By Barbara Van Husen, President

For the last 5 years, the annual MPN Challenge has been the focus of the Foundation’s research strategy. Each November, at the MPN Roundtable, scientists from both academia and industry help the Foundation identify the current unmet needs and unanswered questions in MPN research. Our grant program starting the following year solicits proposals specifically aimed at those areas.

In 2016, the Foundation took a break and did not issue a new Request for Proposals for the MPN Challenge (although we continued to fund multi-year grants begun in 2015). Instead, we spent some time digesting what we had heard at the November 2015 Roundtable, in the hope of creating a revised strategy that would expand our potential impact on MPN science. We began to draw pictures and solicit ideas from our scientific advisors and other outside experts. As our pictures expanded, our enthusiasm grew, along with our determination to take what for us is a big step forward in our support of MPN research.

The resulting 2017-2019 research strategy is depicted in the diagram above. Highlights of the strategy include:

- **Our Primary Goal.** Our research funding for the next several years will be focused on one primary goal: to control MPN disease and halt progression to MF and AML. Research projects we consider will be evaluated against this goal.

- **The MPN Challenge.** Our annual grant program will continue in 2017, soliciting innovative proposals from academic institutions around the world to address key areas of unmet need in MPN science.

- **Patient Registry.** In 2017 we will begin to populate a robust patient registry (myMPN) to collect patient-reported longitudinal data. Over time we believe this registry will become an invaluable asset for MPN researchers.

- **MPN Progression Marker Project.** We are beginning to define a longitudinal study of MPN progression, using patient-reported data from myMPN along with marker testing from partner organizations. As described in last Fall’s newsletter, this data can be the key to understanding MPN progression and how to stop it.

- **MPN Interferon Initiative.** We are currently developing a multi-institutional, multi-year strategic project focused on unraveling the mechanism of action of interferon for MPN patients. We believe this project can not only make interferon more effective and available for patients who can benefit from it, but may have important impact on other blood cancers and solid tumors.

(continued on page 7)
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THE CUBS, THE PIPELINE, AND CLINICAL TRIALS

By Robert Rosen

By now you’ve surely heard that the Cubs won the World Series for the first time in over 100 years. Even though I’ve been a White Sox fan since I was 8 years old, I follow all the teams in our sports-crazed city of Chicago. We take pride in them all and love the action that comes with a winner.

Building a champion took many years of trial and error on the part of the team, its owners, managers, players and fans. To stretch this metaphor, I might say that it feels a little like today’s MPN Research world. For the first time in memory we have a pipeline full of new drugs. Happily, not all are working off the same mechanism of action, Jak Inhibition, like in the early days after the discovery of the JAK2 V617 mutation. Like our sports teams, we do not yet know where the clear winners will be. But in order to have a chance, we have to put players on the field and keep working at it.

These new candidate drugs are addressing our disease from multiple directions. Some are aimed directly at the bone marrow, or are working with an immunotherapy agent, or chasing inhibition through other means like the Aurora Kinase molecule. In this newsletter, our scientific advisor John Crispino has an article lauding the explosion of combination trials. It’s hard to keep track. The options are multiplying, and so are the chances of finding a winning formula for our patient community.

The only way we are going to find new treatments, and perhaps a cure one day, is through persistent and intelligent preclinical research as prelude to the long and winding road of new drug development. At the foundation we have been thinking more about the clinical trial part of this process. Clinical trials entail risk, and we would never recommend them without thorough consideration with your doctor. But at this moment there are a number of trials that are slow to accrue patients, without which we can never know what works.

We encourage you to support the work of the foundation through your donations, and to be open to participating in a clinical trial if appropriate for your medical situation.
In the last newsletter I wrote about myMPN being a tool for patients to change their prognosis. Many MPN patients feel hopeless, powerless and alone. The registry aims to reverse that - to show patients that they are NOT alone and that by sharing their experience with their disease (their own “myMPN”), the research and pharmaceutical community will be better equipped to make decisions that will help them, thereby changing their prognosis! With strong participation in myMPN, treatments for MPNs will potentially move quicker and more efficiently through the development pipeline bringing much needed relief to patients. How does this happen?

Using Patient-Reported Data to Drive Research

The drug development and approval process has many steps. Some are guided by the researchers, some by the pharmaceutical companies, and some by the Food and Drug Administration (FDA). Along the way, hurdles often arise which slow things down. Examples of common hurdles include lack of funding or financial sponsorship to take a drug from the laboratory to the pre-clinical trial process, availability of eligible patients willing to participate in trials, and insufficient data to prove a point to the FDA.

These three examples were chosen to demonstrate how myMPN can change the dynamic of the drug development and approval process for the benefit of patients. Let’s take them one at a time:

1. Demonstrating financial viability of a drug or therapy in the early stages

This is tricky – especially for researchers working in the rare disease space. Potential financial sponsors and/or drug companies need to clear high hurdles to justify the considerable cost of taking a drug or potential therapy into clinical trials.

With rare diseases, data about the number of patients who stand to gain from a specific therapy is often difficult or even impossible to come by.

myMPN aims to change that. By establishing a centralized repository for patient data that is secure and available 24/7, we hope that the numbers of patients suffering specific MPN symptoms or meeting other criteria will provide compelling proof to decision makers in pharmaceutical companies to move forward with a therapy. We’re going to need a lot of data to make these cases, but we know that the patients are out there and we are counting on you to participate!

2. Availability of patients for FDA trials

The current approval process works, but has its flaws. One of the flaws is that it is SLOW. If a drug is approved for trial, the primary investigators work with the FDA and other interested parties to structure the trial and then often recruit participants by speaking to eligible patients when they come to their office for appointments. The participation in the trial is limited to a set of patients who meet certain criteria and visit certain doctors. What if we let patients know through myMPN when there was a clinical trial that was relevant to them? Patients could find out sooner that there are trials which they are eligible for, and contact their doctor’s office to proactively move the process along more quickly. This is just one example of how the clinical trial process can be made more efficient by myMPN.

3. Using data to make a case to the FDA

The FDA is staffed by highly accomplished leaders in the fields of medical care, research and administration. They rely on published articles and networks of clinicians and other practitioners in the field to understand what is happening with patients affected by specific conditions. myMPN is a tool for allowing patients to communicate with the FDA. When a question arises about symptom burden, quality of life or another subject covered by myMPN surveys, we can produce a report based on the testimony of patients on the frontlines. We believe this is more powerful than any secondhand information the FDA may receive.

Making myMPN a Success

The key to the success of the MPNRF registry is the participation of the patients. There is power in numbers. The more patients who share their experience, the better equipped the MPNRF is to make a case to the pharmaceutical industry and research community for therapies and research needed to change your prognosis.

Our registry is in the beta testing process now but we will be launching it to the MPN community for full participation by the end of this year. Look out for an announcement of the full launch on our website, Facebook page and other outlets. Register yourself or your loved one, and SPREAD THE WORD! For more information or questions, contact Lindsey at myMPN@mpnresearchfoundation.org.
Clinical News for MF

Interferons
1. Ropeginterferon Alpha 2b
Dr. Gisslinger reported results of the PROUD-PV study comparing this new longer acting version of Interferon versus HU. Investigators found that ropeginterferon has a similar (i.e. non-inferior) activity to HU at 12 months.

2. Pegasys
Dr. Mascarenhas presented data from the Phase III PNRC study of 168 patients treated with Pegasys or HU. The study did not show a clear difference in the primary endpoint of complete hematologic remission nor in other outcomes. As with ropeginterferon, the data were analyzed at the one-year time point.

JAK inhibitors
1. Pacritinib
In a late-breaking presentation, Dr. Mascarenhas presented an update on the Phase III study of pacritinib in MF. This study of 311 patients compared pacritinib against best available therapy, which included ruxolitinib. Pacritinib was significantly more effective for spleen volume reduction and a trend toward superiority for a reduction in total symptom score.

2. Momelotinib
Gilead reported mixed results from their Phase III study in mid-November, with non-inferiority to ruxolitinib for spleen volume reduction, but not for a response in total symptom score. The data demonstrated that patients with the CALR mutation showed a significantly better spleen response and relapse-free survival as compared to patients with other mutations.

Combination Studies
1. Ruxolitinib plus Azacitidine
This study, presented by Dr. Daver, examined the effect of combining ruxolitinib with the DNA methyltransferase inhibitor 5-azacytidine (AZA). The combination led to improvements in spleen volume and total symptom score, which was accompanied by a modest reduction in allele burden and degree of fibrosis.

2. Ruxolitinib plus a PI3Kd inhibitor
In this small study, the investigators found the combination to be overall well tolerated with an 83% rate of clinical improvement. Further studies of this combination should be pursued.

3. Ruxolitinib plus PIM and CDK4/6 inhibitors
The combination of ruxolitinib, PIM447 (a drug that targets PIM kinases) and LEE011 (a drug that targets the cell cycle by blocking CDK4/6), was effective at suppressing the growth of JAK2 mutant cells in vitro and in vivo. Treatment somewhat reduced the allele burden and prevented the development of fibrosis.

Novel Agents
1. Nuclear to cytoplasm transport inhibitor
A presentation by Dr. Yan revealed that treatment of MPN cells lines with KPT-330, an inhibitor of nuclear to cytoplasmic transport (i.e. the shuttling of proteins such as tumor suppressors out of the cell nucleus), arrested the growth of the cells.

2. Sotatercept (ACE-011) as a therapy for anemia in MF
Dr. Bose presented data from a Phase II study of sotatercept, a drug that inhibits TGF-b signaling and allows for enhanced red cell production.

Novel Studies on MF Progression

Clinical
1. Ruxolitinib plus Decitibine
There was enough of a positive response to warrant a Phase 2 study.

For more information, you can read the ASH 2016 Meeting Report in its entirety online at http://bit.ly/2naTTNA.
My husband Eugene was diagnosed with Essential Thrombocytopenia (ET) in 1991 when it was classified as a blood disorder. The hematologist said that he could go on hydroxyurea, or watch and wait. In those days, they really didn’t know much about this blood disorder. It was found mostly in older people.

In 2010, Eugene developed severe bruising, and lost a great deal of weight quickly. After a regular blood test for gout, the General Practitioner/Primary Care Physician called us on a Sunday and asked my husband to come in on Monday as he had an elevated white blood count. When the GP/PCP told him that he found blasts in his blood, we knew that it was serious because my mother-in-law had been diagnosed with leukemia. We immediately saw a specialist at the Cross Cancer Institute in Edmonton. Within the hour, he had my husband diagnosed with Myelofibrosis.

We left his office in a daze, with nothing in our hands to tell us what my husband really had. I researched all I could about MF. Information ranged from saying that he would die very quickly, to saying he could live a full and normal life. We still didn’t know the magnitude of what having a rare disease meant. I called the Canadian Organization of Rare Diseases (CORD). I credit founder Durhane Wong-Reigher for gathering a group of us together who all had a similar diagnosis with an MPN. CORD brought us together and the rest is history.

In 2014, a group of patients and caregivers came together in Montreal to discuss the formation of a Canadian advocacy group for MPN patients. We established the group with twelve members representing five provinces in Canada, covering the country from coast to coast to address unmet needs for Canadian patients. We wanted to make sure patients had access to information about MPNS, information about their diagnosis and to not feel like they were alone in a diagnosis of a rare blood cancer.

For the past three years, the Canadian MPN Network has organized very successful patient conferences held annually in Toronto during the month of September. This year’s conference will be in September as well. Amongst other things, we provide materials for MPN Doctors to share with their patients about MPNS and the Patient Advocacy Group.

The Canadian MPN Network Patient Advocacy Group also provides support to local grassroots groups. Currently we support local groups in Hamilton, Ottawa, Edmonton, and Vancouver. New support groups are up and coming in both Montreal and Calgary.

I took on being the group’s Chairperson to bring together patients and their families (care partner, care givers, family members and friends) to learn more about this disease and to empower patients in their journey. Since it has no cure, other than a SCT (stem cell transplant), one of the only things that patients have control over is the knowledge of their disease. And for them, knowledge is the power to control something that is uncontrollable.

It was also an opportunity to use my previously developed skills in leading voluntary non-profit organizations. As a Human Resources professional, working with people is my passion. Providing patients with resources, contacts with other MPN Patients, and the peace of mind that they are not alone has been the greatest reward for my involvement. I truly believe that the more we know and understand about our journey with an MPN, the more control we will have.

From the original diagnosis we received in 2010, when we felt that there was no hope, to today. I now have hope on a new frontier of treatments that MPNS will become a “chronic” disease like CML or diabetes, allowing patients to live rich, full, and abundant lives.
LIVING THROUGH THIS: 
CHRONIC ILLNESS AND MPN

By Michelle Woehrle, Executive Director

Concepts that are foreign to many people abound in the world of MPN; Rare disease, chronic cancer, bone marrow niche, cytokine storm. These are just a few terms a person might add to his vocabulary.

But let’s focus on a concept that seems like a contradiction in terms: chronic cancer. Because that’s what MPNs are - chronic cancers. Even though it is technically cancer, defined as an overproduction of cells, to the outside world of concerned friends and family they don’t look like a “real” cancer. But they are. If you don’t believe us, take it from the World Health Organization, which declared MPNs to be categorized as cancer in 2008.

PV, ET and MF can be experienced very often as chronic and even benign diseases. While this isn’t the case for everyone, many people with an MPN live relatively normal lives for decades, although always on the alert for signs of a thrombotic event of ET, PV and MF. On top of that, people with an MPN diagnosis live with the symptoms we know can be so disruptive to normal life - particularly fatigue, which can have a domino effect on quality of life if it impedes work, socializing, family responsibility or hobbies that people enjoy and which make them feel "normal".

This is why we feel so strongly about sharing patient stories so that people who have been diagnosed can benefit from the experiences of others. They can even use these to illustrate to their friends, families, and co-workers that what they are experiencing is a real burden that others share. It’s also why we are keen to get myMPN - our patient registry - off the ground, so that people at all points in the life cycle of MPN, from benign to acute, can share what they live with. The goal of this patient self-reporting (eventually to be merged with objective metrics) is to inform the research process in the interest of our Foundation’s larger goal: to stop progression and/or cure MPN.

PAIR IT UP

By Dr. John Crispino, Scientific Advisor

Although ruxolitinib provides many benefits, it isn’t a cure. One strategy to enhance its activity is to pair it with a second anti-tumor agent that targets a distinct biological pathway. In this way, scientists hope for “synergy,” defined as an anti-tumor activity that goes beyond simply adding the effects of the two drugs. Think of synergy as creating Reese’s peanut butter cups from peanut butter and chocolate – or of discovering the color purple by combining red and blue.

Clinicaltrials.gov lists more than a dozen active Phase 1 and 2 combination trials of ruxolitinib and a second agent for myelofibrosis. Among these second drugs, there are four notable categories:

- Drugs that inhibit PI3K delta, a gene that regulates the PI3K/AKT signaling pathway which cooperates with JAK/STAT signaling to drive cell proliferation
- Histone deacetylase (HDAC) inhibitors, which have shown modest activity as single agents in MF
- Immunomodulatory agents such as lenalidomide, which is effective against a sub-group of MDS cases but hasn’t shown potent activity in MF as a single agent
- Drugs that inhibit the hedgehog pathway, another signaling pathway that controls cell growth and maturation.

Other combination trials seek to leverage the effects of ruxolitinib with chemotherapy or with pegylated interferon. An interesting combination that was presented at the 2016 ASH Annual Meeting is the addition of two novel agents, PIM447 (a PIM kinase inhibitor) and LEE001 (a CDK4/6 inhibitor) to ruxolitinib therapy. Dr. Raajit Rampal reported that this three-drug combination showed strong anti-tumor activity, without toxicity, in pre-clinical models of myelofibrosis. This Phase 1/2 study for patients with MF is currently underway at multiple sites.

The idea behind all of these trials is to hit the cells in two diverse ways, lessening the chances that they will quickly figure out a strategy to evade ruxolitinib.

Combination therapy is the mainstay for many other malignancies. Although a slow process, testing different combinations and treatment regimens is an essential step in the development of long lasting curative therapies.

Meet Dr. Katya Ravid. She’s a professor of medicine and biochemistry at the Boston University School of Medicine. With funding from MPN Research Foundation, Dr. Ravid discovered that it’s possible to detect bone marrow fibrosis in mice using in vivo MRI. If implemented, this project could relieve MPN patients from the need to have as many bone marrow biopsies, which are crucial for verifying the state and progression of their disease.

By helping us support researchers like Dr. Ravid, you can change MPN patient prognoses and find a cure for these rare diseases.

Visit www.mpnresearchfoundation.org today for more information.
HAVING A WILL IS OVERRATED

By Bill Crowley, Director of Development

You have heard many times how important a will is. While there is no law that says you have to make a will, have you ever thought about what would happen without one? Here are three things that may happen:

You have spent a lifetime working, saving and stretching your savings to fund your retirement. Now that your money has outlasted you, it will be awesome to see how the government divides your assets. Governments always make amazing decisions about other people’s money.

The idea that a will simplifies matters for your family after you die is so overrated. Why deny your family that special moment when they gather at your funeral and one relative whispers, “I wonder how the jewelry will be divided” and another relative answers: “What jewelry?”

If you die (I say “if” because you may be the first to live forever) the grieving process is enriched when family hunts through your personal files and possessions in an attempt to figure out what you owned. This is like a scavenger hunt, but with more zeroes. The whole family can play this game. In truth, the whole family will play this game because everyone wants to make sure others get more.

If you do not have an estate plan, you need one, regardless of the size of your estate. Estate planning is about focusing on life. With an estate plan, you can help ensure that you are remembered for the impact you had on your community and your world.

Many people are helping find a cure for MPN’s. Some have found that a good way to accomplish that is to include the Foundation in their estate plans. To learn more about how to include the MPN Research Foundation in your own estate plans, contact Bill Crowley at wcrowley@mpnresearchfoundation.org or (312) 683-7226.

MPNRF EXPANDS RESEARCH STRATEGY FOR 2017-2019

(continued from page 1)

But this ambitious agenda comes with a cost. The Foundation will need to expand its fundraising efforts beyond our current capacity to even begin to meet the objectives of this strategy. MPN patients have been steadfastly generous in supporting research in the past, but to reach this next level the Foundation must consider additional sources. These might include:

- **Partnerships with other non-profit organizations.** Our close partnership with the Leukemia & Lymphoma Society (LLS) on the MPN Challenge has enhanced the effectiveness of this program greatly. We also partner with the AAMDSI Foundation to develop materials on MPN/MDS overlap syndromes. We plan to continue to develop relationships with like-minded non-profits to expand our ability to fund MPN science projects.

- **Direct application for governmental funds.** To date we have not attempted to tap funds available from NCI, NHLBI or other NIH centers. We want to make sure that recent enhancements to the federal government’s cancer research programs (e.g., the Cancer Moonshot) include work focused in MPNs.

- **Public/private partnerships with corporations with whom MPN patients share interests and goals.** Other disease foundations (e.g., LLS, MMRF) have successfully developed programs with biotech and pharma companies that address the shared interests of both patients and those companies. We will continue to inform the MPN community of our direction and progress as this strategy and its funding take shape, and we will always be guided by our Independence Policy for any corporate donations.

The MPN community should be pleased and hopeful about the amount of effort being devoted to MPN research today. Compared to 10 years ago, it’s a monumental change. But until there are effective treatments for all of our patients, and until the progression of these diseases can be reliably halted, we must continue to think boldly and broadly. The 2017 MPN Research Strategy is one step in that direction.

**FUND RESEARCH. FIGHT MPNs. CREATE SUCCESS STORIES.**
When Dad came home from work on an especially hot summer day, we would try and go for a quick swim together before dinner. It was a short walk through the woods to our neighborhood pool. Dad and I had a routine. He would throw his keys into the pool, and I would dive down and find them, gradually building up my stamina until I could reach them in the deepest part of the pool, some nine feet down. "Again, again, again!" I would demand. This was our end of the day father-daughter summertime routine.

Two years after my father’s diagnosis of polycythemia vera, I had a dream that has stayed with me. We had just left an appointment at the cancer center, and I was walking to the edge of a dock looking out at a dark lake. The sun was missing from the sky; and as I glanced back from the edge of the dock, Dad was standing at the shore looking out to me. I knew what I had to do. I was terrified. I knew his keys were in the water, floating somewhere toward the bottom. How was I going to find them? Heart racing, I braced myself and dove in.

Afraid to open my eyes, afraid of what I might find, of what I may see, I put my hands out in front of me, blindly reaching for those keys. I soon understood this was impossible. Even with eyes open, I couldn’t see. No matter how hard I tried, I couldn’t get to the bottom. I couldn’t find the keys. When I decided to swim to the surface in defeat, this time it was different. I wasn’t that same little girl out of breath, but full of pride, holding his keys above my head. I wasn’t even sure how I surfaced with the weight of this sadness. My hands were empty, and my heart was heavy, and Dad was standing there, waiting for me.

I haven’t found the keys to solve the riddle of polycythemia vera yet, but I am hopeful new treatments are on the horizon. And it is my hope that through sharing our experiences, connecting patients, advocates, and caregivers, together we can join forces and become stronger to beat this.

Because everyone has a story, and a unique journey, and by capturing them, we can find inspiration, comfort, healing, and maybe even a friend to lean on who understands what it means to be diagnosed with, or love someone with an MPN.

If you’d like to share your story, I’d love to help you! Let’s chat. You can reach me at jenniferacker2@gmail.com.

Jennifer lives in Pennsylvania with her husband and two daughters. Her father was diagnosed with polycythemia vera in 2013. Since then, she has been fierce in her resolve to help empower those diagnosed with MPNs. She has a passion for writing, and helping others find their voice through writing. She is a volunteer contributing writer for the MPN Foundation. Jennifer studied English and Secondary Education at Moravian College, received her Master’s in English from the University of New Hampshire, and has taught English in New Hampshire and Pennsylvania.