

MPN RESEARCH FOUNDATION YEAR IN REVIEW: 2016



By: Michelle Woehrle, MPA Executive Director

The mission of the MPN Research Foundation is to stimulate original research in pursuit of new treatments -- and eventually a cure -- for the blood cancers polycythemia vera, essential thrombocythemia and myelofibrosis, known collectively as myeloproliferative neoplasms (MPN).

(Please see Audited Financial Statements and 990 for a detailed look at our finances)

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ACTIVITIES

In 2016, MPN Research Foundation (MPNRF) took a break from our annual grant program to reflect on past granting strategies and develop a new strategy to guide our future investments in MPN research. Our goal was to understand what was currently being pursued either by academic or industry scientists; what remained an unmet need; and finally, given that analysis, whether MPNRF could make an impact with our resources of time, expertise and funding.

We found two areas where we felt we could be of particular use: understanding and delineation of the metrics related to Progression (from ET and PV to MF and from MF to AML) and understanding the mechanisms of action of Pegylated Interferon. Conversion to a more acute MPN is on the minds of all MPN patients, and in our view, not enough is being done to prevent or reverse it. Interferon has long been the elephant in the room; it reduces the mutant JAK2 mutation for some patients, and others find it too toxic to take long term. We felt it was time to get to the bottom of what was going on.

Additionally, we determined to continue underwriting our annual grant program, allowing us to keep a consistent presence among MPN researchers doing this important work for our community. Every year we prioritize focus areas for research. This year our focus is on understanding and disrupting the bone marrow environment. We still leave the door open for new ideas from researchers focused on MPNs. This was the time we also decided to go forward with a registry for MPN patients, which we're calling myMPN.



In February Raquel Nunez helped 100 MPN patients participate in Rare Disease Day by collecting and sharing their stories of living with PV, ET or MF. This initiative and others we participate in helps raise the profile of the need to fund research for people living with an MPN, and lets patients know they are not alone.

With our proposed strategy in hand, we began our walking and talking tour of key opinion leaders in the MPN space. Including fellow patient advocates, academic researchers, industry and our scientific

advisers, we took our proposed research strategy (Interferon, Progression, registry, annual grant program) and solicited input on both the strategy and tactics needed to solve these research questions. We continued to refine the research strategy based on feedback we received.

Our legwork included prioritization of the strategic projects (Interferon and Progression), to decide how much money we could commit to each, and in what order they could be staged. Because there were some concrete research approaches around Interferon already, we began pursuing that project first, and established a budget of about \$700,000 in grants possible to go out on this effort in 2017. Along with Leonidas Plataniias of Northwestern University, we convened a panel of Interferon experts from MPN and beyond to discuss its mechanism of action, what was yet unknown about this drug, and where next steps in basic science research could be aimed to find out why this suppresses the mutant JAK2 gene in some MPN patients, why some patients cannot tolerate it, and how to create more perfect versions of this compound so that more could use it.



After deciding to go forward in creating myMPN - the MPN patient registry / natural history database -we hired Lindsey Whyte to be our Registry Project Manager. We also recruited a group of clinicians, statisticians, and basic scientists to serve on our Steering Committee, who will have the final say in the content of the surveys, how information gets shared (with patient permission), and how to make this be a useful tool for researchers.

Steering Committee for myMPN:

Ruben Mesa, Mayo Clinic (Chair)

Michelle Woehrle, MPN Research Foundation (Chair)

Srdan Verstovsek, MD Anderson

Robyn Scherber, Oregon Health Sciences

Brady Stein, Northwestern

John Mascarenhas, Mt. Sinai School of Medicine

Claire Harrison, MPN Voice & Guys & St. Vincent Hospital

Amy Lou Dueck, Mayo Clinic

Camelia Iancu-Rubin, MT Sinai School of Medicine

Our ultimate goal in pursuing this has always been to create something that would be useful for researchers to either test or develop hypotheses, and to warehouse natural history information from patients, entered by patients. We selected Genetic Alliance's PEER (Patients Engaging Everyone Responsibly) platform on which to build myMPN. Once we launch patients can begin to self-report information about themselves including demographics, disease history, current symptoms, and disease changes. In addition to contributing to the wealth of knowledge about MPN, we hope patients learn something about others with PV, ET and MF in the process and recognize they are part of a relatively large group living with MPN.



We planned and hosted a meeting of the MPN Patient Support Group Coordinators coinciding with Blood Cancer Awareness Month, which is September. During September, our awareness campaign was centered around, again, raising the profile of the diseases and empowering patients to share the message that research funding is needed. Through our campaign patients and their friends and family around the globe changed their social media profile picture, and also contributed to us and other organizations who are doing work to fight blood cancer.

We also attended a plenary meeting for the MPN Advocates Network first meeting, an international group of MPN patient

advocates who began meeting in 2014 to see how we can best work together in serving patients globally.

We renewed 8 current grants (funded in 2015) who we had evaluated and who made sufficient progress in year one:

CRISPR Projects (This is a form of gene editing.)"Establishment of isogenic human induced pluripotent stem cell (hiPSC) lines containing CRISPR engineered MPN mutations" George Church, PhD, Harvard Medical School "Precise Genome Editing for Targeting Malignant Clones in MPNs" Zhaohui Ye, PhD , Johns Hopkins

"Correction of JAK2 mutation in myeloproliferative neoplasms by gene editing" Zhijian Qian, PhD and Wen-Shu Wu, PhD, University of Illinois at Chicago

Immunotherapy Projects

"Defining the immunomodulatory properties of mutated calreticulin in MPN" Camelia Iancu-Rubin, PhD and Nina Bhardwaj, MD, PhD Icahn School of Medicine at Mount Sinai

"Anti-PDL1 therapy for patients with Myelofibrosis" Learn more! Brady Stein, MD Northwestern Feinberg School of Medicine *Brady Stein was awarded his grant in 2015, but began year one of his 10 person trial in 2016 due to delays.

"Immunologic Targeting of Calreticulin Gene Mutations in MPN" Robert Kralovics, CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences Inflammation & the Bone Marrow Niche

"Impact of the inflamed bone marrow niche on the progression of Myeloproliferative Neoplasia and marrow fibrosis" Nadia Carlesso, MD, PhD, Herman B. Wells Center for Pediatric Research, Indiana University School of Medicine

Improvement in Utilizing Non-Invasive Techniques to Measure Bone Marrow

"Nanoplatfoms for Imaging Bone Marrow Fibrosis" Katya Ravid, MD, PhD, Boston University School of Medicine Genomic Research into MPN

"Identifying factors that promote clonal dominance in zebrafish hematopoiesis for the treatment of myeloproliferative neoplasms"

In MPN drug development news, we saw Pacritinib be put on full clinical hold by the FDA for safety reasons, and experienced the strife and frustration of the patients who looked at this as the next probable approved drug, which would allow another option beyond Jakafi for people with MPN. We began speaking to the FDA about how we as patient advocates and funders of research can be more of use to them and the drug development process, so that people living

with MPN can get more medicine options, sooner. We are continuing to learn more about how this fits into our mission, and how the 21st Century Cures Act and the Cancer Moonshot may make this type of advocacy more fruitful.



In 2016 we hosted our 4th annual MPN Roundtable. This is an event in which we showcase the work of our most recent grantees, who present to a room of industry scientists and fellow grantees. It is kicked off by a keynote address in the morning (this year's speaker was Ronald Hoffman, who spoke about the bone marrow environment). We use the Roundtable not only to hear and share the progress of our grantees, but also to stimulate a discussion about unmet need in MPN research. This informs how we go about creating our research priorities for the following year.

What we heard this time was that our efforts would be well spent seeking proposals that would eliminate the mutant JAK2 gene, either

indirectly or directly, as well as proposals that would disrupt the bone marrow microenvironment which plays a role in creating the atmosphere in which cancerous behavior can thrive. It is not well understood what role eliminating the mutant JAK2 gene, which forces on a switch in your body that is in control of production of components of your blood. Although there are several companies that have produced JAK inhibitors (including Incyte, which took the first MPN drug to market in Jakafi in 2011), none of them attack the mutated JAK2 specifically. There is some evidence that Pegasys and Jakafi both reduce this, but not consistently among MPN patients, and not permanently based on data we have now.

During 2016 Our MPN Information Kit was accessed, either online or by mail by almost 6,000 individuals searching for information or resources related to PV, ET and MF. In these kits, as well as on our website we provide basic information about the diseases, a list of organizations offering support and services, how to get in touch with local support groups, a list of clinical trials and more in every MPN Information Kit. This is part of our ongoing campaign to make sure that patients get the education and support they need, either through us or through another organization, while a search for a cure and better treatments is ongoing.

SUMMARY

In 2016 we've gone outside of our comfort zone of "merely" raising money and giving it away for research, in order to build strategic projects that hit at the heart of a few hard-to-answer questions that have tantalized the MPN community for too long. Our goal, as always, is to fund research that will unlock the next clue that will lead to better treatments, better quality of life, longer life spans, for people living with ET, MF and PV. That is the mandate of our board of directors and it is a mission that we are proud to carry through year after year until it is finally time to close up shop because all patients have the treatments they need.

We are patient-funded and led by a board of directors mainly comprised of patients and their family members. Thank you for walking this path with us.