

Personalized Medicine

Summer 2005 • Volume 1, Number 1



Inside

From the Director 2

Five Ws can answer questions about family health risks 2

Question & Answer 3

Hewitt residents most likely to say 'yes' to PMRP enrollment 3

In the media 3

How informed are those who give 'informed consent' 3

Peer-reviewed publications 3

Alzheimer's study benefits from Personalized Medicine project

It is estimated that by 2025 the United States and its aging population will experience a 44 percent increase in Alzheimer's disease.

Currently, there is no cure for Alzheimer's disease, but "there are many clinical trials in progress that hopefully within the coming 5-10 years will lead to a cure," said Nader Ghebraniou, Ph.D., head of the Clinic's Molecular Diagnostics Laboratory.

Dr. Ghebraniou is leading a study on Alzheimer's based on data from the Personalized Medicine Research Project (PMRP). The objective of the study is to identify common genetic information carried by people with Alzheimer's, and also to learn more about the biology of Alzheimer's and environmental factors that might influence whether a person gets the disease.

Study results could help lead to early individual screening and detection. Although there is no cure for Alzheimer's, there are five FDA-approved drugs that can control symptoms.



MARSHFIELD CLINIC®
Research Foundation

Continued on page 4

From the Director



Cathy McCarty, Ph.D.

You may (or may not!) have been wondering what we have been up to since you enrolled in the Personalized Medicine Research Project (PMRP). In this first newsletter,

you can read about how PMRP data are being used in the Alzheimer's disease project. Hopefully we can share some results with you in the next newsletter.

The PMRP has received a lot of attention in newspapers (local, state and national)

and scientific articles. Dr. Francis Collins, director of the National Human Genome Research Institute at the National Institutes of Health, identified the PMRP as the future for genomic research. Dr. Muin Khoury, director of the Office of Genomics and Disease Prevention at the Centers for Disease Control and Prevention (CDC), recently wrote that projects such as the PMRP are, "among the most ambitious plans to make use of the information stemming from the Human Genome Project."

I was honored to be asked by Dr. Khoury to participate in a two-day meeting at the CDC in Atlanta in February to discuss the

PMRP and meet with other scientists from the U.S., Canada, England, Estonia, and Germany who are conducting, or are hoping to conduct, studies similar to ours. As a result of this meeting, I hope to collaborate with a German scientist to study the genetics of obesity. This will be particularly interesting because 78 percent of the PMRP participants report German ancestry.

News flash! I just received word from the American Health Assistance Foundation that they have awarded us \$90,000 to study the genetic basis of response to eye drops to lower pressure in the eyes for people with glaucoma.

Five Ws can answer questions about family health risks

In some ways, questions asked and answered by Marshfield Clinic's Department of Medical Genetics are no different than basic journalism: who, what, when, where, and why?

Who: Individuals of all ages who are concerned about their own health or that of other family members.

What: Gathering information, assessing genetic risks, educating, offering testing, providing support and counseling, referring as needed to other specialists and services.

When: At the time of a diagnosis for themselves or a loved one, or when considering risks of other family members, including unborn children.

Where: Marshfield Clinic Department of Medical Genetics, which includes two medical geneticists and three genetic counselors.

Why: To help clarify risks, provide a diagnosis for unexplained symptoms, provide information and services for family members, and identify a new need for specialized care.

Many people seen in Medical Genetics are concerned about problems within their families, according to Medical Geneticist Philip F. Giampietro, M.D., Ph.D. Once



information is gathered about the family, some choose to have testing done while others do not.

Some may decide at a later date if they want to know if they or their children have a greater risk for a medical problem, such as breast cancer, Huntington's disease or others with confirmed genetic links.

"It is an individual choice whether they go through with testing," Dr. Giampietro said.

Understanding a risk can help reassure parents or prepare them for what is ahead. Knowing about medical conditions of an unborn infant can ready medical providers.

"If you know a baby has Down's syndrome and has heart problems, you can have a cardiologist ready to take care of the baby," he said.

Medical genetics also sees adults with unusual combinations of symptoms seeking a diagnosis. Other times, even before symptoms develop, genetic information alerts providers to look out for and manage genetic conditions.

"We can offer tests that could help make diagnoses and help influence patient management for different adult conditions," Dr. Giampietro said. "If we know a patient is at risk for developing tumors and cysts in the kidneys, we can make sure not to put the blinders on. We can look for that condition."

Genetics tests are not a substitute for counseling, however. "People need to be referred to Genetics for counseling, whether or not testing is done," Dr. Giampietro said.

"My role is to help explain complex genetic information to the family," said Genetics Counselor Christina Zaleski, M.S. "There are many emotional issues that go along with making a diagnosis that we need to be sensitive to."

Online: A family history is the simplest, most cost-effective way to begin to understand your family's health risk. A worksheet is available at: http://www2.marshfieldclinic.org/family_history/MCFamHealthHistory.pdf.

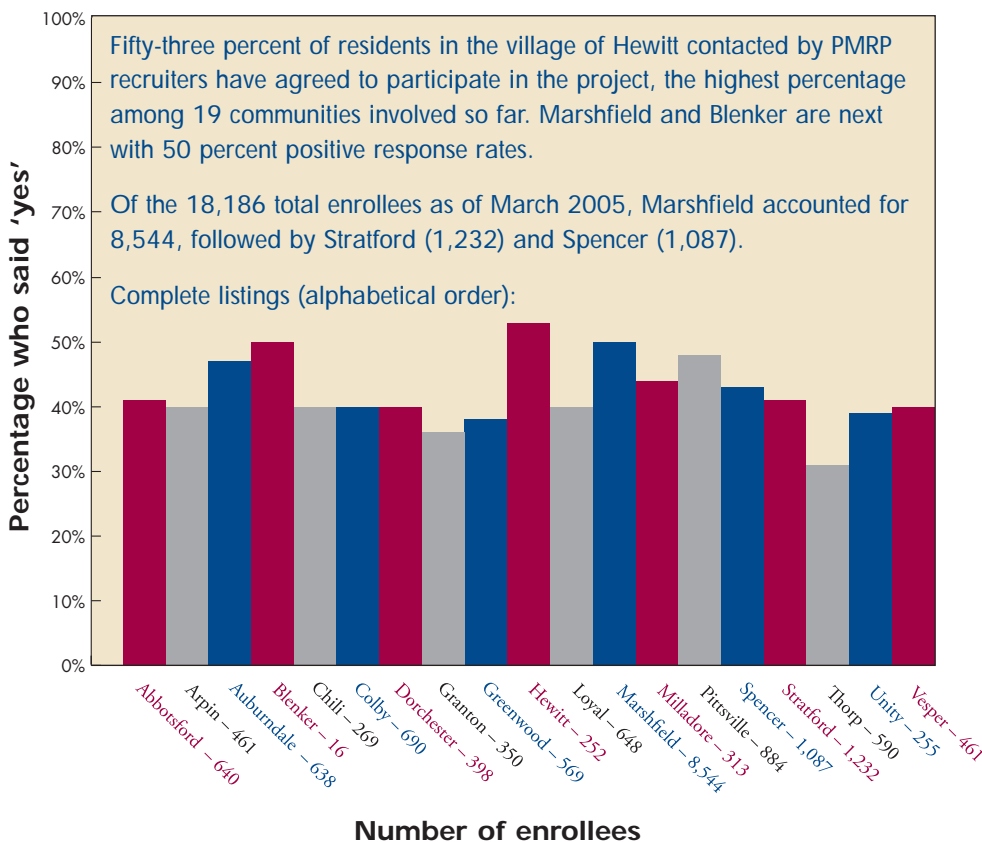
Q & A

Question: How did you get my name? How did you pick me?

Answer: You've been invited to participate in the Personalized Medicine Research Project if you live in a geographical area selected for this project, are at least 18 years of age and receive health care at any Marshfield Clinic center. Recruitment so far has concentrated on 19 ZIP codes in central Wisconsin.

The scientific value of this project, as with other long-term studies of the health of a population, increases as the percentage of the population that participates increases. Therefore, the project's goal is to enroll as many adult residents of the study area as possible. In the future, it is anticipated that the project will incorporate a northern study area of 10 ZIP codes including towns such as Park Falls, Phillips and Ladysmith.

Hewitt residents most likely to say 'yes' to PMRP enrollment



Note: Enrollment is still open to anyone age 18 and over living in these communities. Please call the PMRP at 888-334-2232 or 715-389-7733.

In the media

Articles mentioning or featuring the PMRP have appeared in numerous mainstream media publications, including Parade Magazine, Chicago Tribune, Madison Capital Times, Marshfield News-Herald, New York Times, Pittsville Record, Milwaukee Journal-Sentinel, Minneapolis

Star-Tribune, San Diego Union-Tribune, San Jose Mercury News, Wausau Daily Herald and the Wisconsin State Journal, in addition to the science journals Nature and the New England Journal of Medicine.

How informed are those who give 'informed consent'

Researchers, such as those working on the PMRP, take great pains to make certain that study recruits understand the project they are volunteering for. But do participants truly absorb the sometimes extensive information?

Cathy McCarty, Ph.D., posed that question in a spinoff study from the PMRP.

Questionnaires were sent to nearly 1,600 participants. More than 900 were returned (58 percent). Results showed that although the majority of study participants had a good level of understanding and knowledge of the purpose of the PMRP and did not feel undue coercion to participate, a large number of participants did not demonstrate an understanding of key issues related to the PMRP. Women answered a higher percentage of questions correctly than men, and younger people scored better than older respondents.

"Research coordinators may need to take more time informing males and older individuals about project details so that they are making truly informed decisions about study participation," Dr. McCarty said. "An important point missed by many participants is that they will not get individual genetic information returned to them."

Peer-reviewed publications

A manuscript based on the PMRP and describing, "Design, Methods and Recruitment for a Large Population-Based Bio-Bank," has been published in the science journal Personalized Medicine (Volume 2, No. 1). Authors are Catherine McCarty, Ph.D.; Russell Wilke, M.D., Ph.D.; Philip Giampietro, M.D., Ph.D.; Steve Westbrook, Ph.D.; and Michael Caldwell, M.D., Ph.D.

Did you know?

10 percent of chronic diseases (heart, diabetes, arthritis) have a significant genetic component, and 12 percent of adult hospital admissions are for genetic causes.

Alzheimer's study benefits from Personalized Medicine project

(continued from page 1)

"Understanding which genes and environmental factors are involved in the disease may help better target the disease with specific drug medications that affect these particular pathways," Dr. Ghebranious said.

Like all projects related to the PMRP, the Alzheimer's study is based on linking an individual's genotype (internally coded, inheritable information) to phenotype (observable traits such as the presence or absence of a disease), and also considering the influence of environmental exposures (smoking, use of cholesterol-lowering statin drugs).

Currently, researchers are in the phenotyping stage: they are combing anonymous medical charts of PMRP volunteers ages 65 and older to find individuals diagnosed with Alzheimer's. Researchers are also recruiting additional Alzheimer's cases from nursing homes through the PMRP. Typically, 80 to 90 percent of nursing home residents have Alzheimer's.

Individuals who do not have Alzheimer's are being recruited through the PMRP to serve as control cases.

The goal is to enroll 150 Alzheimer's patients and 300 control patients.

"Once the phenotyping phase is complete, we will start with the genotyping phase where we identify genetic markers that associate with the disease," Dr. Ghebranious said. "We are also collecting environmental exposure information on all cases and controls.

"Eventually, data collected from phenotyping, genotyping and environmental exposure phases of the project will be put into a model to predict the risk for future development of Alzheimer's," Dr. Ghebranious said.

A secondary aim is to use data on smoking and alcohol intake and the use of statins (medications to lower blood cholesterol) among index cases and controls, two environmental factors that may represent risk factors for Alzheimer's.

Co-investigators on the study include: Catherine McCarty, Ph.D.; Philip Giampietro, M.D., Ph.D.; Susan Mickel, M.D.; Russell Wilke, M.D., Ph.D.; and Christa Brown-Switzer, D.O.

Alzheimer's is one of several disorders that causes the gradual loss of brain cells. It is the leading cause of dementia, an umbrella term for several symptoms related to a decline in thinking skills.



PMRP Advisors

Tom Berger
Marshfield

Sharon Bredl
Stratford

Margaret Brubaker
Stratford

Margy Frey
Marshfield

Jodie Gardner
Spencer

Phil Hein
Stratford

Norm Kommer
Colby

Darlene Krake
Marshfield

Julie Levelius
Stratford

Jerry Minor
Pittsville

Mike Paul
Auburndale

Marlin Schneider
Wisconsin Rapids

Scott Schultz
Loyal

Jean Schwanebeck
Pittsville

Mike Warren
Colby

Diana Wilcott
Marshfield