

Personalized Medicine

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How the world looks for someone with glaucoma, which erodes peripheral vision.

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First published results from PMRP

Marshfield researchers have discovered a gene associated with positive response to the most inexpensive class of drugs prescribed for lowering pressure in the eye, according to the first published results of a study involving the Personalized Medicine Research Project (PMRP).

Persons with glaucoma and ocular hypertension who have a certain version of

the ADRB2 gene have a two-fold greater chance of clinically meaningful decrease in intraocular pressure following treatment with a topical (eye drop) beta-blocker.

Because these eye drops are relatively inexpensive, and people usually use them for many years, "this discovery could mean significant savings in healthcare dollars," said Lead Investigator Cathy McCarty, Ph.D., interim director of the Center for Human Genetics. "I am very excited to share our first results using PMRP with study subjects and the general community."

Dr. McCarty and colleagues have applied for a provisional patent to protect this

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From the Director



Cathy McCarty, Ph.D.

I am writing this column on a beautiful sunny day, the first official day of spring after a very snowy winter. With the new season comes news of new

projects. In the last newsletter, I told you about our exciting new grant from the National Human Genome Research Institute to study the genetic basis of cataracts and low HDL levels, and how those associations are modified by statin use and smoking. We have just learned that we have been awarded a grant from the National Heart Lung and Blood Institute, in collaboration with Dr. Uli Broeckel at the Medical College of Wisconsin, to study the genetic basis of heart attack. We have also received a grant from the Eagles Club with Dr. Russ Wilke from the Medical College of Wisconsin to investigate the role of genetics, diet and activity in the

development of diabetes and high blood cholesterol levels in people with body mass index 40 or greater. The Agency for Health Care Research and Quality has given us funds to study the genetic basis of response to Metformin used to treat type II diabetes. This study will be conducted with collaborators from the Medical College of Wisconsin, University of California San Francisco and Kaiser Permanente Georgia. More details to come in future newsletters.

With this newsletter, we present our first-ever results from a study using the Personalized Medicine Research Project (PMRP) database. As a reminder to PMRP participants, this newsletter is how you will see results of the genetic studies. We will not provide personal genetic data back to you. The study reported in this newsletter investigated the genetic basis of response to topical beta blockers used to treat glaucoma. The results have been published in a national medical journal and have led to a patent filing. The next step will be to evaluate these genetic

markers in a clinical setting and to assess the potential cost savings of implementing genetic-based prescribing.

We have two new Research Coordinators. Wendy Foth comes to us from the Clinical Research Unit, with many years' experience in oncology clinical trials. Wendy will recruit and enroll participants into PMRP. Carol Waudby moved with her husband to Marshfield from Columbia, Missouri. Her main responsibility is the new project funded by the National Human Genome Research Institute. We are delighted to have both on our team!

Finally, I thank Phil Hein for 5 ½ years of dedicated service as a founding member of the PMRP Community Advisory Group. In addition to replacing his position on the Board, we seek to expand membership to include other segments of the local community, specifically, a lawyer, someone in their 20s, a Saint Joseph's Hospital employee and a Clinic employee. Please see the article below and consider applying!

Community Advisory Group vital to success of PMRP

They advance genomic research and its role in health care, but they don't have degrees in medicine or science.

Realtor, editor, fire chief, legislator, pastor, farmer, homemaker, banker, teacher – they and others comprise the Community Advisory Group of the Marshfield Clinic Personalized Medicine Research Project (PMRP).

They were chosen for the advisory group precisely because they aren't scientists.

"From the beginning, the PMRP leaders knew they needed strong public understanding and cooperation to get participation," said Norman Fost, M.D., M.P.H., director of the Program in

Medical Ethics at the University of Wisconsin Medical School in Madison and chair of the PMRP Ethics and Security Advisory Board, which advises the PMRP on issues such as privacy and non-disclosure of personal genetic results.

The PMRP convened the Community Advisory Group before it began recruiting subjects in the fall of 2002. Since then, the group has met on a regular basis and is asked its opinions on medical, scientific, legal, ethical and social issues related to the PMRP. Most of the 18 members have been with the group since inception.

"In the first meeting, many of the community members expressed doubt as to what they could add to the discussion,"

recalled Cathy McCarty, Ph.D., Interim Director of the Center for Human Genetics.

"But by the third meeting they were so excited," Dr. McCarty said. "They saw how they could contribute by providing their perspective on the project in ways such as sharing feedback with the researchers on how to best convey information about the project's mission."

"I look forward to every meeting," said Mark Krueger, Pastor of Christ Lutheran Church in Marshfield. "What's impressive about the advisory group is the listening and caring ability of our community people, who give of their time and expertise and are willing to share their thoughts and ideas."

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The group meets two to three times per year. For their time, advisory group members are reimbursed for travel costs and given a modest stipend.

Like all members, Marshfield realtor Margy Frey enjoys getting a sneak preview of research before it is widely disseminated. But she said the most important function of the group is to help “get the word out and encourage people to participate.”

During a typical meeting, Dr. McCarty briefs the group on research results and progress, as does one of the other PMRP researchers in their specific area (e.g., osteoporosis, fibromyalgia, breast cancer,

glaucoma). Dr. McCarty then poses a question to the group, and lively discussion usually ensues, with group members asking questions and giving feedback that will help PMRP leaders better communicate with PMRP enrollees and the general public.

ADDITIONAL MEMBERS SOUGHT: The PMRP seeks to broaden the representation on the Community Advisory Group by adding a lawyer, a person in their 20s, a Saint Joseph’s Hospital employee and a Clinic employee. To inquire or nominate someone, please contact the PMRP at 715-389-7733. We need your help!



The Community Advisory Group at a recent meeting, front (from left): Phil Hein, Jodie Gardner, Rev. Mark Krueger, Phil Boehning, Jean Schwanebeck, Colleen Kelly. Back row (from left): Julie Levelius, Teresa Derfus, Jerry Minor, Mike Kobs, Darlene Krake. Not pictured: Tom Berger, Mike Paul, Sharon Bredl, Margaret Brubaker, Nancy Kaster, Norm Kommer, Marlin Schneider, Scott Schultz.



National DNA Day was established to commemorate the completion of the Human Genome Project in April 2003, and the discovery of DNA’s double helix. The National Human Genome Research Institute (<http://www.genome.gov/>) uses this day to encourage students, teachers and the general public to learn more about genetics and genomics.

Genetics counselor honored by March of Dimes

Marshfield Clinic genetics counselor Christina Zaleski, M.S., was named the 2007 Community Service winner for the March of Dimes’ “Saving Babies Together” leadership award.



Christina Zaleski, M.S.

Zaleski’s work resulted in development of brochures and posters that explain proper protocol for assessing genetic counseling for families of high-risk newborns or families who have had miscarriages, a stillbirth or other infant death. The work was funded by a March of Dimes grant to Marshfield Clinic Research Foundation (MCRF).

Zaleski is a Marshfield-area native who earned a bachelor’s degree from the University of Wisconsin-Eau Claire and master’s degree in human genetics/genetic counseling from Sarah Lawrence College in New York.

Congratulations Christina!

We keep growing

The PMRP had enrolled 19,692 subjects as of April 5, 2008. Enrollment is open to anyone age 18 and older living in Abbotsford, Arpin, Auburndale, Blenker, Chili, Colby, Dorchester, Granton, Greenwood, Hewitt, Loyal, Marshfield, Milladore, Pittsville, Spencer, Stratford, Thorp, Unity or Vesper. Contact the PMRP at 1-888-334-2232 or 715-389-7733.

Participants sought for survey on diet, activity

We seek PMRP participants interested in completing a diet and physical activity questionnaire so that we can better understand the relationship between these factors, genetics and disease. We will compensate you with \$10. If you are enrolled in the PMRP and are interested, contact the PMRP at 1-888-334-2232 or 715-389-7733.

Gene associated with positive response to glaucoma drugs

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discovery. Next steps include an evaluation of additional commonly prescribed medications, as well as a prospective study of the potential economic impact of gene-based prescribing on health care costs for glaucoma.

The study included nearly 20,000 adults enrolled in the PMRP. Topical beta-blockers were prescribed for 253 PMRP subjects, and it was this group that was genotyped. The overall rate of glaucoma in PMRP enrollees ages 50 and older was 2.07 percent, and the rate of treated ocular hypertension was 1.42 percent.

Among the findings:

- A 20 percent or greater reduction in intraocular pressure in one or both eyes was observed in 61 percent of the subjects.
- Males were significantly more likely to have either one or both eyes respond with a 20 percent or greater drop in intraocular pressure (69.3 percent vs. 54.9 percent of women).
- Over a 20-year period, beta-blockers went from being the most commonly prescribed medication to the second-most common.

The implications are potentially far-reaching, said co-investigator Richard Patchett, M.D., a Clinic ophthalmologist.

"We may find ourselves able to target glaucoma therapy on a more personal level in the future as we find genetic profiles that tell us which medications are most likely to work for a given patient," Dr. Patchett said.

Dr. McCarty and co-investigators Dr. Patchett; Russell Wilke, M.D.; and James Burmester, Ph.D.; were funded by National Glaucoma Research, the American Health Assistance Foundation.

Glaucoma is a group of diseases that can damage the eye's optic nerve and result in vision loss and blindness. Glaucoma occurs when the normal fluid pressure inside the eyes slowly rises. An estimated 2.2 million Americans have been diagnosed with glaucoma, and an additional 2 million do not know they have it. Untreated, people with glaucoma will lose their peripheral (side) vision until it appears to them as if they are looking through a tunnel. Blindness can result. Early detection and treatment are key to preventing vision loss. Everyone over the age of 40 should have an eye exam at least once every two years. For more information, go to the National Eye Institute Web site, www.nei.nih.gov.

Contact Us

This newsletter is a publication of the Personalized Medicine Research Project, Marshfield Clinic Research Foundation, 1000 N. Oak Ave., Marshfield, WI 54449-5790.

To contact the PMRP, phone 1-888-334-2232 or 715-389-7733, or visit the PMRP on the Web at <http://marshfieldclinic.org/chg/pages/default.aspx>.

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