THE MPD FOUNDATION
Annual Report: 2008

MPD FOUNDATION Searching for a cure for Myeloproliferative Disorders

INTRODUCTION

In 2008 intense focus on the JAK2 mutation (discovered in 2005) began to yield results for MPD patients as several JAK2 inhibitor compounds went into human trials in both Phase I and Phase 2 FDA testing. The MPD Foundation is proud to have supported much of the research which produced these results. In addition, the discovery of additional and potentially significant mutations guarantees that MPD researchers will continue to push the frontiers of knowledge of the MPDs in 2009 and years to come. This report summarizes the achievements made and opportunities identified in 2008 by the MPD Foundation and its researchers on behalf of all MPD patients.

MISSION

The MPD Foundation is a patient run organization whose primary mission is to stimulate and finance meaningful research in pursuit of new treatments and eventually a cure for the Philadelphia chromosome negative Myeloproliferative Disorders. The foundation values innovative and collaborative scientific investigation. In addition, the MPD Foundation serves as a resource to patients and their families to help them understand this relatively rare disorder, providing information about drug development, clinical trials and patient support activities.

The Philadelphia chromosome negative MPD's include polycythemia vera, essential thrombocythemia, and myelofibrosis.

PROGRAM SERVICE ACCOMPLISHMENTS FOR 2008

2008 saw the completion of Year 2 of the MPD Research Alliance, the MPD Foundation's innovative, collaborative effort to accelerate the development of treatments for the MPDs based on the discovery of the underlying JAK2 mutation in 2005. The three MPDRA researchers reported significant results at the end of Year 2, including the following:

- Dr. Gary Gilliland (Harvard) reported progress in the development of innovative mouse models for in vivo testing of new compounds. His most significant results this year used these mouse models to test candidate JAK2 inhibitors in collaboration with Dr. Ayalew Tefferi, who does similar testing on human cell cultures at the Mayo clinic. As a result of this successful collaboration an extremely promising drug (TG101348) is now in Phase 1 clinical testing.

- Dr. Ayalew Tefferi (the Mayo Clinic) reported that, in additional to his ongoing collaboration with Dr. Gilliland, he continued to build his database of cell and serum samples, which now includes tissues from more than 1,384 MPD patients. He continues to use these samples to further characterize MPD patients who are both JAK2 positive and negative.

- Dr. Ron Hoffman (Mount Sinai Medical Center) reported successful engraftment of high and low-burden JAK2 mutations in specially-developed NOD/SCID mice. In addition to studying the consequences of these different levels of mutation, he studied heterozygosity vs. homozygosity of the mutation and their implications.

Based on Year 2 progress, the Scientific Advisory Board of the MPD Foundation approved grant renewals to Drs. Hoffman, Tefferi and Gilliland. Year 3 of the MPD Research Alliance began on April 1, 2008.

The progress of JAK2 compounds in various stages of FDA testing continue to be of high interest to the MPD Foundation as well as to the researchers we support. Some of the first compounds to go into Phase 1 testing failed due to toxicity issues; at least 1 proceeded to Phase 2 testing which was close to completion at the end of 2008. Others are anticipated to continue Phase 1 and 2 testing in 2009. All clinical trials during 2008 were for MF patients specifically (i.e., not PV or ET).

Initial results of these tests are mixed. While some compounds alleviate symptoms (e.g., spleen size, itching), their effect on levels of JAK2 mutation have been less than hoped for. While development of JAK2 inhibitors continue, researchers agree that additional basic research must be done to understand the underlying causes of MPDs.

Some promising signs began to emerge late in 2008. Some existing FDA-approved drugs (e.g., pegylated interferon) are demonstrating results in tests with MPD patients, showing both symptom reduction and reduction of JAK2 allele burden. Also, scientists in the U.S. and Europe believe additional genetic targets, potentially affecting the hematopoietic stem cell, are on the near horizon. This news motivates the MPD Foundation to strive even harder to broaden the number of researchers studying the MPDs and to strengthen their focus.

EXPANDING THE FRONTIERS OF MPD RESEARCH

The MPD Foundation is proud of the accomplishments of the MPD Research Alliance, but believes that the number of questions still to be answered about the MPDs requires the attention of as many of the best minds as can be brought to bear on this subject. To that end, in 2008 the MPD Board of Directors decided to expand the number of researchers participating in the Research Alliance, to the level of our funding ability.

In addition, we believe that it is critical to encourage new minds to focus on this work. Eight years ago when the MPD Foundation was established few researchers were focused on these little-known, underserved disorders. The small group of researchers

who did concentrate on them struggled for funding and recognition, but their years of effort resulted in the stunning discovery of the JAK2 mutation in 2005.

Since that discovery, these researchers have been joined by an increasing number of scientists who have contributed to the wave of drug development activities we see today. But new investigators (or those wishing to change their area of scientific focus) find it increasingly difficult to fund their endeavors. While scientific advances in the understanding of the human genome and other aspects of microbiology continue to expand rapidly, funding for new researchers is shrinking dramatically; the National Institute of Health, the largest source of scientific career development grants in the U.S., has seen applications increase but success rates for those applications fall for the last 5 years. In this funding environment, it is difficult for new researchers to make the commitment that will ultimately benefit MPD and other patients.

The MPD Foundation believes that we need to invest in tomorrow's researchers today to ensure that today's discoveries turn into tomorrow's treatments. For that reason, the MPD Foundation determined in 2008 to begin a New Investigator grant program to encourage new investigators to focus on the MPDs. This new grant program is aimed at

- Emerging investigators who are considering a career related to research in the MPDs
- Established investigators in other fields who are interested in bringing their experience, skills and ideas to research in the MPDs

Calls for proposals for both the expanded MPD Research Alliance and the New Investigator grant program were issued by the MPD Foundation in July, 2008. The Foundation's Scientific Advisory Board reviewed proposals in November, 2008. The Board of Directors anticipates announcement of awards for both of these programs in early 2009.

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