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Marshfield Clinic
Research Foundation

Personalized Medicine
Research Project

PMRP is part of a network to study the genes for glaucoma

Marshfield Clinic has joined with 15 other research teams in the United States to study the genes for glaucoma, a serious eye disease that can cause blindness. This network of research teams (known as NEIGHBORHOOD) will focus on the most common type of glaucoma, primary open-angle glaucoma. Murray Brilliant, Ph.D., heads the project at Marshfield Clinic, while Cathy McCarty, Ph.D., is a collaborator. The NEIGHBORHOOD network receives funding from the National Eye Institute.

Primary open-angle glaucoma typically happens when the drainage canals of the eye become blocked over time. The correct amount of fluid cannot drain out of the eye causing the pressure of the inner eye to rise. The disease develops slowly and is painless. Most people have no symptoms and no early warning signs. Often, the patient does not realize that he or she is slowly losing vision until the later stages of the disease. However, by this time, any lost sight cannot be restored. There is no cure at present, but the progress of the disease can be slowed if the disease is detected early and treated.

Glaucoma is the second leading cause of blindness in the world. Over 2.2 million Americans have glaucoma but only half know they have it. In the United States, more than 120,000 persons are blind from glaucoma. Everyone is at risk for getting glaucoma but it occurs mainly in people over the age of 50 years. Persons with diabetes, who are severely near-sighted, or who have family members diagnosed with glaucoma are also at higher risk for getting glaucoma.

By identifying the genes that increase our chances of getting glaucoma, the NEIGHBORHOOD network hopes to find out more about the events in our bodies that cause the disease to occur. This information could help researchers prevent the disease, create screening tests to detect the disease in its early stages, and develop methods of treatment for the disease.

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Inside

From the Director, Center for Human Genetics

Murray Brilliant, Ph.D.

Recently, I attended three different scientific meetings in three weeks. The lesson learned from each of these three meetings is that genetics is very important in our health and health care. Our genes help to determine what kind of person we are. They control how tall we can be, what our hair and eye hair color will be, and other features that we can see. They also determine what we can't see- how our body works inside, including how well we fight infections, how well we tolerate certain drugs and what our risks are for certain diseases. To be able to focus the right health care to the right person, we need to take into account each person's genes and we need effective government policy and research.

The first meeting in my three meeting tour was "Genomic Medicine 5", a planning meeting, sponsored by the National Institutes of Health in Bethesda, Maryland. This meeting was the fifth in a series of meetings to bring together leaders in Personalized Medicine to discuss and plan for the future. The focus of this meeting was to uncover and sort out what federal government agencies are doing in this field. Representatives from various federal agencies were in attendance, including: Centers for Disease Control and Prevention, Centers for Medicare and Medicaid Services, Department of Veterans Affairs, Food and Drug Administration, National Cancer Institute, National Human Genome Research Institute, Office of the Assistant Secretary for Health, Office of the Assistant Secretary for Planning and Evaluation, Presidential Commission for the Study of Bioethical Issues, US Air Force Medical Support Agency, US Army Medical Corps, US Coast Guard, and US Navy Bureau of Medicine and Surgery, among others. Agreement was reached that federal agencies should work together to use genomic technology to improve health care in a way that maximizes health benefits, minimizes costs and inefficiencies, avoids harms, and ensures equitable access. We also agreed on the need to provide strong evidence that supports the use of genomic information to improve health care and outcomes, the need to have standards for use of genomic information in health care and the need to harmonize our health care records. This was very encouraging to those of us who are working to personalize and improve health care using genetic information.

The second meeting was with the eMERGE National Network (that PMRP is part of) in Philadelphia. At this meeting, the nine sites that make up the eMERGE Network discussed our progress and plans for future research. Some of the highlights discussed at the meeting were individual studies that have uncovered genetic variants that are associated with dozens of diseases, progress towards implementation of genetic testing for how a person might respond to different drugs (see the article on this in this issue), and plans for future funding for the eMERGE Network.

The third meeting was held in Cork, Ireland on "Hereditary Hemorrhagic Telangiectasia" or HHT, a rare genetic disease affecting blood vessels. I serve on the HHT Global Research Medical Advisory Board and presented the case of a Marshfield Clinic patient with HHT who was given a common drug that led to a severe adverse drug reaction that could have been avoided with proper genetic testing. HHT is a great example of the value of genetic testing. It is often undiagnosed, but if known, there are relatively easy tests and procedures that can allow people with HHT to lead healthy lives.

These three meetings give me hope that one day soon, we will routinely evaluate each patient for genetic variants that will help us guide that person's specific health care. You, the people who volunteered for PMRP have made achieving that goal a little closer. Thank you.

From the eMERGE Principal Investigator

Cathy McCarty, Ph.D.

We've been setting weather records ever since I moved to Duluth two years ago. Last summer we experienced a 500-year flood that left many of the streets in need of repair. In April this year, we had 51 inches of snow, not just a record for the month of April, but an all-time record for ANY month in Duluth! Like the weather in Duluth, we are setting records with eMERGE. We are definitely the first network of researchers working together to use electronic medical records to identify who has disease and then combining de-identified data across sites to conduct significant genetic research. This collaboration to increase the number of subjects in studies has allowed us to make novel genetic discoveries.

eMERGE was originally funded by the National Human Genome Research Institute (NHGRI) for four years, with no anticipation of additional funding. Because of the many successes in phase 1, NHGRI made funds available for a second phase of four years and we were successful when we applied for the grant. We are just starting the third year. Our Project Officer at NHGRI started talking about the possibility of a third round of funding for eMERGE. There will be a one-day meeting in January 2014 (on my birthday!) with outside experts to review our progress and make recommendations about the direction for phase three, if there is one. Stay tuned.

I want to thank this opportunity to acknowledge the contributions of Dr.

The Pharmacogenetics Research Project (PGx)

Pharmacogenomics is the study of how a person's genetics (DNA) affects the body's reaction to drugs (medicines). It is the hope that, one day, medicines will be chosen for each person based on their own genetic makeup. Our response to medicines can be affected by our age, lifestyle, what we eat, where we live and our state of health. A person's genetic makeup is also key to prescribing medicines that **work better** and are **safer** for you.

Through the eMERGE Network and the Pharmacogenomics Research Network, we have begun to recruit Marshfield Clinic patients for a project (PGx) that aims to help doctors to reduce unwanted drug reactions. This project will identify specific genetic variants that affect how medicines work in our bodies (pharmacogenetic variants). Murray Brilliant, Ph.D., oversees PGx at Marshfield Clinic and can be seen discussing the project at www.myresults.org/.

We will enroll people into the study if they are not currently taking any of the following medicines: simvastatin (Zocor), clopidogrel (Plavix), and warfarin (Coumadin). DNA from participants will be tested to see if participants have any pharmacogenetic variants that cause these drugs to be harmful to our bodies. Then, if, in future, doctors should need to prescribe one of these medicines for participants, this genetic information will be available to help doctors prescribe the correct medicines that will work safely in the body. Each person's genetic result will be placed in their electronic health record, along with advice to their doctor that shows up at the time that one of these medicines is prescribed. Doctors will take this advice into account in their overall plans for care of the patient.

We are well on our way to our goal of recruiting 750 participants for this study. We hope that this study will pave the way to expand this to all Marshfield Clinic patients in the future as a "standard of care". Recruitment is open to people who receive their primary health care at the Marshfield Clinic, who are 50 to 90 years old, and who have never taken simvastatin (Zocor), clopidogrel (Plavix), and warfarin (Coumadin). Participants will be asked to meet with a research coordinator for a one-time meeting to enroll in the study. This appointment can be combined with a time when the participant already has a scheduled appointment at the Clinic. After giving informed consent, participants will be asked to donate a blood sample. Researchers will extract DNA from the blood samples, perform genetic tests on the DNA, and put the genetic test results in the participants' electronic health records.

Unlike the Personalized Medicine Research Project (PMRP), this study will return your genetic information to your medical records. Therefore, this is a new and exciting direction for research here at the Marshfield Clinic Research Foundation.

There is no cost to the participant or their insurance company for participating. Also, the study does not offer money for participation. We hope that participants might benefit by having a lower rate of adverse drug reactions, if they are prescribed simvastatin, clopidogrel, or warfarin in the future. Like all such studies, there is a small risk of breach of confidentiality, but we take many precautions to ensure participants' confidentiality.

If you fit the above description and would like to volunteer for the study, please call 1-888-334-2232 or 715-389-7733 for more information.

This study is an important first step in the process of transforming medicine from a "one size fits all" approach to one that tailors care for each individual patient, based on their unique features that include their genetic make-up.

More than 10 years ago we started PMRP and we have learned a lot about how a person's genes influence their health and how these same genes help to determine how different people respond to medicines. With this new project, we have begun a new chapter in Personalized Medicine – applying what we have learned to actual patient care.

Deanna Cross to the development and growth of the Personalized Medicine Research Project (PMRP). Deanna was involved with PMRP from the early days when we met weekly to discuss study design and logistics. She led a project to identify a DNA "fingerprint" to identify the 20,000 DNA samples in the PMRP. The paper that she wrote describing this project is highly read and cited by other scientists. Deanna received funding from the Clinical and Translational Science Award (CTSA) through the University of Wisconsin to identify genetic predictors of adverse outcomes to treatment of prostate cancer. Last month, Deanna left Marshfield Clinic to take up a position as Assistant Professor in the Department of Forensic and Investigative Genetics at the University of North Texas Health Sciences Center in Fort Worth, Texas. We wish Deanna the very best in this new adventure and look forward to continued collaborations.

One final thought. Given my profession, my son and I regularly discuss the latest scientific discoveries reported in the news. The article on family history in our last newsletter prompted further discussion about things than run in our family. He likes to say that he inherited his klutz gene from me (sad, but true if there is such a thing!). Consider discussing family health history when you gather with your family this summer and fall and remember to update your physician where there are any changes to your family health history. Until we have genetic information incorporated into medical records like we are studying in eMERGE, family health history is how physicians personalize medicine.

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The study sites in the NEIGHBORHOOD network have donated DNA samples for genetic research on glaucoma. DNA samples were collected from persons with primary open-angle glaucoma as well as persons who do not have the disease. Researchers will compare genetic information between the two groups of persons to find out the genes associated with the disease. As part of this effort, Marshfield Clinic provided samples that were part of the eMERGE (Electronic Medical Records and Genomics) data set. Persons in this data set were participants in Marshfield Clinic's Personalized Medicine Research Project (PMRP), were 50 years of age or older, and had an eye test in the past five years. The medical records of these PMRP participants were used to confirm a diagnosis of glaucoma and to collect other information about disease in the eye.

To date, the NEIGHBORHOOD network has collected health information and DNA samples for 2,517 persons with glaucoma and 2,428 persons without the disease. The health information includes age, presence of diabetes or high blood pressure, pressure in the inner eye, whether a person has ever smoked, and presence of glaucoma in family members.

The NEIGHBORHOOD network will also use DNA samples from another glaucoma study, the GLAUGEN study, in its research. The GLAUGEN study collected DNA samples from 1,000 persons with glaucoma and 1,183 persons without the disease. Combining the NEIGHBORHOOD and GLAUGEN samples in a special type of study called a meta-analysis will improve the ability of researchers to find the genes that cause disease. Researchers have already used the combined data sets to confirm the results of another study that the CDKN2BAS gene is involved in glaucoma. This gene interacts with other genes to regulate the growth of cells. Thus, the NEIGHBORHOOD and GLAUGEN data sets have started to provide information useful for working out how glaucoma develops. PMRP participants are a valuable part of this ongoing research on glaucoma, and we look forward to future findings from the NEIGHBORHOOD network.

Details about the NEIGHBORHOOD network were obtained from the publication: *"The NEIGHBOR Consortium primary open-angle glaucoma genome-wide association study: rationale, study design, and clinical variables," Janey L. Wiggs, et al. Journal of Glaucoma. 2012, July 23.*

Contact Us

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PMRP Advisors

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