

Personalized Medicine

Research Project



The Personalized Medicine Research Project (PMRP) has several groups to help guide it. The Ethics and Security Advisory Board met in Marshfield in July, 2009. Attending were (from left): Cathy McCarty, Ph.D., PMRP Principal Investigator; Warner Slack, M.D., Harvard University; Geraldine McQuillan, Ph.D., Centers for Disease Control and Prevention; Norman Fost, M.D., M.P.H.; University of Wisconsin (chair); Jon Merz, J.D., Ph.D., University of Pennsylvania; Karen Rothenberg, J.D., M.P.A., University of Maryland; Jeffrey Botkin, M.D., University of Utah.

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Project nears 20,000

Sometime this winter, the 20,000th person will join the Personalized Medicine Research Project. Marshfield Clinic researchers began recruiting voluntary participants in 2002 and reached 15,000 early in 2004. Participants mostly live in one of 19 ZIP codes from these communities: Abbotsford, Arpin, Auburndale, Blenker, Chili, Colby, Dorchester, Hewitt, Marshfield, Milladore, Pittsville, Spencer, Stratford, Unity, Vesper, Granton and Thorp.

External boards advise PMRP on complex genetics issues

Like an airline pilot checking in-flight data, the Personalized Medicine Research Project (PMRP) at Marshfield Clinic monitors feedback from several external advisory groups as it navigates the ever-changing horizon of human genetics.

The largest population-based genetic research project in the United States solicits feedback via a system that includes:

- Community Advisory Group
- Ethics and Security Advisory Board
- Scientific Advisory Board
- Focus groups

(Advisory group members are listed online. Go to <http://www.marshfieldclinic.org/chg/> and click "Personalized Medicine Research Project" and then "Advisory Boards" in the righthand directory.)

The Community Advisory Group was a unique concept in 2002 when it was established to advise the PMRP. Other genetic research projects nationwide have followed suit, some after consulting with and visiting PMRP personnel, and observing firsthand the project interaction with the Community Advisory Group. The group is comprised of 20 central Wisconsin residents from various walks of life. The group provides a direct link to the community at-large, and helps facilitate public understanding and participation in the project. The group meets regularly to discuss questions regarding medical, scientific, legal, ethical and social issues.

The Ethics and Advisory Board, chaired by Norman Fost, M.D., M.P.H., University of Wisconsin Medical School, consists of recognized experts in fields of bioethics,

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From the Director



Cathy McCarty, Ph.D.

Welcome to our revised PMRP newsletter! Based on comments from our Community Advisory Group and from focus group participants, we have revised the study newsletter to better meet your

needs. Since we do not send personal genetic results back to you, nor enter any research results into your medical record, this newsletter is our way to tell study participants about ongoing studies using the PMRP database and to seek your input on any proposed study protocol changes. We are busy working on approximately 20 projects using the PMRP database. Some are mentioned in the "News in Brief" section. We will plan to have a summary table on all active projects in our next newsletter.

We received some of the federal economic stimulus funds in the form of research grants. We are involved in a consortium to study the effectiveness of KRAS genetic testing for metastatic colon cancer. KRAS is a protein that performs an essential function in normal tissue signaling, which coordinates the production and renewal of parts of your body. But mutated KRAS genes play a role in a number of cancers.

PMRP scientists continue to be asked to speak at national and international meetings. Several posters were presented at the annual meeting of the American Society of Human Genetics in Hawaii in October. A poster was presented at the inaugural meeting of EGAAP (Evaluation of Genomic Applications in Practice and Prevention), a Centers for Disease Control and Prevention initiative, in Michigan at the end of October. We also were represented at the PRIMR (Public Responsibility in Medicine and Research) conference in Nashville in November.

We'd like to welcome Murray Brilliant, Ph.D., as the new director of the Center for Human Genetics, and first holder of the Dr. James Weber Endowed Chair of Human Genetics. Dr. Brilliant will serve on the PMRP Oversight Committee. (Please see story on page 4.)

PMRP enrollment is still open. If you know anyone who is 18 years or older and lives in one of the 19 Zip codes around Marshfield and would like to participate in PMRP, please tell them to stop by the Lawton Center on the Marshfield campus or to call our toll free number, 1-888-334-2232 or 715-389-7733. In addition to our general recruitment, we are specifically recruiting women with endometriosis who live in Wisconsin and use the Marshfield Clinic for their health care.

I want to take the opportunity to thank all PMRP participants. Our research would not be possible without you! I wish you all a wonderful holiday season.

News in Brief



New Studies

- A study to identify genetic predictors of **ACE inhibitor-associated angioedema** is underway. ACE inhibitors are a group of drugs used primarily in the treatment

of hypertension and congestive heart failure. In some people, these drugs can cause an allergic reaction characterized by swelling of skin around the mouth, tongue and throat. In severe cases, breathing can be cut off. This is a genome-wide association study, meaning it examines genetic variation across the entire human genome. Cathy McCarty, Ph.D., is Principal Investigator at Marshfield, and Nancy Brown, M.D., is Principal Investigator at Vanderbilt University. Since 35-40 million people take ACE inhibitors worldwide, the number of people at risk for this drug side effect is substantial.

- A study has been initiated to determine whether genetic variations are associated with the risk of an **allergic reaction to the antibiotic drug sulfamethoxazole (SMX)**. The Principal Investigator is Cathy McCarty, Ph.D., and the Co-PI is Steven Yale, M.D. The study is funded by the University

of Wisconsin Institute for Clinical and Translational Research.

In Print

- A paper recently published in the journal *Pharmacogenomics* concludes from a PMRP study that a common genetic variation in vitamin D-dependent signaling is associated with **congestive heart failure** in patients with hypertension. Lead author is Russell Wilke, M.D. The study's Principal Investigator is Cathy McCarty, Ph.D.
- A recently published study using PMRP participants indicated that variation in two particular genetic markers was associated with risk for **osteoporosis** in women, with one of the markers showing an association only in smokers, suggesting a role for environmental interaction. Principal Investigator and lead author Philip Giampietro, M.D., published the study in the journal *Osteoporosis International*.

External boards advise PMRP on complex issues *(continued from page 1)*

law, theology, education, medical ethics, and clinical computing and information security. This board advises the PMRP on issues such as informed consent and non-disclosure of personal genetic results.

The Scientific Advisory Board is chaired by David Altshuler, M.D., Ph.D., Assistant Professor of Genetics and Medicine, Harvard Medical School. The board advises the leadership of the Marshfield Clinic Research Foundation on research design and scientific matters associated with the Personalized Medicine Research Project

In addition, the PMRP occasionally consults with a local private marketing firm to convene focus groups of project participants to address specific questions.

"The advisory groups play a key role in tempering research efforts with frank and open discussions about the research, methodologies, and decisions that are being made within the PMRP," said Community Advisory Group member Mathew J. Bartkowiak, Ph.D., University of Wisconsin-Marshfield/Wood County assistant professor of English.

Adapting to Change

These advisory boards allow the PMRP to adapt to unforeseen issues, and provide the PMRP flexibility to grow.

Take the question of ethical and appropriate usage of tissue samples, which came up in late 2008.

Technology is now available to analyze the DNA material in stored clinical tissue samples, potentially unlocking a wealth of information that can lead to new treatments and diagnostic tests. But stored tissue samples were not part of the original consent form signed by PMRP participants at enrollment. Did this mean additional consent on the matter of tissue should be obtained from all participants? The ethics board might have said "yes." But the Community Advisory Group asked for the opinions of project participants through an article in this newsletter. Response from readers was overwhelmingly positive to include all possible tissue samples. In fact, many individuals called the contact number to give specific days on which procedures were done to ensure that no sample would be missed. Given the response, it was decided that re-consent was not necessary.

Different Perspectives

The advisory groups don't always agree, and that's seen as healthy by Cathy McCarty, Ph.D., Principal Investigator of the PMRP. The ethics board and Community Advisory Group met face-to-face for the first time in July 2009. The meeting led to an enhanced mutual respect for the groups' respective roles.

"That was an historic meeting for us," Dr. McCarty said. "And it led to comments from most of the ethics board

members about the effectiveness of the Community Advisory Group and the amazing support of the community in general for the Personalized Medicine Research Project."

Community Advisory Group Member Jodie Gardner, a project manager at Saint Joseph's Hospital, said the July meeting helped both advisory groups better understand where the other was coming from.

"The ethics board members tend to live in big cities and what I think they learned from us is that there is a lot of trust in Marshfield and the surrounding communities for Marshfield Clinic," Gardner said.

As the number of PMRP participants edges toward 20,000, Dr. Bartkowiak said he is "impressed with the project's efforts to have our population maintain a strong voice in the discussions."

Additional reading: "Community consultation and communication for a population-based DNA biobank: the Marshfield clinic personalized medicine research project." McCarty CA, Chapman-Stone D, Derfus T, Giampietro PF, Fost N; Marshfield Clinic PMRP Community Advisory Group. *Am J Med Genet A.* 2008 Dec 1;146A(23):3026-33.

Genetics physician named Wisconsin Stillbirth Service project director



Elizabeth McPherson, M.D.

Elizabeth McPherson, M.D., a medical genetics specialist at Marshfield Clinic, was recently named director of the Wisconsin Stillbirth Service Program (WiSSP). Dr. McPherson replaces Richard

M. Pauli, M.D., Ph.D., a nationally recognized expert in stillbirth assessment and related fields. Pauli founded WiSSP and served as its director from 1983 until March 2009.

Since 1983, the program has provided a statewide service to families who experience stillborn births and the health care providers who help those families. Over 70 hospitals across the state are affiliated with WiSSP.

GINA takes effect

On November 21, 2009, the Genetic Information Nondiscrimination Act (GINA) of 2008 went into effect. This Act is intended to prevent employers and health insurers from discriminating against individuals based on genetic tests and information. GINA requires that covered entities obtain and post notices informing covered individuals of their rights under the law. For more information, go to <http://www.genome.gov/10002077>.

Human Genetics director named



Murray Brilliant, Ph.D.

Murray Brilliant, Ph.D., has been named director of the Marshfield Clinic Research Foundation Center for Human Genetics, and is the first holder of the Dr. James Weber Endowed

Chair in Human Genetics.

Dr. Brilliant comes to Marshfield from the University of Arizona School of Medicine in Tucson, where he was Lindholm Professor of Mammalian Genetics and chair of the Graduate Interdisciplinary Program in Genetics. He previously was a member of the Institute for Cancer Research in Philadelphia, an associate staff scientist at The Jackson Laboratory in

Bar Harbor, Maine, and a postdoctoral research associate in the Tufts University Neuroscience Program.

"I had heard of the excellent work being done at the Foundation," he said, "and the more I found out about the Personalized Medicine Research Project, the more excited I became."

James Weber, Ph.D., was a research scientist at the Foundation from 1986 to 2005. He is credited with helping to revolutionize the study of human genetics.

Dr. Brilliant replaces Cathy McCarty, Ph.D., who had been serving as acting director of the Center for Human Genetics. Dr. McCarty is Principal Investigator of the Personalized Medicine Research Project.

Dr. Brilliant will serve on the PMRP Oversight Committee, the final committee to approve access to the PMRP biobank after scientific and ethical approval.

Resistant hypertension selected for study

The eMERGE network has chosen resistant hypertension for its cross-site phenotype. Resistant hypertension is defined as high blood pressure that does not come down after three or more blood pressure medications. An additional 2,000 people are to be genotyped across the network, including perhaps 500 from Marshfield. "This means that we will have close to 5,000 people with full whole genome genotyping, allowing us to investigate many different outcomes," said

Cathy McCarty, Ph.D., Principal Investigator of the PMRP. The eMERGE Network is a national consortium formed to conduct research that combines DNA biorepositories such as Marshfield's Personalized Medicine Research Project with electronic medical record systems for large-scale genetic research. Network members are: Marshfield Clinic, Mayo Clinic, Group Health Cooperative with the University of Washington, Northwestern University and Vanderbilt University.

Contact Us

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