ISSUE 11 WINTER 2015

BioNews

> FOR PARTICIPANTS AND FRIENDS OF THE MAYO CLINIC BIOBANK

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Welcome to another edition of *BioNews.*

In our last newsletter, we discussed what it takes to run the Biobank and announced the creation of Mayo Clinic Bioservices to ensure ongoing support of the Biobank. (If you missed our last newsletter, you can find it – and other previous newsletters – on our website: http://goo.gl/K7O1Q8.) Several of you reached out to us with questions. Some of these questions were about samples being used outside Mayo Clinic for research purposes. We thought others may have similar questions about how Mayo Clinic Biobank samples are used for research.

In this newsletter, we give an inside look as to how research happens beyond the Mayo Clinic Biobank, as well as articles on new technologies being used on samples within the Biobank, recent studies using Biobank samples, and how the Mayo Clinic Biobank is partnering with philanthropic donors to improve health.

As we enter 2015, we are getting very close to reaching our goal – **50,000 PARTICIPANTS!** We appreciate the generous donation made by each and every one of you. Because of you, the Mayo Clinic Biobank is contributing to research with the goal to improve health in many areas. Stay tuned for updates on our progress in future newsletters.

As always, we enjoy hearing from participants of the Mayo Clinic Biobank and encourage you to contact us by phone (866-613-2386) or email (biobank@mayo.edu) if you have a question or comment.

INSIDE THIS ISSUE

YOUR QUESTIONS ANSWERED: **SAMPLE USE OUTSIDE OF MAYO CLINIC**

Giving More Power to Biological Samples.

Some participants have expressed concern about researchers outside of Mayo Clinic having access to samples and medical information in the Mayo Clinic Biobank. Though we spoke with these individuals directly, we thought others may be interested in hearing some of the ways that Biobank samples are being used.

There are many reasons that samples leave Mayo Clinic and this has been happening since the Biobank began over 5 years ago. Over the past decade, many important changes have occurred in the research world. One of these has been the huge advances made in technology, allowing researchers to dig deeply into the human genome. Recently the cost of using these technologies (such as whole genome sequencing – see page 3) has decreased dramatically making it feasible to use for research. Another important change has been a shift from working in isolation at just one institution but instead to collaborating with other researchers around the world. This is due, in part, to the advances in knowledge and technology we just mentioned. It is also driven by the fact that larger studies are needed to identify new causes of disease. This has led to the creation of many national and international consortia that combine their data into very large studies that have the ability to find things no one could have found on their own.

One example of this type of study is the OncoChip Project which combines researchers from hundreds of institutions around the world who together are pooling data on over 400,000 patients with breast, prostate, ovarian, lung and colon cancers as well as persons without cancer. Dr. Fergus Couch, a breast cancer researcher at Mayo Clinic, recently requested 200 Biobank samples of individuals without breast cancer to be included with his previously collected samples from individuals with breast cancer to contribute to this project. By combining samples and data from around the world, the goal is to provide reliable assessment of the cancer risks associated with genetic and environmental factors.

In addition to collaborating with other researchers for purposes of pooling samples and data, Biobank samples are provided to other institutions, organizations, or companies based on unique areas of expertise and capabilities for research. Researchers outside of Mayo Clinic may have access to important technologies yet they may not have access to the samples needed to do this research. By providing Biobank samples for research at outside institutions, we are able to facilitate important research, while furthering our mission to improve clinical care. Biobank staff will continue to perform a stringent review of each and every sample request before giving approval for a researcher to access samples and health information. Additionally, all researchers outside Mayo Clinic will be required to work with a researcher at Mayo when they use Biobank resources.

In future newsletters, we will continue to address questions asked by our participants, including expansion of our Community Advisory Board and our policies for the return of research results. If you have any questions that you would like to see addressed in a future newsletter, please contact us by phone (866-613-2386) or email (biobank@mayo.edu).

GENETIC TECHNOLOGY: WHAT IS WHOLE GENOME SEQUENCING?

Since the Mayo Clinic Biobank's inception in April of 2009, rapid technological advances have vastly improved our ability to study our genes. We wanted to share with you more details about one of these technologies, known as whole genome sequencing, and its application within the Biobank.

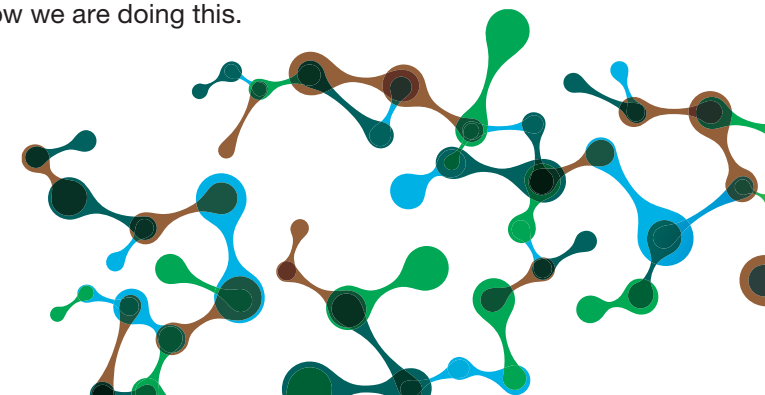
In an effort to better discuss this, let us take a step back and start with some general information about genetics:

- Our bodies are made of trillions of cells. In every cell of our body (eye cell, skin cell, heart cell, brain cell, etc.) are packages of genetic information.
- The packages of genetic information are known as chromosomes. We get our chromosomes in pairs. One of each chromosome pair comes from our mother and one comes from our father.
- Our chromosomes are made up of deoxyribonucleic acid, or DNA.
- Our DNA is made up of 4 bases (**A** for Adenine, **G** for Guanine, **C** for Cytosine, and **T** for Thymine) that exist in pairs and are repeated about 6 billion times to make up the DNA strands.
- Within the long strands of DNA in our chromosomes are smaller structures known as genes. We currently believe there are approximately 20,000 genes in each cell of our body. Our genes are the instructions that tell our bodies how to grow and develop properly.
- Each gene contains a specific sequence of these four chemical bases ("letters") **A**, **T**, **C**, and **G**.
- If there is a change of even a single base ("letter") in a gene, it is called a genetic variation ('misspelling").
- We all have variations in our genes. Most of this variation appears to do nothing. Some of this variation makes us appear unique.
- Other variations affect how a gene works and can increase risk for disease. We can find gene variations through a test called DNA sequencing, which allows us to read through all the 6 billion letters to see how each gene is spelled.

For years scientists and doctors have been able to figure out the DNA sequence (sequencing) of some genes. However, only recently have tests become available to sequence most of the human genes (genome) at one time. One of these tests is known as Whole Genome Sequencing (WGS). This test generates data for the entire DNA sequence in an individual!

It is important to know that whole genome sequencing will uncover thousands of variations in an individual's DNA sequence and that most of these variations are unlikely to be associated with risk for disease. Moreover, there is still a lot that scientists do not understand about all of the human genes, including how the environment interacts with genes to impact disease risk. It is through research projects, like those using the Mayo Clinic Biobank, that scientists will learn more about what genetic information means for patients' health and risk for disease and how to use that information to implement individualized medicine.

So far, the Mayo Clinic Biobank has generated this type of large-scale data on approximately 90 Biobank participants. These data have been some of the most highly used data within the Biobank. Currently, we are actively working to collect this data on all participants within the Biobank. See page 4 for more information on how we are doing this.



PARTNERING DONATIONS TO ACCOMPLISH BIG THINGS:

PHILANTHROPY & BIOLOGICAL SAMPLES COME TOGETHER TO IMPROVE HEALTH ACCESS

When you agreed to join the Mayo Clinic Biobank and provided a blood sample and access to your medical history, you made an important gift that is helping to accelerate research and improve clinical care. In fact, many generous donors have recognized this commitment you have made to advancing medical research and have chosen to join you in accomplishing this goal through financial contributions to support infrastructure and projects (such as whole genome sequencing) in the Biobank. We are indebted to all those who contribute to our mission, which could not be achieved without this support. Philanthropy is a great way to generate the financial resources to support biobanking activities, providing researchers with access to high-quality biological specimens and data. By having access to Biobank samples, researchers can now do in weeks what used to take years and, ultimately, alter patients' lives in the near future instead of in decades.

We are currently working with the Mayo Clinic Department of Development to raise the money needed to generate whole genome sequencing data on all 50,000 participants of the Mayo Clinic Biobank. We are grateful to all who have donated to the Mayo Clinic Biobank, whether it be samples or financial contributions. **Thank you!**

HELP US TO LEARN MORE ABOUT YOU!

We are continuing to send out a short (8-page) follow-up questionnaire to all participants. The purpose of this questionnaire is to find out about certain health conditions that may have developed since you first enrolled in the Mayo Clinic Biobank. It includes a series of questions about gastric symptoms that would help us identify if you have an undiagnosed GI condition called irritable bowel syndrome. In addition, there are general health questions that your doctor would not typically ask.

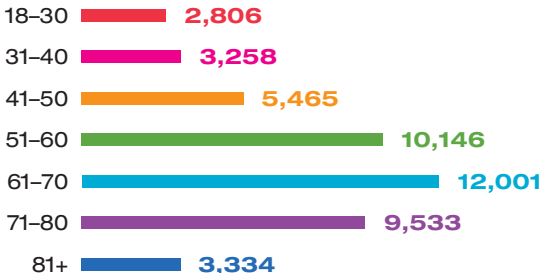
We will use this information to determine if your data and samples are appropriate for use in various studies. For example, if you have developed a particular disease since you enrolled in the Biobank, we could use your sample as a "case" (someone with the disease), while if you have never had a specific disease (e.g., heart disease), you may serve as a "control" for a study heart disease cases. Although some of this information may be in the Mayo medical records, we know that many people enrolled in the Biobank seek medical care at non-Mayo Clinic facilities. This questionnaire will allow us to collect the same information from everyone.

You can expect to receive this questionnaire about four years after you enrolled. If you enrolled in 2011, you can expect to receive the questionnaire in 2015. If you enrolled in 2012, you will receive your questionnaire in 2016, and so on.

For those who have already completed this questionnaire, thank you! If you enrolled more than 4 years ago and have not filled this out yet, please call or send us an email and we will mail you another questionnaire.

UPDATES ON RECRUITMENT STATS

AGE

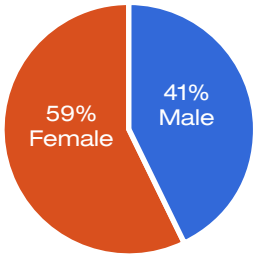


RESIDENCE

Olmsted County: **14,161**
SE MN: **5,839**
Rest of MN: **6,854**
Iowa: **2,739**
Wisconsin: **3,731**
Dakotas: **809**
Florida: **4,913**
Other US: **7,462**
Missing: **35**

GENDER

Total: **46,543**
Female: **27,337**
Male: **19,206**



NEW RESEARCH PROJECTS **USING THE BIOBANK**

The purpose of the Biobank is to enable research. We are pleased that the Mayo Clinic Biobank continues to be used for a wide variety of research projects. Overall, we now have 134 approved projects requesting samples and data from Biobank participants. Several new projects have been approved since the last issue of BioNews. Included are a subset of the recent studies that have been approved for Biobank sample and/or data use. For a complete list of projects, visit our website (http://www.mayo.edu/research/centers-programs/mayo-clinic-biobank/projects).

Knowledge and Preferences of Mayo Clinic Biobank Participants Regarding the Return of Genetic Test Results

Janet E. Olson, Ph.D. and Suzette J. Bielinski, Ph.D. are researching knowledge and preferences of Mayo Clinic Biobank participants regarding the return of genetic test results. They have requested to send a survey to 1200 Biobank participants. The increase in genetic studies out of the Mayo Clinic Biobank has the potential to discover incidental research findings. In some cases, these have clinical actionability and should be offered back to participants. The goal of the survey is 3-fold: 1) to assess genetic health literacy among participants; 2) to determine preferences of mode of returning research results related to Biobank participation; 3) to determine preferences of mode of returning clinical genetic tests unrelated to Biobank participation.

Impact of Genetic Variants on Hospital Utilization

Paul Y. Takahashi, M.D. is researching hospital utilization. He has requested genome wide association data from 454 Biobank participants who were patients in Employee Community Health. He is researching genetic risk factors for prediction hospitalization. His goal is to better predict those at the highest risk for hospitalization to provide services like care management to prevent adverse outcomes.

International Bicuspid Aortic Valve Consortium (BAVCon)

Hector I. Michelena, M.D. and colleagues are researching the genetics of bicuspid aortic valve disease. He has requested samples from 300 Biobank participants with a history of bicuspid aortic valve disease and 300 Biobank participants without a history of bicuspid aortic valve disease. His goal is to improve the diagnosis and management of patients with bicuspid aortic valve disease. This project is part of a large, multi-site international consortium.

Autoantibody Biomarker Discovery in Inflammatory Bowel Disease Using Immunoproteomics

Shabana F. Pasha, M.D. is researching Crohn's disease. Crohn's disease causes inflammation of the digestive tract, which can lead to abdominal pain, severe diarrhea, fatigue, weight loss and malnutrition. She has requested samples from 100 Biobank participants without a history of inflammatory bowel disease, celiac disease, or irritable bowel syndrome to compare to patients who have Crohn's disease that she has recruited through a separate study. Her goal is to identify specific antibodies against human proteins in patients with Crohn's disease and determine if these antibodies can differentiate inflammatory bowel disease from healthy individuals and differentiate between aggressive and nonaggressive Crohn's disease.

Genetics of Alzheimer's Disease

Nilufer Ertekin-Taner, M.D., Ph.D. is studying genetic factors that protect against Alzheimer's Disease (AD) in a high-risk population. She has requested whole exome sequencing data from 89 Biobank participants without AD to compare to patients who have the genetic risk factor APOE 4/4 for AD but are cognitively normal that she has recruited through a separate study. Her goal is to identify strong protective genetic factors against AD and gain a better understanding of their role in AD and may possibly shed light on a novel pathway which may influence this common, complex disease.

Chronic Lymphocytic Leukemia Exome and GWAS

Susan Slager, Ph.D. is researching chronic lymphocytic lymphoma. She has requested whole exome sequencing data from 89 Biobank participants to compare to patients who have chronic lymphocytic lymphoma that she has recruited through a separate study. Her goal is to determine genetic markers associated with risk of chronic lymphocytic leukemia.

A Pilot Study to Evaluate the Prevalence of Nephrolithiasis (kidney stones) within Liver Disease

William E. Haley, M.D. is researching kidney stones in liver disease. He has requested to mail a short questionnaire to 500 Biobank participants without a history of liver disease that will assess the frequency of kidney stones. The responses will be compared with responses from individuals with liver disease that Dr. Haley has recruited through a separate study. He hopes to determine whether kidney stones are more common in those with liver disease. If this is true, it may lead to increased awareness of the risks for kidney stones in those with liver disease, as well as development and application of management strategies for appropriate screening aimed at reducing kidney stone formation and associated complications.

Genetic Variation in Alcohol Metabolizing Genes on the Inverse Association of Alcohol Consumption and Renal Cell Carcinoma Development

Alexander S. Parker, Ph.D. is researching renal cell carcinoma (RCC). Incidence and mortality rates for RCC are steadily rising. To date, cigarette smoking and obesity are accepted risk factors with growing evidence that moderate alcohol consumption provides a protective effect against RCC development. Dr. Parker has requested samples from 1000 Biobank participants without a history of cancer to compare to patients with RCC that he has recruited through a separate study. He is researching interactions between alcohol consumption and genetic variation in alcohol metabolism on RCC risk. His goal is to enhance knowledge of the causes of RCC and to inform new prevention and treatment options.

Comparison of the Framingham Risk Score and QRISK Score for Heart Disease

Suzette J. Bielinski, Ph.D. is researching heart disease risk. She has requested questionnaire data from Biobank participants. She is researching the accuracy of heart disease risk scores. Heart disease risk scores are used in clinical practice to identify patients who would most benefit from intervention. The Framingham Risk Score (FRS) and QRISK are two commonly used scores. Dr. Bielinski wants to use EMR and Biobank data to compare the performance of the two risk scores. Her goal is to provide more information about how to more accurately identify those at low, intermediate, and high risk for heart disease.

PSA Levels

W. Edward Highsmith, Ph.D. is researching prostate specific antigen (PSA) levels in men. PSA is a protein made in the prostate and is used to screen for prostate cancer. High PSA levels may indicate the presence of prostate cancer. However, many other conditions can also cause high PSA levels. Additionally, it has been estimated that 40-45% of the variability in PSA levels can be explained by genetic factors. Dr. Highsmith has requested samples from 2000 male Biobank participants with an elevated PSA level who had a prostate biopsy. He is studying genetic factors that distinguish between men with high PSA levels who have prostate cancer and men with high PSA levels who do not have prostate cancer. His goal is to better understand the variation in PSA levels and to improve screening for prostate cancer.

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CONTACT US

If you have questions or need information about the Mayo Clinic Biobank, please contact us at:

507-293-0203 (Minnesota)
904-953-2504 (Florida)
1-866-613-2386 (toll free)
biobank@mayo.edu (e-mail)
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