.net.

With your help, we can find a cure.

EVENT UPDATES

by Ann Brazeau, VP of Development

NYC Patient Symposium coming up November 4

The MPD Foundation and the Cancer Research and Treatment Fund will be co-hosting the 5th MPD Patient Symposium in New York on November 4, 2009. Guest speakers include Drs. Ayalew Tefferi, Richard Silver, Ruben Mesa, Jerry Spivak, Richard Champlin, Tiziano Barbui, Srdan Verstovsek and Robert Rosen, from the Foundation. This day-long event will be held at the New York Athletic Club. Attendees will enjoy a unique opportunity to engage with guest speakers from the most prestigious cancer centers and share their experiences with fellow patients. For more information and to register, call 212-288-6604 or visit **www.crt.org.**

Over 150 Participate in the 4th Annual Al Bolea Memorial Ride

In 2006, Al Bolea passed away from myelofibrosis. Every year since, his friends and family have gathered to celebrate his life and raise money for MPD research by hosting a charity bicycle ride. Al was an avid cyclist. This year the ride, which took place near Boston, included a BBQ and raffle. Over 150 cyclists participated, topping previous years' participation. In addition to making this annual ride a reality, Al's family served and catered the BBQ.

The MPD Foundation greatly appreciates the effort and dedication this group has exhibited over the years. Every contribution brings us closer to finding the answers MPD patients and their families want to know.

A Faster, Greener Way to Receive MPD Related News

Send your email address to: **mwoehrle@mpdfoundation.org** or just fill out the enclosed card to receive regular email updates on research, clinical trials, MPD community events and more.

OUR GLOBAL SEARCH FOR BREAKTHROUGH RESEARCH

by Barbara Van Husen

The MPD research community may be small in numbers, but it's decidedly spread out geographically. And because we're always searching for the most promising investigators to support, the MPD Foundation has become increasingly active beyond the borders of the USA.

In 2005 the Foundation provided funding to help establish the International MPD Consortium, a group of researchers from the United States and Europe that ultimately received $19.6 million in grants from the National Cancer Institute. The Consortium exemplifies one of our key principles at work: It's far more productive for researchers at different institutions to cooperate with each other than to compete.

First European researchers join MPD Research Alliance

In 2008, for the first time, the MPD Foundation invited overseas as well as US researchers to apply for grants and to join our own MPD Research Alliance. Proposals came in from Italy, Austria, France and the United Kingdom, and after extensive review two European researchers joined our previously All-American team: François Delhommeau at Saint-Antoine Hospital in Paris and Robert Kralovics at the Austrian Academy of Sciences. We'll be giving you updates on their research in future newsletters.

The MPD Foundation's connection with patients has also become increasingly global. We now work with patient support groups in Canada, India, Japan and many countries in Europe. The MPD patient brochure has been translated into Spanish and Japanese, with additional languages to come.

We may never all meet each other, but the more we act as members of one global community, the better off we'll all be.

MPD PATIENT SUPPORT GROUPS CONTINUE TO FLOURISH

There are now thirty MPD patient support groups, eight of which are out of the country and two online. The newest additions are in New York City, San Diego, Phoenix and New England.

These groups offer a safe place for MPD patients and their families to share their stories and learn up-to-date information on MPD research, current drug therapies and clinical trials. Participants can hear from experts in the field either in person or through conference calls.

The MPD Foundation posts meeting information and collateral materials on its web site, assists with securing speakers and helps support groups use constant contact e-mails to reach out to patients in specific areas.

If you are interested in attending a support group meeting, please visit our website at **www.mpdfoundation.org** and click on "Patient Resources" for a list of cities and contacts. If you would like to learn more about forming a group, contact Ann Brazeau, VP of Development, at 312-683-7226 or abrazeau@mpdfoundation.org.

MPD FOUNDATION WEB SITE LAUNCHES CLINICAL TRIALS FEATURE

Patients, physicians, researchers and other interested individuals and companies can now get up-to-date, accurate information on current MPD clinical trials on our website. This new feature will highlight leading MPD trials and provide links to learn more about the drugs, enrollment criteria and trial outcomes as they become available. You will find:

- Study name
- Drug being tested
- Company name
- Trial site locations
- Patient recruitment information
- Study timeline
- Contact information

You will also find comprehensive explanations about clinical trials and what you should know before considering participation. Some trials will have additional information including audio and video presentations.

PATIENTS AS PLAYERS

(continued from page 1)

The Foundation is proud to have been instrumental in the early development of JAK2V617F inhibitors. You have helped us fund preclinical testing of many of the JAK2 inhibiting drugs. At last count there were about half a dozen of them in development or in clinical trials. These early breakthroughs by academic scientists have been followed by further exploration on the part of bio/pharma companies, allowing us to invest again in more early stage scientific inquiry.

You have helped us both to fund promising new investigators whose work is already starting to pay off, and to continue funding the work of seasoned investigators who have led the field in the past. We have funded early research into the puzzling TET2 discovery, funded the discovery of the MPL mutation and promoted collaborative research between major investigators. We provided seed money for the International MPD Research Consortium, resulting in a $19.6 million NIH grant.

Your donations enable us to provide assistance to patient support groups, organize symposia, keep our website up to date as an important MPD educational resource and fund these newsletters.

Patients, their families and friends are no longer passive spectators in this game. You are making a difference, promoting progress and bringing us closer to our goals. We thank you for your support and commitment.

Thanks to you, we're nearly $8 million closer to a cure

The goal is almost in sight, and with your continued support we'll get there. Please be generous.

BBB ACCREDITED CHARITY
bbb.org/charity

MPD FOUNDATION

MPD Foundation Update is a periodic newsletter published by the MPD Foundation to provide members of the MPD community with information on current research and the Foundation's activities.

Update Editorial Staff
Woody Woodruff, Editor
Amanda Friedeman, Layout Editor

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

MPD Foundation
233 South Wacker Drive, Suite 375
Chicago, IL 60606
Tel (312) 683-7243 Fax (312) 332-0840
www.mpdfoundation.org