

MPD Gene Mutation Discovered!

After years of searching, a major breakthrough.

- The first news came out on March 17, 2005: A team of researchers at the Cambridge Institute for Medical Research, UK, led by Dr. Tony Green, announced that they had discovered a single point mutation in the JAK2 gene that appeared in 97% of polycythemia vera patients they studied, in 57% of essential thrombocythemia patients and in 50% of patients with idiopathic myelofibrosis. The mutation was not detected in any of the control patients.

Only days later, on March 24, a team at Brigham and Women's Hospital in Boston, led by Dr. Gary Gilliland, reported almost identical findings.

Many readers of this Web site may have participated in the Boston study. Dr. Gilliland's team recruited more than 600 volunteers in a matter of weeks by posting a request at MPDInfo.org and on the MPD-Net listserve.

Anatomy of the discovery

- JAK2 actually isn't a gene. It's an enzyme called a tyrosine kinase, which acts as a molecular signaling pathway – essentially, an on-off switch – that triggers the generation of hematopoietic (blood) cells. The researchers believe that the mutation causes the switch to remain in an “on” position, thus causing the uncontrolled cell proliferation for which the myeloproliferative disorders are named. Tyrosine kinases have been implicated in many cancers, including CML.

JAK2 is also known as Janus protein tyrosine kinase. You can find plenty of references by looking up either one on Google, although most of the studies cited are earlier ones unrelated to myeloproliferative disorders.

What this means to MPD patients

It's big news! This is truly a major discovery that gives all MPD patients a great deal to be thankful for. The optimum result will be a drug that targets the JAK2 mutation, just as Gleevec targets the tyrosine kinase responsible for CML. That would mean better control of our counts, fewer side effects and healthier, longer lives.

However, researchers have a way to go before they can develop such a drug and demonstrate that it is both safe and effective in humans. Meanwhile, there may be opportunities to participate in clinical trials of any emerging treatment; Dr. Gilliland has announced that his team is still recruiting patients for the Boston trial. And since not all MPD patients have the JAK2 mutation, the team continues to search for other mutations that may be implicated in causing MPDs.

More information

The British study, "Identification of the Val617Phe JAK2 mutation lays the foundation for new approaches to the diagnosis, classification, and treatment of myeloproliferative disorders," by E. Joanna Baxter et al, appears in The Lancet, Volume 365, Number 9464, 19 March 2005. The full text is available at <http://www.thelancet.com/> for a fee of \$30.

Articles reporting the study results are available at

<http://www.medicalnewstoday.com/medicalnews.php?newsid=21467>

http://www.ivanhoe.com/channels/p_channelstory.cfm?storyid=10807

<http://www.washingtontimes.com/upi-breaking/20050317-105747-8880r.htm>

The Boston Study, “Activating mutation in the tyrosine kinase JAK2 in polycythemia vera, essential thrombocythemia, and myeloid metaplasia with myelofibrosis,” by Ross L. Levine et al, appears in Cancer Cell, Vol 7, Issue 4, 24 March 2005. Both an abstract and the full text are available free at cancer.org.

<http://www.cancer.org/content/article/abstract?uid=PIIS1535610805000942>

News stories announcing the discovery appear at

http://www.bio-itworld.com/news/032405_report7908.html

http://www.eurekalert.org/pub_releases/2005-03/hhmi-to1032405.php

<http://www.medicalnewstoday.com/medicalnews.php?newsid=21777>

All of the articles mistakenly classify MPDs as leukemias. Don't worry. The study doesn't say that. It's just that the job of reporters is to attract readers, and more people are likely to read an article with “leukemia” in the headline than one featuring “myeloproliferative disorders.”