

Personalized Medicine

Research Project

Community Advisory Group a model for large biobanks

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The Community Advisory Group was established to provide guidance to the PMRP, but the work of these 20 Marshfield-area residents is informing scientists, administrators and policy makers far beyond central Wisconsin.

At the 2011 summer Steering Committee Meeting of the eMERGE Network, July 25-26, in Bethesda, Maryland, Community Advisory Group member Sharon Bredl and eMERGE Marshfield site Principal Investigator Cathy McCarty, Ph.D., told the Marshfield story during a panel titled "Community Perspectives on Data Sharing."

Dr. McCarty is used to speaking at such conferences. Not so, Bredl.

The dairy producer from Stratford joked that she was the only attendee without a bunch of letters behind her name. But the conference didn't need another expert with academic credentials. It needed an articulate community perspective, and Bredl delivered.

Not that it was easy.

"It was the most stressful thing I have done in my life," said Bredl, who was invited to participate in two panel discussions. "I was thrown into a foreign country where I did not know the language."

"She did an outstanding job," said Dr. McCarty. "I was challenged by a federal employee about a remark that I made and Sharon confirmed that the community trusts Marshfield Clinic to do the right thing. She lent credibility to the discussion as a community member that I couldn't provide as the scientist."

The PMRP has been part of eMERGE since 2007. The eMERGE Network, funded



Dairy producer Sharon Bredl, shown here at last year's Meet the Cheesemaker Gala in Madison, Wisconsin, spoke on behalf of the Community Advisory Group at the eMERGE Network meeting in July.

primarily through the National Human Genome Research Institute, encourages rapid sharing of resulting data with the broad scientific community, and it also focuses on ethical issues such as confidentiality.

Each eMERGE Network member has dealt with community involvement in different ways. The Community Advisory Group was a unique concept in 2002 when it was established. It continues to be studied and emulated by other genetic research projects, whose leaders recognize the need for community voices in the planning and governance of large biobanks.

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From the eMERGE Principal Investigator



**Cathy
McCarty, Ph.D.**

Greetings from Duluth! I never tire of watching the ships on the lake but I do miss my friends and colleagues in Marshfield. I'm glad that we have the eMERGE project to keep us in regular contact.

For those of you who kid me about the weather in Duluth, I've been checking and the temperature has often been warmer in Duluth. I suspect that may not be the case in January, however.

At the end of July in Bethesda, Maryland, we had the final meeting of the first phase of eMERGE, and the initial meeting of the next phase. Recall that eMERGE is a multi-center study funded by the National Human Genome Research Institute to leverage the wealth of information available in electronic health records to identify genetic markers of disease. All of the initial five sites in eMERGE 1 were refunded through a competitive grant

application process. Two new sites were added – Mount Sinai Medical Center in New York and Geisinger Health System in Danville, Pennsylvania, one of our partners in the HMO Research Network.

Sharon Bredl, a member of the PMRP Community Advisory Group (CAG) since it started in 2002, represented the CAG on two speaking panels at the eMERGE steering committee meeting. Read more about her visit in this newsletter. One of my fellow Principal Investigators commented to me that he thought that Sharon's presentation was the best of all the community members. Way to go Sharon!

In September, Dr. Murray Brilliant and I attended a meeting of the newly formed PhenX RISING network, also funded by the National Human Genome Research Institute. Seven sites have been funded to use standardized questionnaires to collect information that can be used together with genetic information to conduct gene/environment studies. In our case, we will use the large amount of genetic information from eMERGE 1 to study gene/environment interactions that lead to increased risk of cataract or low HDL

(the "good" cholesterol) levels. Read more about this study in this newsletter. Thank you in advance to everyone who receives the questionnaire to complete and takes the time to do so. Our research depends on you and I continue to be very grateful for your participation!

I want to take this opportunity to thank Luke Rasmussen for his contribution to eMERGE. Until mid-September, Luke worked in the Biomedical Informatics Research Center. Much of his time was devoted to eMERGE and he helped develop novel methods and implement "natural language processing" to use the information in the electronic medical records to identify who does and does not have a specific disease, such as cataract. This allows us to efficiently conduct our research and identify genetic predictors of disease faster. Luke has accepted a similar position at Northwestern University. He is very talented and was a pleasure to work with. We will miss him but we look forward to continued collaboration with him because Northwestern is also an eMERGE site. Thanks and good luck Luke!

From the Director, Center for Human Genetics



**Murray
Brilliant, Ph.D.**

The human genome is extremely complex with about 23,000 genes. Our genes are coded for by only a small part of our DNA. Some of the non-coding parts of our DNA contain information directing where and when these

genes are turned on and off. However, we really do not know what most of the DNA does. DNA is composed of four different units called bases that form a ladder-like structure. Each human genome has approximately 3 billion bases. Except for identical twins, we each have unique differences (or variant bases) in our DNA that make us who we are – what we look like and what our health risks will be.

This is an exciting time for PMRP. By the end of 2011, we will have information on between 600,000 and 2 million of the more common variant bases for almost 5,000 PMRP participants. These data continue to provide important information on how genetics influences health risks and treatment response.

In late August 2011, we began a new chapter in our efforts to understand the role of genetics in our health and how we can use genetics to tailor medical care. We sent de-identified DNAs of 23 PMRP participants to the University of Wisconsin Biotech Center. They have determined the DNA sequence for virtually all 23,000 genes for these participants. They also determined the entire DNA sequence of one PMRP participant. This is an enormous amount of data that can further PMRP research projects. This represents the first steps in a new level of genetic analysis.

Our goal is to determine the DNA sequence of more and more PMRP Participants in the next few years, greatly improving our ability to do important research linking genes and health.

Cataract study begins with surveys going to selected PMRP participants

Discovering genetic markers associated with disease is only the first step in genetic research. It's also necessary to look at environmental factors that may contribute to the cause and influence of various diseases.

PMRP researchers are currently interested in gene-environment interactions for age related cataract. They'll be asking some participants for more information, and then use a genome-wide association tool to multiply the statistical power of the collected data.

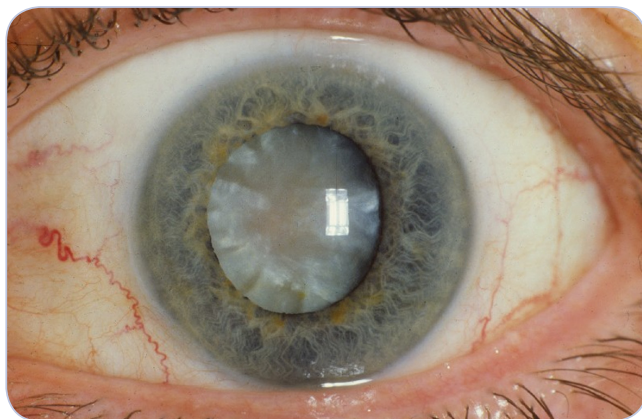
"A questionnaire is being sent to some PMRP participants, and it's an opportunity to make an important contribution to vital research," said Cathy McCarty, Ph.D., eMERGE Principal Investigator. "The questionnaire is voluntary, and should take no more than 45 minutes to complete. Names and all data will be coded and protected."

Questions are related to health insurance coverage, education, eye dominance, birth weight, UV light exposure, air contaminants in the home environment, characteristics of current place of residence, and birth order compared to any siblings -- exposures known to be associated with age-related cataract

from previous studies. This information will be combined with genetic data to see if there are interactions between genetics and environmental factors that increase the risk of cataract. Those who choose to complete and return the questionnaire will be compensated \$10.

The questionnaire will be sent to the approximately 3,700 PMRP participants with genome-wide association data who agreed in their original written informed consent document to be re-contacted for future studies. These participants' data are part of eMERGE, the newly-expanded network of seven biobank sites that can combine de-identified data from different studies.

PMRP researchers will then take data from the questionnaire, along with previously-collected data, and plug them into something called the PhenX Toolkit, which incorporates consensus-developed measures across multiple studies. PhenX facilitates consistency in replication studies, detection of modest genetic associations, and detection of gene-gene and gene-



By age 80, more than half of all Americans either have a cataract or have had cataract surgery. Photo courtesy National Eye Institute.

environment interactions. The PhenX project is funded by a \$150,000 grant from the National Institutes of Health, National Human Genome Research Institute. The most recent PhenX newsletter can be found at <https://www.phenx.org/Default.aspx?tabid=736>.

Study results are anticipated in about a year, and will then be uploaded to dbGaP (the database of Genotypes and Phenotypes hosted by the National Center for Biotechnology Information) for possible use by researchers worldwide with proper approvals (<http://www.ncbi.nlm.nih.gov/gap>).

A unique resource for gene-diet interaction studies

A study has confirmed the PMRP as a useful resource in studies examining gene-diet interactions and development of common diseases. Lending strength to the study was the size of the PMRP cohort

and a high response rate (63 percent) to a 124-item diet history questionnaire, yielding more than 11,000 questionnaires.

In addition, dietary intake in PMRP subjects was found to be relatively consistent with data from the National Health and Nutrition Examination Survey (NHANES), enabling future researchers to study this large cohort consuming a typical American diet and linked to Marshfield Clinic's comprehensive electronic health record.

Furthermore, the findings suggested a possible correlation between the use of dietary supplements and the APOE4

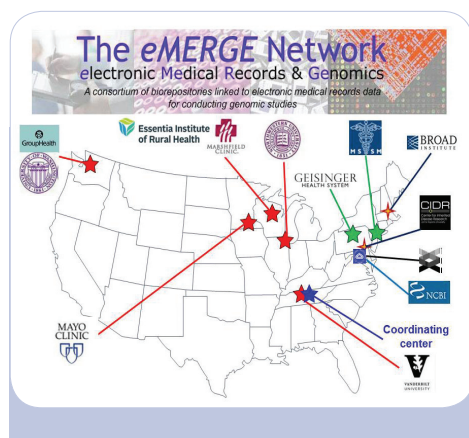
gene. Non-smokers in both genders used more supplements.

Lead author on the study was Lacie Strobush, Neillsville, a biomedical science major at the University of Wisconsin, La Crosse. Strobush was one of three summer 2010 interns who conducted work related to PMRP and the genome-wide association project of the electronic Medical Records & Genomics (eMERGE) Network, www.gwas.net. Her mentor was Cathy McCarty, Ph.D.

"Dietary intake in the Personalized Medicine Research Project: a resource for studies of gene-diet interaction," Lacie Strobush, et al. Nutrition Journal. 2011; 10:13, accessible at www.nutritionj.com/content/10/1/13.



Community Advisory Group a model for large biobanks *(continued from page 1)*



"The planned duration of the PMRP biobank extends for decades; therefore regular, ongoing communication to enrollees is necessary to maintain awareness and trust, especially relating to protocol changes reflecting evolving science," Dr. McCarty said.

In addition to the panel discussion on community interactions from the original five eMERGE sites, the July Steering Committee meeting featured updates and highlights from the various workgroups in eMERGE. Each of the five original sites and the two new sites presented information on the strengths and resources of their biobanks and their electronic medical records. Attendees also discussed future cooperation and sharing of de-identified data.

"I was amazed at how these competitive campuses were working together," Bredl said. "Everyone realizes it's vitally important to share research and policies so that we don't reinvent the wheel across the country."

Speaking of efficiency, Bredl used her position on the panels to emphasize the importance of maximizing research dollars for research, and minimizing money spent on procedural matters such as re-consent of participants, an ethical issue that biobanks wrestle with as technology accelerates.

"We owe that to the donors and taxpayers providing the funds," Bredl said.

The five original Network members are: Marshfield Clinic/Essentia Institute of Rural Health, Mayo Clinic, Group Health Cooperative with the University of Washington, Northwestern University and Vanderbilt University. The two new members: Geisinger Health System (Pennsylvania) and Mount Sinai School of Medicine (New York).

To see a list of members of the PMRP Community Advisory Group (CAG) and Ethics and Security Advisory Board (ESAB), go to <http://www.marshfieldclinic.org/pmrp/> and click "Advisory Boards" in the righthand directory.

To learn more about the eMERGE Network, go to www.gwas.net.

Contact Us

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