

MPN RESEARCH FOUNDATION

CHANGE YOUR PROGNOSIS

UPDATE

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COMING SOON: THE FIRST-EVER MPN PATIENT REGISTRY

There have been many surveys and studies conducted in the MPN community over the past several years to collect information on patients, ranging from their quality of life to their medications. These are excellent ways to learn more about the impact of living with PV, ET and MF.

Incyte Corporation sponsored the comprehensive REVEAL study in order to learn more about Polycythemia Vera; the Landmark survey assessed disease burden and patient-doctor communication for ET, PV and MF.

THE MISSING LINK: AN MPN PATIENT REGISTRY

There's another option for studying a patient population that can provide insights that could lead to real progress for new treatments: a patient registry. A patient registry, or natural history database, is simply a repository of information that could include age at diagnosis, recent symptoms, history of exposure to chemicals, other illnesses and much more, that is updated over time.

It is meant to be everlasting, in contrast to longitudinal studies which offer a great deal of value (such as Landmark), but often look at a span of time, and do have an end point. A registry is almost its own organism, which can evolve and grow over time as information is collected and new variables are added.

There is no MPN patient registry, and it is a void that we believe we are equipped to fill on behalf of patients internationally. We want to know more about the people living with MPNs, and to let patients drive this process. Are there trends that research hasn't picked up on yet? Are there patterns that could benefit our understanding of the disease and maybe even lead to a cure? Is it possible to keep patients informed in real time about clinical trials they are uniquely qualified for because of their

(CONTINUED ON PAGE 6)



PERIODIC NEWSLETTER FOR THE MYELOPROLIFERATIVE NEOPLASMS COMMUNITY

NEW LOGO. NEW TAGLINE. NEW ENERGY.

You may have noticed a change to our logo and tagline, which went live Tuesday on our web site August 18th. Our new logo is bolder, with a tagline to match.

The updated tagline, "Change your prognosis," articulates the essence of what the MPN Research Foundation is all about. We help you improve your life and prognosis by:

- Funding original research to drive understanding of MPN disease pathways ultimately leading to new, more targeted therapies.
- Making you aware of available therapies and clinical trials.
- Educating you on your disease.

We are excited about this inspirational tagline. As we prepare to embark on our 15th year of grant making we are more focused than ever on doing what it is we do best: driving scientific interest and funding research to develop new treatments and ultimately a cure for Polycythemia Vera, Essential Thrombocythemia and Myelofibrosis.

We need your help to do it. Please be generous.



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MISSION The primary mission of the MPN Research Foundation is to stimulate original research in pursuit of new treatments — and eventually a cure — for myeloproliferative neoplasms (MPNs). In addition, the MPN Research Foundation promotes collaboration in the scientific community to accelerate research, and serves as a powerful patient advocacy group for patients and their families.

www.MPNResearchFoundation.org

MPN RESEARCH FOUNDATION

CHANGE YOUR PROGNOSIS

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PICKING WINNERS IN THE COMPETITION FOR MPN RESEARCH FUNDING

By Robert Rosen

I've always been something of a sports nut, which is easy to be in Chicago where I was born and have spent most of my life. What's so wonderful about our city if you are a sports fan is our 5 major professional sports teams, (7 if you count soccer and women's basketball) and numerous college teams. Every neighborhood has softball and basketball leagues and if you play your cards right you can keep playing in age appropriate leagues for much of your life.

Of course there is a great intersection between sports and medicine. Advances in overall wellness, joint management, cardiac and cardio and so much else have been indispensable to keeping all of us on the move.

It's a stretch to relate our scientific selection process at the MPN Research Foundation to being a Chicago sports fan but I'm going to try anyway. Although I support all our teams I can't help but play favorites. For me it's the Bulls and the White Sox. In the same way I cheer for all good medical science and anything that will advance us closer to new treatments.

But we cheer for some harder than others, and the way we show our favoritism is by funding the science that we think has the best chance of becoming a winner, or leading to a breakthrough that can contribute directly to new therapies. At the foundation we continue to refine this process and seek new ways to focus on those that have the best chance, as it were, of making the playoffs.

A hallmark of our organization is flexibility. We're fast on our feet. When we see new research ideas that need attention we can turn quickly in that direction. Last year we picked four specific focus areas where we solicited grant applications. Our decisions are informed by our scientific advisors and our own sense of where innovative and transformative research is most needed.

This year we solicited proposals in CRISPR (gene editing), immunotherapy, specific JAK2 inhibition, and new mechanisms of action. We received over 30 proposals but only five made it to the finals and were selected for funding. In addition we are providing continuation funding for four grants from the previous cycle. So nine altogether. We root for all relevant medical research but we only fund the ones that feel most like winners.

THE MPN RESEARCH FOUNDATION HAS PROVIDED KEY SUPPORT FOR VIRTUALLY EVERY MAJOR ADVANCE IN MPN RESEARCH SINCE 2000.

– Andrew Schafer, MD, Director of the Richard T. Silver, MD Myeloproliferative Neoplasm Center at Weill Cornell and Chairman, MPN Research Foundation Scientific Advisory Board.

FEATURED PARTNERS CORNER: MPN EDUCATION FOUNDATION

Excerpts from an interview with Antje Hjerpe, Director, MPN Education Foundation:

How did you first get involved with The MPN Education Foundation?

In 1999 I joined MPN-NET, the world-wide, online education and support group founded by Joyce Niblack, who also started the MPN Education Foundation. MPN-NET provides education and support services in the Listerv format and the MPN Education Foundation provides education via its acclaimed doctor/patient conferences held every other February.

Because of my participation in MPN-NET, Joyce Niblack nominated me to be a Director of the MPN Education Foundation in 2009.

What was your first impression of the MPN Education Foundation?

The MPN Education Foundation provided the best MPN education conference and still does to this day.

It also provides an educational website and link for joining MPN-NET so that patients have support available to them every day.

What can you tell us about the history of the MPN Education Foundation?

As your readers may already know, Joyce Niblack, an ET patient diagnosed in 1988, and her husband Robert – both patent lawyers – started what became MPN-NET with the late Dr. Harriet Gilbert because they determined that MPN patients were not able to find up to date, accurate information on MPNs. She started the biennial MPN Education Foundation conference with preeminent physicians from the Mayo Clinic in order to provide access to education regarding the MPNs directly from world class experts.

We have helped thousands of patients when they needed help. I admit, I am proud to be a part of that.

How long have the conferences been going on?

For the past 18 years the Education Foundation with the collaboration of the Mayo Clinic has held 9 MPN patient-doctor conferences.

That's a long time. What has changed since you started working with the MPN Education Foundation?

When I was diagnosed there was virtually no reliable information available on MPNs, research was also limited. All this has changed so much for the better.



ANTJE HJERPE, DIRECTOR, MPN EDUCATION FOUNDATION, WITH HER GRANDSON, TREVOR, WHO JUST CELEBRATED HIS 12TH BIRTHDAY.

What's the best thing to happen since you started working with the MPN Education Foundation?

I think it's how the information can empower the patients to best advocate for themselves, which is further enforced with excellent information given on MPN-NET.

What do you want our readers to know about the MPN Education Foundation?

The MPN Education Foundation is the oldest and one of the few organizations devoted solely to patient education. We are privileged to have world-known MPN specialists to talk directly to patients at our conferences. Also, the Foundation is run solely with unpaid patient volunteers.

The interest in MPNs seems to be growing. Why do you think that is?

It's all about spreading awareness. The more patients know, the more informed they can speak to their doctors about MPNs. More research is conducted in the MPN field which leads to new discoveries and new treatments. And as more drug companies work in the field, they have an understandable interest in raising awareness too.

What would you tell someone who is thinking about volunteering?

Wonderful idea! When can you start?

To contact the MPN Education Foundation or to join the MPN-NET online support group, visit mpninfo.org.

HOW WE CHOOSE RESEARCH FOCUS AREAS

by Barbara Van Husen

Our strategy for funding research is based on one simple premise: that patients can, if thoughtful and united, accelerate and affect the course of scientific research that can ultimately change the course of their disease, for their own benefit and that of the patient population as a whole. We also recognize that the amount of money we as a patient population can raise will never equal the potential investments of governmental and other large organizations. But by being very careful about how and where we direct our funding dollars, we can:

- Fund scientific research of the highest quality and potential for impact on the MPNs.
- Catalyze areas of science not being stimulated by other funding sources, opening the door to new potential treatments.
- Focus on research with the highest potential to have transformative effects on patient care and treatment.
- Leverage our limited funds to get the largest possible benefit for every dollar we invest.

In the early years of the Foundation, when little MPN research was being done, we were happy to receive any requests for funding, regardless of the project. But when the JAK2 mutation was discovered in 2005, we began to take a more targeted approach. We designed a single project to accelerate preclinical testing of JAK inhibitors, and invested over four years to make sure that this discovery delivered results as quickly as possible. When it became clear that both academia and industry were heavily invested in this work we began to look for different funding opportunities.

For several years we funded a broad range of projects, with a focus on bringing new investigators (both beginning and established scientists) to MPN science. Then in 2012, we once again began to focus our attention on a single topic where the need for additional research was acute. We named this initiative the MF Challenge.

The MF Challenge, currently in its third year (and renamed the MPN Challenge since it affects all MPN patients), seeks to stimulate new ideas related to Myelofibrosis and the diseases that lead up to it (PV and ET). We seek new and innovative ideas that are not currently being pursued, and we attempt to build collaborations among scientific constituents who hold the keys to discovery in this area. The vehicle we use to focus our funding is the annual MPN Roundtable.

THE MPN ROUNDTABLE

The purpose of the first MPN Roundtable in 2013 was to encourage collaboration on advancing MPN science, and to identify areas of unmet need for the Foundation and our partners at LLS to pursue in the MPN Challenge. We invited our current grantees, other MPN scientists, and representatives from

each of the companies then currently active in MPN research and/or product development.

We used the meeting to showcase our grantees' projects, and held a wide-ranging discussion of the unmet needs in MPN research. The meeting was lively and interesting, and several new collaborations were started that day. Our 2014 grant program was based on the results of this meeting. Based on the success of the first MPN Roundtable, we now hold the Roundtable as an annual event, which will meet again this year on November 9 and 10.

The importance of bringing together the best scientific minds from both academia and industry to identify and discuss new approaches to our research cannot be overestimated. The more input we get, from multiple sources, the surer we can be that – with your generous help – the research we fund will make a significant difference to the well-being of MPN patients today and in the future.

WE CAN'T DO IT WITHOUT YOU

Like it or not, MPNs are rare diseases, and they don't attract widespread publicity. So it's up to us in the MPN community – patients, family, friends and caregivers – to do everything possible to help develop new treatments and, one day, a cure. And we can do it – if we do it together. Please be generous.

mpnresearchfoundation.org



PATIENTS GET A VOTE IN THIS YEAR'S RESEARCH

It is not very often that patients get a say in how to explore new treatments and a cure for their disease. 120 MPN patients did get that unique opportunity this year. With a gift during Blood Cancer Awareness Month last September, they were able to tell us what research project they felt was the most beneficial from the research projects submitted this year.

While many MPN patients are very well informed about their disease and MPN science, as you can imagine, reviewing cutting-edge research can be very challenging for a non-scientist. To help patients be informed voters, we provided background on some of the transformational science we were investigating this year. Those voting received a short course explaining gene-editing techniques and immunology.

When it came time to make a choice, each patient was provided abstracts and a short explanation for each of six projects. They then had to weigh the potential benefits for all MPN patients. Even after providing those voting with information about the current science and extensive on-line research, many found it tough to choose from the projects.

However, we did have a clear winner. Dr. Brady Stein and Dr. Frank Giles from Northwestern Medicine Development Therapeutics Institute, at the Robert H. Lurie Comprehensive Cancer Center, received almost twice as many votes as the next project. This project will be a small pilot study with 10 patients exploring the possible effectiveness of immunotherapy by using a drug called a PDL-1 inhibitor to determine a patient's response to anti-PDL1 therapy. If this project is successful, the immune system of MF patients will be restored to attack the cancer cell.

Many reported that it was very exciting to see all the new proposed research in MPN science. Those voting also have a better appreciation of how difficult it can be to choose which project most merits funding.



MATT WEISMANTEL VOTED – AND YOU CAN, TOO. JUST MAKE A GIFT TO THE MPN RESEARCH FOUNDATION THIS SEPTEMBER, DURING BLOOD CANCER AWARENESS MONTH. A GIFT GETS YOU A VOTE.

HIKING THE EXTRA MILE FOR A CURE

On August 19, 2014, Julie Libon was diagnosed with Myelofibrosis. She learned that MF is a rare blood cancer that affects approximately 16,500 to 18,000 people in the United States with no cure. (For our work to find a cure, see article on page 4.)

After her diagnosis, she and her family felt compelled to act. They formed HikeMF, an organization that sponsors an annual hike with the sole purpose fund research on Myelofibrosis. The funds raised from the hike support the work of the MPN Research Foundation.

On Saturday, May 30th they had their first annual hike at beautiful Moose Hill Wildlife Sanctuary in Sharon, MA. Over 125 people laced up their boots and joined the fun. After hiking for about 90 minutes on the Bluff Overlook Trail, the hikers had refreshments, a silent auction, and raffles in the main building. They raised over \$25,000. Not bad when their original goal was \$10,000 and they expected about 25 people hiking.

If you're inspired by Julie's actions email Bill Crowley at wcrowley@mpnresearchfoundation.org with your idea, big or small.



COMING SOON: THE FIRST-EVER MPN PATIENT REGISTRY

(CONTINUED FROM PAGE 1)

diagnosis, age or medication history? These are questions we would seek to have answered via a registry.

We have seen the power of what a registry can do for diseases like cystic fibrosis, and we want to put that power to drive research in the hands of MPN patients as well.

Since 2010 we've been contemplating whether and how to proceed, but in 2012 the National Organizations of Rare Disorders (NORD) launched their own secure, patient-centered platform, which is available for use by their member organizations.

We've been in talks with them since their launch and have recently decided to put our stake in the sand. We are excited to announce that we're moving forward with an MPN patient registry, which we hope to launch in 2016.

NORD has launched four registries, with two in implementation as of this publication. They have worked closely with the NIH to conform with their common data elements, and their registries are equipped to share data with the Patient Centered Outcomes Research Institute (PCORI) which seeks to close the information gap in order to provide evidence around outcomes for patients across disease states.

Like us, NORD takes patient privacy and choice extremely seriously and there will be multiple controls in place so that patients involved can control their experience while still contributing to the research.

There will be a section in the registry for people to learn about clinical trials that they'd be suitable for as well as a calendar of community events. And we'd like to allow patients to ask questions of the dataset and report back in a way that is respectful of privacy. The driver behind this registry will be the patients who contribute to it.

We're currently putting together a steering committee that includes other leaders in the MPN community such as Ruben Mesa, who will be the Committee Chair. We will include the perspectives from industry as well, since the hope is that this registry will also help them develop more and better treatments for MPNs.

There is much to be decided about the questions that we'll ask, the process for allowing researchers to query the registry, how best to recruit patients to participate (and keep them updating their information) and how to engage the whole universe of constituents in making this something that everyone in the community can embrace and be proud of.

We very much welcome questions and comments about this plan. Please direct them to mwoehrle@mpnresearchfoundation.org or **312-683-7243**.

A WASHINGTON PARTY FOR POLYCYTHEMIA VERA RESEARCH

The Mason family – JoAnn, John and their daughter, Jaclyn; longtime supporters of the MPN Research Foundation – hosted a party at their Washington, DC home to thank their many friends who have supported Polycythemia Vera research.

JoAnn, a member of the MPN Board of Directors, thanked the guests and spoke about the journey their family has made over the past years since Jaclyn received a diagnosis of an MPN. She expressed her appreciation to the MPN Research Foundation for the support and important information they have provided that has helped them understand Jaclyn's disease.



THE MASON FAMILY

The Mason's felt it was important to do their part by supporting the MPN Research Foundation's efforts to raise awareness and advocate for new treatment options. With the help of their many friends, they have raised substantial funds for Polycythemia Vera research.

While demonstrating the skills of a wonderful host and hostess, John and JoAnn used the occasion to offer each of their friends a very personal thank you. "There are so many exciting things happening, and hopes are running high for better diagnosis, new therapies, and an eventual cure." By the end of the evening, everyone present felt more knowledgeable and confident that their donations were being used effectively to support this important cause.

FROM THE MINDS OF CLINICIAN SCIENTISTS: INVESTIGATOR-INITIATED TRIALS

By John Crispino, PhD, Scientific Advisor

We often think about the ideas for clinical trials emerging from the halls of pharmaceutical companies. Indeed, some of the available trials are company sponsored, that is, ones in which the trial design, execution and analysis are conducted by a pharmaceutical company.

Trials that are conceived, executed and analyzed by academic physicians fall into a different category: investigator initiated studies (IIS). There are a large number of IISs aimed at developing novel therapies or novel combinations of drugs for the MPNs.

Examples of multi-center IISs are those being led by physicians within the Myeloproliferative Disease Research Consortium (MPD-RC), including Dr. John Mascarenhas, Dr. Raajit Rampal, Dr. Adam Mead and Dr. Vikas Gupta. These exciting and innovative trials include::

1) Exploring the Potential of Dual Kinase JAK 1/2 Inhibitor Ruxolitinib (INC424) with Reduced Intensity Allogeneic Hematopoietic Cell Transplantation in Patients with Myelofibrosis.

This is a Phase II trial of ruxolitinib for two months prior to reduced intensity conditioning hematopoietic stem cell transplant with fludarabine and busulfan in intermediate and high-risk patients with MF. The hypothesis is that reduction of splenomegaly, improvement in performance status and reduction in inflammatory cytokine signaling through JAK1/2 inhibition will improve engraftment, reduce transplant related mortality and potentially reduce GVHD in this setting.

2) Multicenter phase I/II trial of ruxolitinib in combination with decitabine in patients with accelerated phase myeloproliferative neoplasms (MPN) or post-MPN AML.

This Phase I/II trial of combination therapy with continuous oral ruxolitinib and five days of decitabine cycled every 28 days is designed for patients with advanced phase MPN. The rationale is based on preclinical studies from Ross Levine and Raajit Rampal as well as clinical experience of decitabine monotherapy.

3) Open label study of single agent MDM2 inhibitor RG7388 in patients with polycythemia vera and essential thrombocythemia, with pilot feasibility study in combination with Pegylated Interferon Alfa 2a.

The trial is based on observations by Dr. Ron Hoffman's laboratory, which show that MDM2 – a protein that inhibits the activation of the P53 tumor suppressor – is over expressed in PV CD34+ cells that have wild-type P53. This drug interrupts the P53-MDM2 interaction and thus relieves the negative regulation of MDM2 on P53, which in turn leads to the activation of the P53 pathway and selective killing of MPN HSC.

4) Single Arm Salvage Therapy with Pegylated Interferon Alfa-2a for Patients with High Risk PV or High Risk ET who are Either Hydroxyurea Resistant or Intolerant or have had Abdominal Vein Thrombosis.

This large phase II trial is enrolling high-risk ET/PV patients who are intolerant to HU or refractory to HU. The goal of this study is to establish Pegasys as a second line therapy in terms of efficacy and tolerability.

5) Randomized Trial of Pegylated (peg) Interferon-2a versus Hydroxyurea Therapy in Treatment of High Risk PV and High Risk ET.

This is a Phase III randomized trial of newly diagnosed treatment naïve patients with high risk ET/PV randomized to either HU or Pegasys. The trial will characterize safety and molecular response rate of IFN therapy and is expected to clarify which drug should be the standard of care for upfront treatment.

In closing, investigator-initiated trials provide an important counterbalance to industry-driven trials. We will continue to bring you updates on these efforts.

WE'RE NOT ALONE. AND TOGETHER WE CAN CHANGE OUR PROGNOSIS.

Please be generous. And don't be shy about asking your friends to help out, too.

MPN RESEARCH FOUNDATION UPDATE

A periodic newsletter published by the MPN Research Foundation to provide members of the MPN community with information on current research and the Foundation's activities.

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WITH **your help**, SINCE 2000 MPNRF HAS

INVESTED

10.5 Million Dollars

FUNDED OVER

55 Research Projects

SUPPORTED

53 Researchers

ENGAGED

31 Institutions

**BUT WE STILL HAVE A LONG WAY TO GO ... AND
WITH YOUR HELP, we will.**