

MPN RESEARCH FOUNDATION

CHANGE YOUR PROGNOSIS UPDATE

VOLUME XVII, NO. 1 SPRING 2018

PERIODIC NEWSLETTER FOR THE MYELOPROLIFERATIVE NEOPLASMS COMMUNITY



IN LOVING MEMORY
OF ROBERT ROSEN
1943-2018

REMEMBERING BOB ROSEN

Barbara Van Husen, President



Bob Rosen and
Barbara Van Husen

By the time you read this newsletter, most of you in the MPN community will know that our founder Bob Rosen passed away on January 3, due to complications related to a stem cell transplant. You will have read tributes to his dedication and sense of purpose in founding the MPN Research Foundation, and praise for the progress that has been made in MPN science since MPNRF was founded in 1999.

You may also remember that each newsletter opened with his essay on current issues in MPN science, impatience at the slowness of treatment development, and occasional reflection about the relationship between science and baseball. For this issue, I am going to take his place and try to express what his loss means to me and to us all.

For those of us in or close to the MPNRF office, Bob's influence was profound and strongly felt. He was dedicated. Relentless. Funny and smart. A voracious reader, and an ardent student of history. Stubborn. Sometimes irritating. He wore funny hats. He interrupted meetings with seemingly offhand remarks that ultimately directed us to either increased vigor or alternative approaches.

For me, he was the perfect business partner. His streaks of vision matched my more deliberative sense of process. He would say 'Why not?'. I would say 'But how?'.

We would often agree to 'marinate' on an idea before taking a step, leading to many jokes about cooking and its relationship to scientific progress. He talked endlessly about his family, and I about mine. We discussed the state of the world and proposed alternatives to save it. The void that his absence will make in my own life is beyond measure.

But the bottom line is this. Bob was diagnosed with PV 20 years before he progressed to MF and immediately to AML. He used those years to make a difference for us all. Without his persistence (and relentlessness, stubbornness, etc.), MPN patients would have fewer options and less hope. The organization he built is strong and full of determination to fulfill his mission. And for each of you who have a connection to these horrible diseases, his example is like a beacon.

DO SOMETHING.
BE INFORMED.
CHANGE YOUR PROGNOSIS.
BE LIKE BOB.

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.

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CHANGE YOUR PROGNOSIS

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WE ALL HAVE A ROLE – AND WE CAN'T WAIT

Michelle Woehrle, Executive Director



Last year we shared our intent to launch a project aimed at helping to predict who will transform to MF. Since then, we have been working on a plan that would allow for better understanding of the genetic, cytogenetic and symptom changes leading up to progression to MF, in hopes of stopping or preventing it. This is the number one concern of most patients: how to stop or prevent progression. It has been an obsession of the Foundation's for years. From launching

the MF Challenge in 2012, through today, as we've seen our nearest and dearest succumb to MPN without any means to stop it.

Our hope is to start enrolling patients at the end of 2018 or early 2019. Anyone 18 or older with PV or ET will be able to participate in order to create a powerful biobank and database that researchers could tap to determine what is driving progression to the deadly myelofibrosis.

As with our patient registry myMPN, patient privacy and access to data will be safeguarded by a steering committee, including MPNRF, ensuring that access to data and samples will be granted to those who seek to help patients. We are very excited to be working with some outstanding MPN thought leaders on this project, including Drs. Srdan Verstovsek, John Crispino and Raajit Rampal. They, in addition to our consultants Rick Winneker and Helena Ellis, are helping us launch this ambitious project.

"THE ANSWERS TO WHO IS
PROGRESSING AND WHY LIVES
IN EACH OF YOU; IT IS WRITTEN
IN YOUR BLOOD AND GENES,
SUGGESTED IN YOUR SYMPTOMS."

We cannot afford to wait on this. As Dr. Crispino says in his article remembering Bob Rosen, featured on Page 9, "We need to do better."

We all have a role to play – MPNRF as patient advocates, researchers working hard around the world and even patients, who might consider participating once this project is up and running. The answers to who is progressing and why lives in each of you; it is written in your blood and genes, suggested in your symptoms. Our role, to bring all the pieces together, is an overdue but necessary step in getting us the answers we need so that patients can live longer and better despite their diagnosis with MPN. Stay tuned and consider participating when enrollment is open. ■

myMPN PARTICIPATION NUMBERS SURGE KEEP UP THE GREAT WORK!

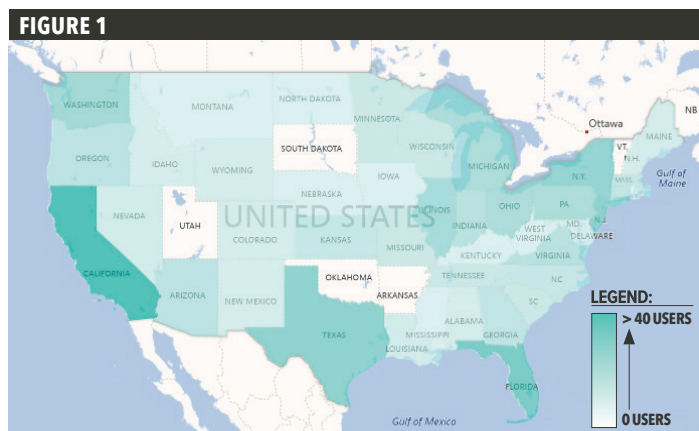


Lindsey J. Whyte, Longitudinal Research Project Manager

If you're not already participating in myMPN, what's holding you back? Since our launch in September 2017, we now have well over 400 users in the US alone! From myMPN registry steering committee member Ruben Mesa, to our contacts at the FDA, everyone is excited at the prospect of our growing repository of real world data from MPN patients. As I've reported in the past, the utility of the data collected in myMPN about symptom burden, current and past treatments and timing and severity of health events makes this a vital tool going forward as we make decisions about where to focus funds for MPN research. The experience and unmet needs of patients are coming through, loud and clear!

Our registry launched in September 2017 and participation has steadily grown with increasing use of the quality-of-life survey ("How do you feel, today"? or HDYFT) and heavy reporting of health events. Over 100 participants have completed a HDYFT at least twice, and our most active user has completed an average of 1 HDYFT per week for a total of 19 surveys! Way to go!

Figure 1 below shows states where myMPN users are located. As you can see, California has the highest participation over 40 users, while Florida ranks second with nearly 35, and Texas and New York are both approaching 30 users. In the coming months, we hope to grow our participation rates nationwide and expand use of the registry in other native English-speaking countries.



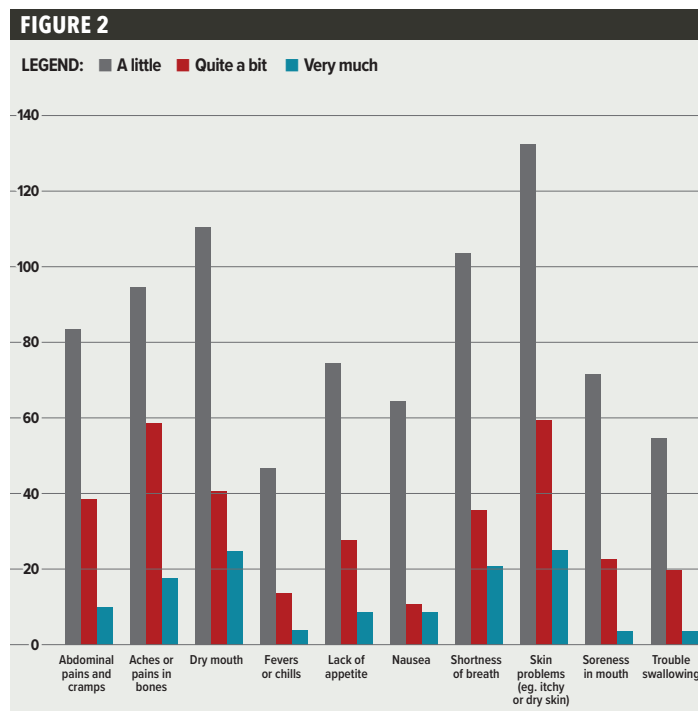
WHAT ARE WE LEARNING FROM THE PARTICIPANT DATA?

The purpose of the initial data screens is two-fold: First, we want to be sure that the data being reported is representative of what previous MPN studies have indicated. This is an important way to ensure that our data is reliable and validated by MPN's research

and pharmaceutical communities. For example, the distribution of myMPN participants by initial diagnosis is 45.1% Essential Thrombocythemia, 39.9% Polycythemia Vera and 12.6% Myelofibrosis which is consistent with past epidemiological studies. When we look at treatments currently being used by patients, baby aspirin ranks highest with approximately 76% of myMPN participants, followed by hydroxyurea (42.1%), JAK inhibitor (17.6%) and interferon (6.0%). Almost 10% of participants report using no therapies at the present time. Again, these data are consistent with what is known about the MPN population.

The second purpose of our initial screens of the data is to establish a baseline from which we can increase participation of the registry tool. We know that some patients are comfortable with, and even embrace, the notion that sharing their personal experience with their disease can help move research in MPNs going forward. Others have a difficult time seeing the connection. We hope to build a compelling case for the registry that will encourage more participation, including among people who are skeptical or hesitant.

Some patients have accessibility challenges, either because they do not have a computer where they can enter their responses to the surveys, or perhaps they have language barriers that preclude them from participating. We hope that the participation in the registry



(CONTINUED ON PAGE 8)

A PATIENT'S STORY



Jon Mathias



It may seem strange that someone who has an incurable blood cancer thinks of himself as a lucky man. But it's true – given that I got Essential Thrombocythaemia for some reason, the journey I've been on since has taken many fortunate turns.

My first bit of luck was that when a blood clot caused me to have a stroke back in 1998, it was a relatively minor event and I

recovered from the stroke quickly. The next break was getting referred to Professor Tom Pearson at St Thomas' hospital in London. Prof. Pearson was probably the leading MPN specialist in the UK at the time and I only ended up seeing him because he was friends with the cardiologist I had seen. It's also very fortunate that I tolerated the side effects of interferon quite well and that the drug has been very effective in keeping my blood relatively normal since my diagnosis.

My story is so different from tens of thousands of people who get MPNs every year. Many may not even be diagnosed until a large blood clot causes a major stroke or heart attack. Others will be diagnosed but may never gain access to accurate information and specialist medical expertise, or have access to effective treatment.

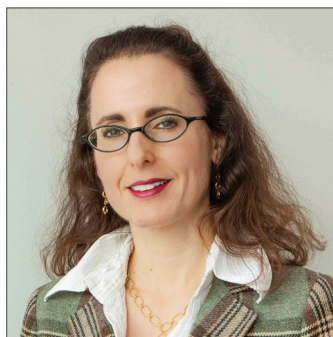
It is the knowledge that I have been so lucky that motivates me to improve outcomes for the huge majority of MPN patients. When my (amazing) doctor Claire Harrison asked if I was interested in creating the patient support group that eventually became MPN Voice, it was great to be able to get involved in practical things like printing information sheets, building a website and organizing patient meetings so that MPN patients can meet each other and share their own stories. Simple stuff, but we soon found out from the patients we met just how valuable the work was.

Having seen the positive effect our group in the UK has had, I am now focused on helping MPN communities form and grow in other countries around the world. We are trying to build an international network of MPN patient organizations so that we can share best practices and work together to be a collective voice for MPN patients everywhere.

Our goal is to get to the point that wherever in the world a person is diagnosed with an MPN, they will have access to the best possible support, expertise and treatment, in the same way that I have been so lucky to have had. ■

NEW STUDY: T CELL IMMUNOTHERAPY TARGETS

Vivian Oehler, Marie Bleakley, Melinda Biernacki



Vivian Oehler



Marie Bleakley

This collaborative project with Vivian Oehler, Marie Bleakley and Melinda Biernacki is one of the first studies to focus on the discovery of targets for T cell immunotherapy in patients with myeloproliferative neoplasms (MPNs).

We will first determine which neoantigens (tumor-specific peptides that are unique to JAK2, CALR, and MPL mutation expressing cells) can be found on MPN cells and MPN stem cells. We will then see if MPN-specific T cells from patients or healthy individuals can mount an immune response against these cells. Our results will inform the development of immune strategies to treat MPN patients, such as adoptive T cell therapy or vaccination, or combination strategies with immune checkpoint inhibitors.

At Fred Hutch, University of Washington, and Seattle Cancer Care Alliance we see many patients with high-risk MPNs. Although current treatment strategies are excellent at alleviating symptoms, these therapies, short of allogeneic transplantation, are rarely curative. Our ultimate goal is to provide a wholly new treatment strategy for MPN patients that could be highly MPN-specific and potentially curative. ■



Melinda Biernacki

"OUR ULTIMATE GOAL IS TO PROVIDE A WHOLLY NEW TREATMENT STRATEGY FOR MPN PATIENTS THAT COULD BE HIGHLY MPN-SPECIFIC AND POTENTIALLY CURATIVE."

CELEBRATING OUR RESEARCH PROGRESS

Rick Winneker, PhD, MPNRF Consultant

Three years ago, the MPN Research Foundation, with support from The Leukemia & Lymphoma Society, announced **The 2015 MPN Challenge**. The goal was to stimulate new avenues of research to strengthen the overall understanding of the cause(s) and potential treatments for all MPNs, with a particular emphasis on using new transformative technologies currently being investigated for other cancers. Given that emphasis, it was not a surprise that after a review of the 35 grant applications received for this program, 3 of the 4 funded grants were focused on the cutting-edge science of gene editing technologies.

RESEARCH GOALS AND PROGRESS

George M. Church, PhD, Harvard Medical School

The goal of this project was to develop a series of cell lines containing common MPN driver mutations using induced pluripotent stem cells derived from Personal Genome Project volunteers. If successful, these cell lines would be a valuable resource for the MPN research community, as they are well characterized and fully consented to be distributed publicly. The Church lab was successful in developing one of these cell lines containing the JAK2V617F mutation, but the successful development of CALR mutation containing cell lines remains problematic. They are also continuing to work on gene editing technology enhancements to correct these mutations in stem cells both in vitro and in vivo.

Linzhao Cheng, PhD, Zhaohui Ye, PhD, Alison Moliterno, MD and Jerry Spivak, MD, Johns Hopkins School of Medicine

The goal of this project was to use gene editing technologies to develop new cellular genetic models of JAK2 and CALR mutations using isogenic human induced pluripotent stem cells and study the differential gene regulation induced by these two very prevalent mutations found in the MPNs. A second goal was to establish a CRISPR-mediated approach to target and eliminate the malignant MPN clones that contain JAK2-V617F. The team had some success developing new cells lines containing

JAK2, CALR and MPL mutations and has started the characterization of these cells. Their results using gene editing technologies to target a point mutation such as the JAK2-V617F MPN mutation in blood stem cells have been met with low efficiency as observed also by others. This remains a significant challenge for the whole hematology field.

Wen-Shu Wu, PhD and Zhijian Qian, PhD, The University of Illinois, Chicago

The goal of this project was to use gene editing technologies to correct the JAK2V617F mutation in MPN hematopoietic stem cell model systems. Ultimately, the development of safe and effective strategies to correct these MPN driver mutations in a patient's stem cell population could lead to cures. The research team used a variety of gene editing approaches and modifications but ultimately two obstacles remained that have slowed progress in this cutting-edge field of science. The gene correction efficiency for the JAK2V617F point mutation is not high (~5-10%) and the CRISPR/Cas9 gene-corrected cells have a disadvantage in proliferation and gradually lose the ability to grow.

Camelia Iancu-Rubin, PhD, Nina Bhardwaj, MD, PhD, Icahn School of Medicine at Mount Sinai

The goal of this project was to define the immunogenicity of the mutant-Calreticulin (mt-CALR) peptide expressed by patient-derived MPN hematopoietic cells. The hypothesis is that mt-CALR may produce a novel tumor antigen that can trigger an adaptive immune response which would support the rationale to develop mutation-specific vaccines or other immune based therapeutic approaches. The results have shown that the mt-CALR epitope is a novel MPN-specific tumor antigen that elicits immune responses in vitro; however, the T cell reactivity in MPN patients is less robust than in healthy donors partially due to immune suppressive mechanisms such as increased expression of checkpoint blockade inhibitors. These findings also provide a strong rationale for testing checkpoint blockade inhibitors in combination with the mt-CALR vaccine for the treatment of MPN patients with CALR mutations. ■

MPN Challenge Grant Recipients (L-R): Zijan Qian | Wenshu Wu | Stephen Oh | Angela Fleischman | Marie Bleakley | Robyn Scherber Vivian Oehler | Camelia Iancu-Rubin | Linzhao Cheng



REPORT: 2017 ASH MEETING

Dr. John Crispino, Scientific Advisor



Although there were no major MPN-focused breakthroughs, this year's American Society of Hematology (ASH) Annual Meeting didn't disappoint. We heard several reports of investigational agents and learned new biological insights into the pathogenesis of the MPNs.

JAK inhibitors: The biggest news is that Fedratinib, a JAK inhibitor

that had shown promising Phase 3 results but was put on hold by the FDA for possible association with Wernicke's Encephalopathy, is back in the mix. Studies by Dr. Harrison and colleagues suggest that the Encephalopathy is unrelated to the drug. Along with this presentation, Fedratinib was in the news for its acquisition from Impact Biosciences by Celgene. This is a promising development which suggests that this JAK inhibitor will be evaluated by the FDA very soon and may become an approved therapy for myelofibrosis.

Interferon: An exciting presentation by Dr. Hans Gesslinger updated us on the clinical development of the new form of interferon known as Ropeginterferon alfa-2b. This formulation requires less frequent dosing than Pegasys and is under consideration by the European Medicines Agency. Dr. Gesslinger presented two-year data on safety and efficacy in PV. Ropeginterferon was found to have significantly better complete hematologic response (CHR) and better CHR with improvement in disease burden. The superiority over hydroxyurea (HU) became evident at the 18-month assessment.

With respect to safety, Ropeginterferon alfa-2b had a similar profile to HU. These promising data increase the likelihood that this agent will be made available to patients. In addition to Ropeginterferon alfa-2b, a presentation by Dr. John Mascarenhas outlined the MPN Research Consortium Global Phase 2 study of Pegasys in high risk PV/ET patients who were intolerant or resistant to HU. The overall response rate at one year was 69% and 60% for PV and ET patients respectively. They also reported that the tolerability was limited due to adverse events. Nevertheless, the outcomes are notable with respect to the advanced nature of the disease in this patient population. This study provides evidence for the efficacy of interferon therapy second line to hydroxyurea and durable hematologic

responses were seen in a subset of patients that can tolerate the medication.

Novel agents: Among the clinical studies of novel therapeutic agents, three stood out.

The first was a phase 1 study of RG7388 (Idasanutlin) in PV and ET patients presented on behalf of the MPN-RC by Dr. Mascarenhas. This drug was well tolerated and led to an overall response rate of 78%, with more than half the patients achieving >50% reduction in total symptom score. From the 12 patients treated with this agent, bone marrow responses and molecular responses were noted in several. Furthermore, the correlative studies suggested that the drug has the predicted on-target effect on p53 activation. These

encouraging results suggest that targeting the p53 pathway will provide benefit to patients. A multicenter phase 2 trial is now underway, evaluating this oral agent in high risk PV patients that are intolerant or resistant to hydroxyurea.

A second notable study, presented by Dr. Nassema Gangat of the Mayo Clinic, provided data from an ongoing phase I study of the aurora kinase inhibitor Alisertib in PMF. She reported that Alisertib was overall well tolerated and led to >50% reduction in total symptom score in more than half of the patients. The study

group also observed a marked improvement in megakaryocyte morphology in the bone marrow of the patients, which is consistent with the pre-clinical data showing that this compound targets these atypical cells in PMF.

Finally, Dr. Prithviraj Bose from MD Anderson presented data from a study of Sotatercept alone or in combination with ruxolitinib in patients with MPN associated myelofibrosis and anemia. Sotatercept acts to improve anemia through sequestration of TGF- β ligands which can suppress red blood cell production. Of note, 35% of the patients displayed a hemoglobin response. Given the current challenges in improving anemia in this disease, this response rate is promising.

Basic Biology: One of the more interesting basic science studies was presented by Dr. Shannon Elf from Dr. Ann Mullally's laboratory. She provided important new insights into the way that mutant calreticulin protein, common in ET and PMF, activates JAK/STAT

"BASED ON WHAT WE HEARD AT ASH, THIS COMING YEAR MAY SEE THE APPROVAL OF NEW AGENTS TO TREAT THE MPNS."

(CONTINUED ON PAGE 7)

POTENTIALS OF THERAPEUTIC CANCER VACCINATION IN MPNS



Morten Orebo Holmström, MD, PhD, Post doc position at Department of Hematology, Zealand University Hospital and Center for Cancer Immune Therapy, Herlev Hospital, Denmark



In vivo vaccination experiments with CALR mutant epitopes are currently running at Center for Cancer Immune Therapy, Department of Hematology, Herlev Hospital, Denmark.

At Department of Hematology, Zealand University Hospital and Center for Cancer Immune Therapy, Herlev Hospital (both in Denmark), we are working on the potentials and perspectives of cancer immune therapy in MPN. In recent years we have published in *Leukemia* that both cells carrying the *JAK2V617F* mutation and cells carrying the *CALR* exon 9 mutations are recognized by specific T cells.

Moreover, we have demonstrated that these T cells are able to kill the mutant cells. These findings have opened an avenue for clinical vaccination trials in patients with both *CALR*-mutant and *JAK2*-mutant MPN. We are currently running proof-of-concept vaccination studies in mice at our institution (pictured) and in collaboration with the Koschmieder group, University of Aachen, Germany. Concurrently, we just published in *Onc Immunology* that patients with *JAK2*-, *CALR*- and *MPL*-mutant MPN harbor frequent and strong immune responses against the cornerstone immune-regulatory protein programmed death ligand-1 (PD-L1). This finding has spurred us to investigate if co-vaccination with PD-L1 derived epitope may enhance the *JAK2/CALR*-mutant specific immune responses. In the lab, we are currently working on the identification of other immune-regulatory mechanisms that may be targeted by therapeutic cancer vaccination in patients with MPN. ■

REPORT: 2017 ASH MEETING

(FROM PAGE 6)

signaling. Through a number of basic biochemical experiments, she mapped out the specific parts of the protein that promote signaling and the expanded growth of blood cells. These new insights shed light on possible new strategies to inhibit mutant *CALR* activity.

Another notable talk was given by Dr. Sara Meyer from Dr. Ross Levine's laboratory. She has been investigating the contributions of an intracellular signaling pathway, named MAPK, to abnormal cell growth in the MPNs, especially in the setting of JAK kinase inhibition. Her pre-clinical studies revealed that combining JAK and MAPK pathway inhibitors gave rise to superior activity in MPN animal models than treatment with either single agent. A clinical trial combining ruxolitinib with a MAPK pathway inhibitor is planned.

Dr. Margaret Nieborowaka-Skorska, with Dr. Thomas Skorski and colleagues, presented a study on the use of Olaparib, an inhibitor of PARP (a protein involved in DNA damage repair) in the MPNs. She demonstrated that deficiencies in DNA damage repair caused by ruxolitinib treatment sensitizes tumor cells to the drug, providing rationale for combining these agents in the MPNs.

CONCLUSIONS

Based on what we heard at ASH, this coming year may see the approval of new agents to treat the MPNs. Furthermore, successful pre-clinical studies may move into the clinic.

Stay tuned to the Foundation's website for important announcements of approvals and new trials. The next updates will come from the European School of Hematology's 8th Annual Conference on the MPNs in May, and the American Society of Clinical Oncology in June. ■

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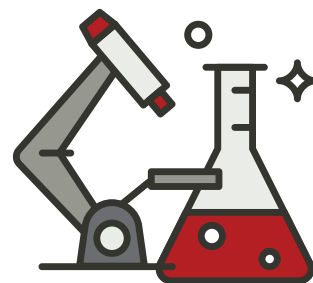


MPN Research Foundation



@MPN_RF

INTRODUCING: MPN INTERFERON INITIATIVE



Rick Winneker, PhD, MPNRF Consultant

We're pleased to announce the launch of the MPN Interferon (IFN) Initiative at the American Society for Hematology (ASH) meeting in Atlanta last December. Given that IFN can achieve molecular remissions in some MPN patients, the MPNRF and its advisors felt the time was right to double down on research efforts to better understand why some patients respond and others do not. The Initiative will also focus on defining the molecular mechanism of action of IFN in this disease, to identify other rationale drug targets that might lead to improved therapies that work in a similar manner.

The IFN Initiative is a multi-institutional and multi-year project currently centered around four research projects, along with support from MPNRF staff and a group of experienced IFN and MPN research advisors. The goal of this collective team is to track progress, develop opportunities for collaboration and exchange expert advice on a regular basis, including annual meetings of the group at ASH. The external advisors for this Initiative include Andrew Schafer, MD (Weill Cornell), John Crispino, PhD (Northwestern), Robert Cohen, MD (Calico) Ron Hoffman, MD (Mt. Sinai), Richard Silver, MD (Weill Cornell), Jean-Jacques Kiladjian, MD (INSERM), Radek Skoda, PhD (U. Basel), William Vainchenker, MD, PhD (Gustave Roussy), Hans Hasselbalch (U. Copenhagen) and Josef Prchal, MD (U. Utah).

THE 4 PROJECTS AND PRINCIPAL INVESTIGATORS ARE AS FOLLOWS:

1. *Overcoming resistance to interferon in MPN stem cells* – Ann Mullally, MD (Brigham & Women's Hospital, Boston MA), Steven Lane, MD, PhD (QIMR Berghofer Medical Research Institute, Brisbane, Australia) and Michael Milsom, PhD (German Cancer Res. Ctr., Heidelberg, Germany).
2. *Mechanism of action of interferon alpha in MPN therapy* – Jean-Luc Villeval, PhD and Isabelle Plo, PhD (INSERM/ Gustave Roussy/University Paris-Saclay, France).
3. *Novel Agents for the Treatment of Malignancies* – Leon Platanius, MD (Northwestern University Feinberg School of Medicine, Chicago IL)
4. *Using a vascular niche platform to develop interferon-based strategies to eradicate MPN stem cells and phenotypes* – Joseph Scandura, MD, PhD (Weill Cornell Medicine, New York, NY)

As the project coordinator for this Initiative, I am looking forward to working closely with this great team of researchers and advisors to reach our goal of improving outcomes for MPN patients, and fully realizing the potential of IFN as a therapeutic option. ■

myMPN PARTICIPATION NUMBERS SURGE

(FROM PAGE 3)

over time will represent a cross-section of all MPN patients and we will begin to strategize on how to make that a reality. Similarly, from a gender perspective, we have a higher representation of women than men in the registry. While this is not consistent with the epidemiology of MPNs, it is commonly known that women are more likely than men to participate in online studies of this sort. Now we know that we need to try harder to engage male patients!

As I alluded to earlier, data from our "How do you feel, today?" survey becomes more valuable with each additional encounter by a single user. We can see how the user's experience changes from day to day and week to week simply by looking at the trends in their responses to various quality-of-life measures. By illustration, Figure 2 (page 3) shows the burden of various common MPN symptoms, based on the data of approximately 400 surveys. This data is aggregate but clearly shows that skin problems (itchy or dry skin) are significant, with nearly a quarter of participants indicating they have had "very much"

or "quite a bit" of a problem in the week preceding their completion of the survey. Aches and pains in the bones and dry mouth are also problematic, according to the responses.

As more users adopt the habit of regularly completing HDYFT surveys and data accumulates in the system, we will be able to parse it by variables such as diagnosis (PV, ET or MF), age of patient, length of time since diagnosis, and more. This will enable researchers to draw conclusions about how symptom burden changes over time, by diagnosis, and perhaps identify other triggers or links that were previously not known.

But first, we need all myMPN patients to keep up the great work of regularly visiting www.mympn.org! ■

PROGRESSION MUST BE STOPPED

Dr. John Crispino, Scientific Advisor

"We're working on it." That was always my answer to Bob Rosen's question of when will we be able to stop progression to myelofibrosis and AML. I can't emphasize enough how sad I am that we didn't work fast enough. We didn't save Bob, or the countless others who have gone before him. It isn't for lack of trying, but we can do better. We need to do better.

A friend once told me: "Listen to what the patients are telling you." He wasn't referring to their world. No, he meant listen to the genetics behind their disease. The MPNRF Progression Project is a great step towards unraveling the mystery of evolution from PV and ET to PMF, and from PV/ET/PMF to AML. This project will enable the genetic voices to be heard, and it will provide us with the clues that we need to solve the progression puzzle. I am committed to making the Progression Project a success and ask you to join the Foundation in this essential undertaking.

I first met Bob almost ten years ago at an MPN Challenge Grant review, and the second time I saw him, he invited me to become the Foundation's Scientific Advisor. It has been a tremendous honor to work closely with him and help bring his dream of finding a cure closer to reality. The Foundation has been behind a number of major discoveries, including pre-clinical studies of JAK inhibitors and the discovery of both the *TET2* and *CALR* mutations. That's part of Bob's legacy. Although we no longer have him leading the charge, I know that the Foundation will be an integral part of curing the MPNs.

Bob, you have been a good friend and you will always be my inspiration. You will be missed. ■



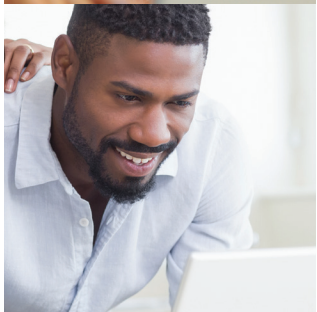
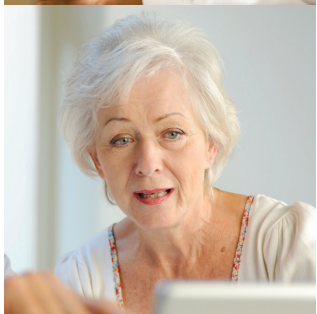
PROVIDING EDUCATION AND RESOURCES FOR A BETTER TODAY. INVESTING IN RESEARCH FOR A BETTER TOMORROW.

Partner. Advocate. Friend. At the MPN Research Foundation, we're committed to standing with you in the fight against polycythemia vera (PV), essential thrombocythemia (ET) and myelofibrosis (MF) – the group of blood cancers collectively known as myeloproliferative neoplasms.

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CONNECTING WITH THE MPN COMMUNITY

Whether you're looking for job leads, new ideas, or a shoulder to cry on – personal connections make us stronger, and strong communities change the world. That's why it's important for members of the MPN community to connect with and support each other.

Looking for a way to support your MPN community? These activities create awareness, encourage charitable giving, and strengthen personal connections.

- **f** **📷** **🐦** **Spread the word! Post and repost!** The Foundation is constantly posting on social media about news and ways people can support our efforts. Comment and repost as much as possible so your friends and family can see the great work we do.
- **Pledge your next birthday to the MPNRF.** Pledge your birthday and we will create a personalized fundraising page that you can send to family and friends on your birthday. Ask them to honor your big day with a gift to the Foundation!

FEELING A BIT MORE AMBITIOUS?

- **Are you looking for a challenge? Join Team MPN.** Sign up to participate in an athletic activity such as a marathon, cycling event, hike; anything you like! We will create a personalized fundraising page so you can share your story and collect pledges for the Foundation.
- **Maybe an athletic event isn't your thing. Throw a party or plan a bake sale.** Do you like to host parties? Make your next event about the MPNRF and ask your friends to chip in what they can. Like to bake? Set up a bake sale at your local school or take orders over email and donate the proceeds to MPNRF.
- **Do you want to connect with other patients? Start a patient support group.** We need to grow the network of support groups across the country, and need volunteers to organize local meetings. Check our website to see if there's a support group in your area

If you're interested in devoting your time and talent to the MPN community in other ways, contact Ellen Bouleanu, Associate Director of Major Gifts. ■



WHEN YOU'RE BOTH DOCTOR AND PATIENT

Jennifer Acker

What kind of insight does a doctor who has treated cancer patients, and who has a rare cancer diagnosis himself, have to offer fellow MPN patients?

Over the course of his career, Dr. Donald Margouleff has treated hundreds of patients with thyroid cancer. He says that early in this career, he learned to never prescribe to a patient exactly long he or she has to live.

"I think to live a fulfilling life, patients need hope and I think it is my obligation to present treatment in that way. None of us know that and quoting the literature on this topic has brought great distress to many patients," says Dr. Margouleff.

"I tell patients that they have a disease, and that they will be treated with the best available medication. I tell them that in my life I have seen a long list of medical advances, such as coronary artery bypasses, and all the vaccines that have eliminated polio and numerous other childhood diseases."

In his years as a medical professional, Dr. Margouleff has witnessed changing treatments for MPNs.

"I've seen the use of radioactive phosphorus discontinued. It was amazing – one dose or two at most by IV dropped the hemoglobin to within normal. There were no side effects and it was used at most centers. Then came the data that indicated that its use increased the risk of leukemia. I remember making a house call to an elderly gentleman who had skipped his phlebotomies and had a stroke. He was housebound. I had a little lead lined box and went to his home and gave him a dose of P-32."

As those who've ever faced a challenging diagnosis know all too well, life can change in the blink of an eye. Thirty years ago, Dr. Margouleff was suddenly looking at life through the foggy lens of a patient when he was confronted with the rare diagnosis of Polycythemia Vera.

He acknowledges he was fortunate to have a mild form of the disease.

"Since I had treated a number of patients with PV with phosphorus P-32, I was quite familiar with the disease and, in fact, performed a blood volume measurement on myself in my own laboratory."

Just over a year ago, Dr. Margouleff became anemic. His hematologist confirmed a new diagnosis of Myelofibrosis.



Dr. Donald Margouleff

Dr. Margouleff confesses, "I often felt well enough that I didn't see him for years at a time; he was not happy with me as a patient."

Over the years I treated hundreds of patients with hyperthyroidism with radioactive iodine I-131. In this condition, there is the unrestrained overproduction of thyroid hormone. It is similar to the uncontrolled overproduction of red cells in PV. That disease is due to autoimmunity, where an antibody takes control and stimulates the cells that produce thyroid hormone. I think we will see new drugs that can control whatever factor is overstimulating red cell production. It is coming."

When asked what wisdom he would impart to the MPN community, this doctor's orders are clear.

"My advice to others with an MPN is to be diligent in following doctor's orders. If you are polycythemic and require phlebotomies, get them as medically indicated. Untreated, there is a real risk of stroke or other cardiovascular event. It is a painless disease and failure to adhere to necessary treatments can be catastrophic."

Finally, remain hopeful. There are significant research developments that could conceivably reverse the course of this spectrum of diseases."

At 88 years young, Dr. Margouleff still keeps busy. He practiced medicine full time until the age of 76, and then began practicing part-time until the age of 83, when his wife became ill.

"I loved being a doctor and still keep up on medical advances. I am the

(CONTINUED ON PAGE 12)

WHEN YOU'RE BOTH DOCTOR AND PATIENT

(FROM PAGE 11)

associate editor of a medical journal and review articles reporting on advances in medical knowledge."

But he's not all business. Dr. Margouleff has been playing the piano since age six; a skill that proved useful during his medical schooling.

"While in medical school I supported myself by playing in bars, restaurants, and ski resorts. I studied in Switzerland and you didn't have to be good to get gigs in the 1950s. All the musicians were killed in the war and I had plenty of work."

He also loves the outdoors (he's kept a fishing boat in Montauk on Long Island since 1968) and enjoys reading *The New York Times* daily.

For this MPN patient, there's not much time for rest. At the moment, Dr. Margouleff is writing his personal memoirs, and has a large extended family. He is a father to seven, grandfather to eight, and great-grandfather to three.

"I have lived beyond my expectations, longer than my father and both grandmothers. I think I am obligated to make the most of this blessing," he acknowledges. ■

Dr. Donald Margouleff, an MPN patient for almost three decades, has practiced medicine for nearly 40 years at North Shore University Hospital in Nassau County on Long Island. He was an attending physician in the Department of Medicine and is board-certified in Internal and Nuclear Medicine.

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WWW.MYMPN.ORG

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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MPN RESEARCH FOUNDATION BELIEVES PATIENTS WITH PV, ET, AND MF SHOULD BE FRONT AND CENTER IN THE RESEARCH PROCESS.

148,363

Polycythemia
Vera
Patients

134,534

Essential
Thrombocythemia
Patients

12,812

Myelofibrosis
Patients

Patients help support research by contributing to our grant program, enrolling in the patient registry myMPN, participating in clinical trials, and sharing information with family, friends, and other patients.

MPNRF has funded
over \$12 million
in research

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64

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67

Research
Projects
Funded

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