



Grant recipients Robert Kralovics and Toshiaki Kawakami with Scientific Advisory Board member Andrew Schafer.



Also seen at the ASH dinner hosted by the MPN Research Foundation: Grant recipients Saghi Ghaffari, Wei Tong and Ross Levine.

## MPN HIGHLIGHTS FROM ASH 2011

*By John Crispino, PhD  
Scientific Adviser*

The December 2011 annual meeting of the American Society of Hematology (ASH) once again provided an opportunity for researchers and clinicians to present and discuss the most current developments in the science of myeloproliferative neoplasms (MPNs). Following is a summary of the topics presented at ASH, including the following highlights:

- Ruxolitinib (Jakafi) was approved by the FDA Nov 2011 for treatment of myelofibrosis.
- SAR302503 (formerly TG101348) showed promising Phase I/II data, which included a decrease in allele burden.
- CYT387 showed favorable spleen and anemia responses in a Phase I/II study
- Additional JAK inhibitors are under development and in early clinical trials.
- Pegasys demonstrates sustained molecular and hematologic remission in patients.

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## NEW INITIATIVE SEEKS INNOVATIVE IDEAS TO REVERSE FIBROSIS

The MPN Research Foundation and The Leukemia & Lymphoma Society have joined forces to sponsor an important new research project, the MF Challenge. Its goal is to discover the causes of bone marrow fibrosis, and to identify opportunities to arrest and reverse fibrosis.

We believe that such a campaign will be a game-changing opportunity for MF science and a life-changing opportunity for MF patients.

### Now Accepting Grant Applications

In January 2012 we jointly issued a Request for Proposals for the MF Challenge. Applicants will have until April 1, 2012 to submit proposals for funding of up to \$100,000 per grant. The grant review will take place in June 2012 in Chicago.

Proposals must describe an innovative idea or approach and a method for testing that approach within a one-year grant period.

Upon completion of the one-year period, we will evaluate applicants on the extent to which their concept has been substantiated by initial testing, and the most promising projects will be eligible for significantly expanded future funding.

Proposals that engage interdisciplinary teams and approaches will *(continued page 5)*

## 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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## ROBERT PRITZKER, IN MEMORIAM

*By Robert Rosen*

Have you ever had a conversation, a small moment, where you sensed something important was about to happen? When that moment went on to signify the beginning of something new and meaningful in your life? It happened when many of us received our diagnosis, but it also happened to me after a brief conversation with Bob Pritzker over 10 years ago.



In the wake of my own diagnosis of PV and my frustration with the low levels of MPN research in American medical labs, I was struggling to channel my energy into something productive. I had heard accidentally that Bob Pritzker, whom I knew causally from business, had recently also been diagnosed.

In need of a strategic and financial partner to enact the plan, I called Bob and re-introduced myself. “Bob,” I said, “I was recently diagnosed with Polycythemia Vera.”

His response, “I know something about that, why don’t you come over and talk?”

That was it, the brief moment that opened the door.

We met at Bob’s office, I explained the outline of the plan, and Bob said, “Well, at least we won’t do any harm, we might save some lives, and the lives we save might even be our own.”

Bob became a founding board member, together with Woody Woodruff and Joyce Niblack, and the MPD Foundation was born.

Bob died last October at 85 from Parkinson’s, not from PV. Those of us who were privileged to sit in board meetings and committee meetings with him will not easily forget his quiet demeanor, delightful sense of humor, and unflinching support of the MPD Foundation, the forerunner of today’s MPN Research Foundation.

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# PATIENT ADVOCACY: WHAT IT MEANS AND WHAT ROLE WE PLAY

*By Ann Brazeau*

Navigating through the current healthcare maze is a source of ongoing frustration. The system is not always understandable and friendly, making it necessary for patients, caregivers and organizations to educate themselves on all the intricacies associated with their diseases, including insurance issues, treatment options, drug development, government policies and overall care.

Recently, a new trend is emerging and gaining momentum in the area of patient advocacy. In fact, patient advocacy is a burgeoning field. The terms Patient Advocate and Patient Advocacy have a broad range of usages and may be applied to various subcategories of individual advocates and organizations providing various levels of advocacy.

The MPN Research Foundation has been advocating for MPN patients since its inception. Research in MPNs was almost nonexistent in 1999. To date, we have funded over 33 grants totaling over \$8 million. Some of that research directly influenced the new drug developments taking place today. Over the past several years we have been very active on behalf of patients in the following ways.

The Foundation:

- Promotes and supports patient support groups in the US and internationally to bring the most current scientific discoveries to the attention of MPN patients and provide a safe forum for patients to discuss their personal issues relating to their diagnosis.
- Lobbied successfully for inclusion of MPNs in SEER data and more accurate ICD.9 codes to promote more accurate counts of the number of MPN patients nationally.
- Actively promotes physician education in MPN science and treatment through face to face meetings and presentations at cancer centers, specifically to hematology groups.
- Continues an ongoing investigation of reimbursement issues faced by MPN patients including the initiation of inclusion of MPN

non-FDA treatments in Compendia used by insurance companies when determining reimbursement issues.

- Successfully obtained coverage through CIGNA for off-label use of Pegasys for PV and ET.
- Built the MPNR Foundation's website to provide MPN information and resources.
- Produces and distributes MPN patient brochures to numerous cancer centers and physicians worldwide.
- Hosts, sponsors and facilitates patient education symposia to bring the experts to the patients and to provide the most up to date information on research, clinical trials, treatment options and general news to empower and equip patients with the knowledge they need when making health care decisions.
- Sponsors the Chicago Roundtable, which is an innovative multi hospital group of Chicago clinicians and researchers dedicated to providing excellent MPN care and education to patients and physicians.
- Was instrumental in bringing attention to the Pennsylvania MPN patient cluster that has now received substantial governmental funding for continued research.

The MPN Research Foundation has been a driving force in research, education, growing awareness and patient empowerment. As a patient driven organization, we will continue to examine ways to improve the lives of MPN patients everywhere.

## **MPN Research Foundation Update**

is 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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## TWO DAYS IN NEW YORK

*By JoAnn Mason*

Last November, I traveled to New York to attend one of the Foundation's board meetings. During lunch, a few of the current MPN Research Foundation grantees presented interim reports on their projects. Grantee Robert Handin spoke about his zebra fish project, Ross Levine discussed his collaboration with Ben Ebert on genome sequencing, and Saghi Ghaffari spoke about her study of a signaling mechanism other than JAK2. For someone who is involved in supporting this kind of research, it was a great opportunity to interface with researchers and to ask questions.



Researcher Saghi Ghaffari and Robert Rosen discussing the search for a different signaling mechanism in JAK2 negative MPN patients.

The following day was the much anticipated 6th International MPD Patient Symposium which was co-hosted by the MPN Research Foundation and CR&T. This event brings together the experts and the patients. It was a wonderful opportunity to ask questions and to hear about new research and drug trials, and to learn more about the day-to-day issues of patients and caregivers.

The symposia the Foundation hosts (like the upcoming events in San Mateo and Chicago) are great for the patients and allow them to spend time

with the experts and to make connections with their fellow patients. For such a dispersed group, I believe that fostering this kind of network is beneficial to both patient and researcher/clinician. The connection is one that lasts beyond the event.

These events, along with the generosity of family and so many wonderful friends, give us in the MPN community all a reason to feel positive about the future and to be very grateful.

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## PV: JUST RUN WITH IT

*by Rob, PV Patient*

I just wanted to pass on some of my experiences with polycythemia. I was diagnosed in November 2009. My mom was treated for 20 years with polycythemia vera, and died from lung cancer which I'm told is not related. She was on hydrea most of that time.

I am a 54 year old athlete. I run numerous marathons a year and currently try to put in 40-60 miles per week. There is no doubt that my blood dictates many of my workouts and races. It may affect my times a bit, but not my resolve to keep on training.

My training for the May 1 Eugene Marathon was horrible. My long 20 mile runs were slow and sluggish for 6 weeks up to the race. I was worried.

My hematocrit a week before the race was in the mid 50's. No wonder I was sluggish. I ended up having two phlebotomies over the next five days. Though the phlebotomies made me quite tired for the two days leading up to the marathon, I was able to run and finish the 26.2 in great fashion. Next up is the Chicago Marathon in October.

In my opinion the key to polycythemia vera is to listen to your body. You may have some tough days, but you must persevere during those days.

## NEW INITIATIVE

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receive favorable attention, as will proposals made by collaborative teams, either within or across research institutions. We expect all grant recipients to share their data with other researchers within a year of being generated.

### A Whole New Approach

For the MPN Research Foundation, it's a whole new approach. "Myelofibrosis is the deadliest of the MPNs, and patients with both polycythemia vera and essential thrombocythemia have the potential to convert to myelofibrosis," said Barbara Van Husen, President of the MPN Research Foundation.

"Despite that, we have never received a request for funding based purely on research into fibrosis. We are going to change that with this grant program."

### The Concept of Concept Grants

Until now, we have focused on supporting research whose findings can be applied as quickly as possible to benefit patients. Instead, the MF Challenge is awarding *concept grants*, which seek to develop as-yet-unproven new approaches that are worth pursuing further.

### Why This Approach? Why Now?

Little is known about the cause of fibrosis in the bone marrow, and there are no treatments that directly address it. Even the new JAK2 inhibitors cannot reduce fibrosis.

"Paradigm-shifting" strategies that use new high throughput technologies for screening molecules and bring a multi-disciplinary approach to identifying the cause of fibrosis could attack this riddle from an entirely new direction.

"LLS looks forward to working with the MPN Research Foundation to meet this challenge," said Richard C. Winneker, LLS Senior Vice President, Research.

Our goal is nothing less than to give new hope to those members of the MPN community who need it most: patients with Myelofibrosis.

## "YOU DON'T LOOK SICK."

By Lina, ET Patient

During my freshman year of college, I was an "otherwise healthy" student, going about my life like anyone else. To look at me you would not know that there was a problem. Inside me was a different story.

After visiting my general practitioner for some strange bruising on my arms, I was diagnosed with Essential Thrombocythemia (ET).

MPNs like ET are "Invisible Illnesses," meaning there really are not many outward signs that show we're sick, but boy do we feel it. I don't know about the rest of you, but no matter how I look, sometimes I feel like I've been run over by a truck.

However well-intended the phrase may be, saying "but you don't LOOK sick..." to a sick person is very insulting. The implication being that we are faking, that it's not real, or it's in our heads. We don't look sick? Well ... what does sick look like, pray tell? Should all sick people be emaciated, bruised, or limping? What does it take to be acceptably sick? This may surprise some...but not all sick people look alike. Shocking, I'm sure. (insert sarcastic eye roll here). True, you cannot see my cancer the way you could someone with breast cancer, or lymphoma. That does not make it less real, less painful or less important.

We all have good days and bad, but for the Invisibly Ill, the bad days often outnumber the good. Most of us, though, are obliged to put on the happy face and get on with things. If we do not, we will not be able get much done. I often feel like I am two completely different people; the one on the outside, who looks just fine, and deceives everyone around her; and the one on the inside who is exhausted, battered and miserable.

I learned to put on a happy face real quick when I got my first "Grown-Up Job." I started at my office as the receptionist, so putting on the perky, bubbly personality, however fake it may have been, became a part of my daily life. Fatigued, sick, headache? Didn't matter. That smile was permanently plastered on. Inside I might have been cursing the phone

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## MPN HIGHLIGHTS FROM ASH 2011

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- Alternative therapies, such as Panobinostat, Imetelstat and Pomalidomide show promise in pre-clinical and early clinical studies.

### JAK Inhibitors

Perhaps the most exciting data from this year's ASH meeting was the progress reported on JAK inhibitors. This November, the FDA approved the first in class JAK kinase inhibitor Ruxolitinib (Jakafi, Incyte) for treatment of myelofibrosis. Several other compounds with promising phase I/II data are following closely behind.

**Ruxolitinib (Incyte):** Verstovsek and colleagues (MD Anderson) presented several abstracts to update the benefits of Ruxolitinib. Results from the Phase III COMFORT-I study in the US showed that Ruxolitinib provided significant and sustained reductions in spleen volume and improvements in MF-related symptoms, including abdominal discomfort, early satiety, itching, night sweats, and bone/muscle pain.

Furthermore, after nearly 1-year follow-up, the study suggests that ruxolitinib may provide a survival advantage compared to placebo. Similarly, data from the Phase III European COMFORT-II study, which compared Ruxolitinib to the best alternative therapy, found significant reductions in spleen size and improvements in the quality of life of MF patients. No difference in survival was noted.

In contrast to the aggregate COMFORT data, long-term outcome of patients treated with Ruxolitinib at the Mayo Clinic in the Phase I/II study was less favorable and no significant differences in survival were noted (Tefferi et al, Mayo Clinic).

With time, we will learn if and how much of a survival advantage is conferred by this drug. Patients should discuss with their physician whether Ruxolitinib is right for them.

**SAR302503 (Sanofi):** Tefferi, Pardanani and colleagues (Mayo Clinic) provided an updated analysis of Phase I/II data for this compound in patients with myelofibrosis. Almost 60% of patients

achieved a  $\geq 50\%$  reduction in spleen size and nearly 82% showed  $\geq 25\%$  decrease. Moreover, the therapy resulted in a durable, general trend of decrease of allele burden, especially in patients with  $\geq 20\%$  JAK2VF allele burden at baseline.

The ability of this compound to reduce JAK mutant allele burden distinguishes it from Ruxolitinib, which does not alter allele burden.

**CYT387 (YM Biosciences):** Tefferi, Pardanani and colleagues (Mayo Clinic) presented data from a Phase I/II study of 166 MF patients treated with CYT387. Almost 90% of patients showed  $\geq 25\%$  reduction in spleen size while 49% showed a  $\geq 50\%$  reduction in spleen size. Common constitutional symptoms also showed marked improvement in the majority of subjects.

Of note, 62% of patients treated with the 300mg dose reached transfusion independence by 12 weeks. Lower doses also showed significant benefits with respect to anemia. Thus, this small molecule appears to offer an additional benefit over Ruxolitinib. Look for the Phase III study to open in 2012.

### Non-JAK2 Drugs

**Panobinostat (Novartis):** Mascarenhas and colleagues (Mt. Sinai) updated results from Phase I study of Panobinostat (LBH589), a histone deacetylase inhibitor, in MF. The final results of the study revealed that majority of patients (10/11) had a 30% median reduction of splenomegaly and at least two patients showed improvement in bone marrow pathology. The Phase II study is ongoing.

**Imetelstat (Geron Corporation):** Imetelstat inhibits telomerase, an enzyme that repairs the ends of chromosomes as cells divide. Cancer cells have aberrantly high activity and it is believed that this activity is needed for immortalization. Brunold and colleagues (University Hospital and University of Bern, Bern, Switzerland) reported that Imetelstat selectively inhibits the growth of megakaryocytes from ET patients compared to those from healthy subjects.

These results suggest that the drug may alter the excessive megakaryocyte and platelet production in patients. Imetelstat is currently in a Phase II trial for ET.

**Pomalidomide (Celgene):** Begna and colleagues (Mayo Clinic) presented results from three consecutive clinical trials for Pomalidomide in the treatment of MF-associated anemia. Among 82 patients in the study, 77% were red cell transfusion dependent at baseline. The overall anemia response rate was 27% (22/82), with the vast majority of responses seen in the first 6 months. The anemia response was better in patients with JAK2VF mutation and in those without marked splenomegaly.

**Pegasys (Roche):** Turlure and colleagues (Service d'Hématologie Clinique, CHU, Limoges, France) reported the long-term results of a Phase II study of Pegasys in PV, which revealed robust hematologic, molecular and histological remissions.

After a median 6.4 year follow-up, 94% patients were in hematologic response with 82% showing complete remission, 29% remained in hematologic response after cessation of therapy, and 83% showed a major and sustained response in JAK2 VF mutation burden. Also, almost 30% of patients showed complete molecular response (i.e. no detectable JAK2 VF mutation).

### **Combinations of JAK Inhibitors and Novel Agents**

Several studies described pre-clinical data to support combining novel therapies with Ruxolitinib or other JAK inhibitors.

- Baffert and colleagues (Novartis) revealed that the combination of Ruxolitinib and Panobinostat showed improved anticancer activity in Jak2 VF mouse model as compared to either treatment alone.
- Vannucchi and colleagues (University of Florence, Italy) reported synergy between PI3K/mTOR inhibitors and JAK1/2 inhibitors in growth of cell lines and primary patient samples.

- Wen and colleagues (Northwestern University) showed that a combination of Ruxolitinib and diMF (a megakaryocyte polyploid inducing agent) provided synergy against growth of megakaryocytic cell lines with activated JAK2 and MPL mutations in vitro and in vivo.

### **Summary**

2011 saw major advances in the development of JAK inhibitors for MPNs, with one approved drug, two following close behind, and at least 2 or 3 others in early phase clinical studies.

In addition, there is continued development of drugs that target other aspects of the disease, which are likely to be used in combination with JAK inhibitors.

Finally, several labs are rushing to sequence MPN patient specimens to identify new mutations related to these diseases. Look for breakthroughs in this area by the next ASH meeting in December 2012.

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## **ROBERT PRITZKER, IN MEMORIAM**

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For years he hosted board meetings in his cozy conference room, plying us with sandwiches and cookies, and offering quiet support for our work. His own entrepreneurial experience with medical device companies helped us understand that scientific progress would not happen overnight, and he agreed with our thoughtful approach to funding research and the ever growing members of our board of directors.

Robert Pritzker was known worldwide in numerous financial and industrial sectors, but to us he was Bob, always there, always appreciated, always loved.

## “YOU DON’T LOOK SICK.”

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for ringing, but I’d still thank you for calling and inquire how I could help. If you didn’t know I was sick...I took great pains to make sure it stayed that way. There are days though when I just can’t fake it any more. On those days, I tend to hear that dreaded “but you don’t LOOK sick...” Also on those days my sarcastic side will often think (or sometimes say, depending on the audience) “And you don’t LOOK like a jerk...but I guess appearances can be deceiving, can’t they?”

Yes, it’s true that we don’t fit the picture in most people’s heads of what sick should look like, but trust me. While these illnesses may be invisible, the reality of our feelings is not.

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## CIGNA NOW COVERS PEGASYS

*by Felisse Sigurdson*

We’re thrilled to inform MPN patients that effective January 15, 2012, Cigna now covers Peginterferon Alfa-2a (Pegasys) for treatment of Polycythemia Vera (PV) and Essential Thrombocythemia (ET). For PV, approval is based on failure, contraindication, or intolerance to both phlebotomy and other myelosuppressive agents.

The change in Cigna’s coverage policy resulted from a request by the MPN Research Foundation to amend its coverage policy for Pegasys in light of the recent clinical trials showing the significant effectiveness in PV and ET patients.

Details of the coverage policy can be found at: [http://www.cigna.com/assets/docs/health-care-professionals/coverage\\_positions/ph\\_6003\\_coveragepositioncriteria\\_peginterferon\\_alfa\\_2a\\_pegasys.pdf](http://www.cigna.com/assets/docs/health-care-professionals/coverage_positions/ph_6003_coveragepositioncriteria_peginterferon_alfa_2a_pegasys.pdf)

Hopefully, this change will improve the coverage process and reduce the number of frustrating and time-consuming appeals for MPN patients insured by CIGNA who want to use Pegasys. The Foundation intends to replicate this process with other insurance companies who are frequently requiring patient appeals for Pegasys.

## UPDATES

### New York Symposium

In November the MPN Research Foundation and the Cancer Research and Treatment Fund co-hosted another symposium in New York City. Over 250 guests attended this daylong event, which included presentations by MPN experts and researchers, breakout sessions and a panel discussion.

### West Palm Beach Patient Symposium

In mid-January, the MPN Research Foundation hosted a symposium for the first time in West Palm Beach, Florida. Speakers included Dr. Ruben Mesa, Mayo Clinic-Arizona. Dr. Mesa’s presentation focused on how to overcome your MPN through proper treatments and lifestyle choices.

Dr. Ross Levine, from Sloan Kettering, shared his insights about genetic studies of MPNs currently underway in collaboration with Harvard researcher, Ben Ebert. Dr. Serge Verstosvek, from M.D. Anderson, explained the intricacies of clinical trials and why JAK2 inhibitors are safe and effective for some patients.

Dr. Robert Jacobson from the Palm Beach Cancer Institute shared his 40 year career in MPN research and in the clinic. Additionally, Board member Stephanie Cedric, who was an ET patient, shared her story and journey from diagnosis to remission.

Her father, Don Milts, gave a wonderful presentation about how he and his wife, Celia, also a Board member, started the non-profit Friends of ET Research to help raise money for MPN research. They have raised nearly \$1 million to date and continue to find ways to grow awareness and funds that they graciously donate to the MPN Research Foundation. (Note: Drs. Mesa and Levine are currently receiving funding for research projects from the MPN Research Foundation).

### Save the Dates

#### Upcoming Patient Symposiums

May 17<sup>th</sup> – San Mateo, California

September 20<sup>th</sup> – Chicago, Illinois

For more information visit our website at

**[www.mpnresearchfoundation.org](http://www.mpnresearchfoundation.org)**