MAYO CLINIC

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BioNews

FOR PARTICIPANTS AND FRIENDS OF THE MAYO CLINIC BIOBANK

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WELCOME TO ANOTHER EDITION OF BIONEWS

Welcome to another edition of BioNews. The Mayo Clinic Biobank continues to be a rich resource for research across Mayo Clinic. To date, over 280 projects have been approved to use Biobank samples and/or data to further health research. At this time, over 130 scientific publications have come from this research, with many more active and ongoing.

In this edition of BioNews, we discuss pharmacogenomic testing and a large study using this type of testing within the Biobank, the RIGHT 10K Study. We also introduce a new research partnership between the Biobank and Regeneron Pharmaceuticals.

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

PROJECT GENERATION:

A NEW COLLABORATION BETWEEN MAYO CLINIC BIOBANK AND REGENERON PHARMACEUTICALS

NEW COLLABORATION

We are excited to announce a new collaboration that will vastly enrich the value of the Mayo Clinic Biobank and make possible many research projects by Mayo Clinic researchers that would otherwise never be done. The Mayo Clinic Biobank is a part of a joint research partnership between The Mayo Clinic Center for Individualized Medicine and Regeneron Pharmaceuticals that will yield whole exome sequencing data on the entire Mayo Clinic Biobank of approximately 56,000 participants as well as another 44,000 Mayo participants from Mayo studies on patients with cancer, cardiovascular, neurologic and other conditions. This collaboration is a result of many years of planning and discussion. The goal of this research partnership, called Project Generation, is to learn more about the genetic causes of disease and the role of genetics in treatment and outcomes from disease. This is one of the most promising areas of medical research, as we know people who have similar risk factors do not all get a disease, and that some

drugs work for some people and not others. We think genetics has a lot to do with this, and if we can understand the underlying genetics we can develop better ways to prevent, treat and cure disease.

PROJECT GENERATION

When we launched the Biobank in 2009 it was not feasible to conduct whole exome sequencing on this scale, but we knew it would be in the not too distant future. Advances in technology now make this type of testing on large numbers of samples possible, and new medical breakthroughs require data on thousands to hundreds of thousands of participants. Thus, having sequence data on every biobank sample increases the ability of our biobank and Mayo Clinic researchers to continue to lead in this type of research. However, the cost of sequencing is still a major barrier for individual investigators and even for Mayo Clinic overall. This lead the Biobank to explore a partnership with Regeneron Pharmaceuticals, a leading pharmaceutical company that has worked with other biobanks and academic medical centers, studied hundreds of thousands of subjects, and earned an excellent reputation in this area. Regeneron has an impressive track record of research and development and bringing new drugs to the market that treat or prevent important diseases. Our agreement with Regeneron was reached after a year of negotiation to assure that Mayo Clinic patient data was secure and could be utilized to research and advance patient care.

DNA samples from each biobank participant will be sent to Regeneron for sequencing. In addition, questionnaire and medical record data will be shared after identifying information has been removed. Regeneron will return the sequence data to us for research studies at Mayo Clinic. We will also conduct joint research projects using these data. The partnership with Regeneron involves the exchange of DNA and data, not money. The samples and health information have not been sold. After sequencing is complete, Regeneron will also retain the sequence data for their own research, which is focused on drug discovery. Under our agreement, they cannot sell the Mayo Clinic data to a third party.

COMMUNITY ENGAGEMENT

The Mayo Clinic Community Advisory Boards (CAB) have been discussing the goal of whole exome sequencing with biobank leadership since 2012. If you want to read more, in several past issues of this newsletter we have discussed whole exome sequencing and the return of results of this type of testing to our participants (link below). In addition to discussions on whole exome and whole genome sequencing, the CABs have also had a number of discussions on how to collaborate with outside groups, both academic and industry like pharmaceutical companies. We recognized early on that Mayo Clinic would not be able to do all types of research alone and that partnerships and involvement with others would be an important strategy for us. All of these early conversations have allowed us to get ready for this large endeavor, and have put us in a good position to continue community engagement throughout this and other future collaborations.

WHAT DOES THIS MEAN FOR THE BIOBANK?

Biobanks support research by gathering biological samples, like your blood, in one place. Otherwise, each researcher would need to go looking for people willing to give samples for every new study. When combined with medical record data and the biobank surveys you have filled out, researchers can learn more about the bigger picture of disease and health. Whole exome sequencing is important for the biobank because it again saves each researcher time and resources because they do not have to genetically sequence the samples for each new study.

WHAT DOES THIS MEAN FOR YOU?

We recognize that biobank contributors might have questions

about this new step for the Mayo Clinic Biobank. The unpredictability of biobank research for future decades is both why biobanking research is so exciting, but also why ongoing community engagement is important. For example, one common question is: what information about me will Regeneron be able to access? As with all research involving samples given to researchers outside Mayo Clinic, our collaborators at Regeneron will not have access to any identifying information. This means, they will not have names, birthdates, Mayo Clinic IDs, or the contact information of any biobank contributor. We share biospecimens (just enough to do this research), medical record information, and questionnaire data with barcodes, and only the Mayo Clinic Biobank can link this code to you personally.

WHAT ABOUT WORKING WITH FOR PROFIT COMPANIES AND COMMERCIALIZATION?

The Biobank was set up to work with a variety of researchers at Mayo, other medical centers, the National Institutes of Health, and industry, including pharmaceutical companies. All of these groups help fund and contribute to advancing medical care. For this project, we could not afford to sequence this number of samples without a partner. We carefully selected Regeneron as a partner. Regeneron is providing millions of dollars of sequencing to create an asset that will be used to find better drugs for patient care and to conduct research into the causes of many diseases. Mayo Clinic and Regeneron might profit if a new drug is discovered from this research collaboration. As we note in the consent form, Mayo is a non-for-profit organization, and uses all profits from products to support ongoing research and education activities. The topic of commercialization, and how best to collaborate with private companies, has been and will continue to be discussed by the Mayo Clinic Biobank Community Advisory Boards.

STAY TUNED

We will provide periodic updates in future editions of BioNews and on the website. As always, we are happy to address any questions you may have about this or any other study. You can email the Mayo Clinic Biobank at biobank@mayo.edu or call us at 507-293-0203 or 1-866-613-2386. If you have concerns about Project Generation and prefer to withdraw from the Biobank, please let us know no later than the end of 2019.

READ MORE

Past issues of BioNews have also described whole exome sequencing. https://www.mayo.edu/research/centers-programs/mayo-clinic-biobank/about/resources

PROJECT GENERATION:

A GENETIC RESEARCH PROJECT FOR ALL CONTRIBUTORS TO THE BIOBANK

WHAT WILL THE BIOBANK LEARN THROUGH PROJECT GENERATION?

Your complete genetic code is made up of 3 billion DNA letters and includes more than 22,000 genes. We don't understand the function of most of the human genes at this time. So, even though the project will generate a great deal of new information, the current Biobank policy is to return results on only 59 genes at this time. These 59 genes, often referred to as the American College of Medical Genetics (ACMG) 59, were reviewed and chosen by a national panel of experts as genes that should be reported when patients were undergoing whole exome sequencing.

The 59 genes that will be analyzed contribute to many different health conditions, most of which are adult-onset disorders. This research project will include looking at genes associated with an increased risk for hereditary breast and ovarian cancer, hereditary colon cancers and other cancers, increased risk for hereditary forms of heart disease, and, risk for a genetic form of high cholesterol called familial

hypercholesterolemia. The results of this genetic testing will not diagnose a health problem, but may tell you that you have an increased risk for a certain condition. **Some biobank contributors will learn about increased personal health risk, but most will not.** In research projects that look at these 59 genes, only about 2-3% of participants will test positive for a gene variant associated with a health risk. **If you have a positive result the biobank will reach out to you to find out if you would like to know about these findings. Most biobank contributors will not receive any personal genetic results.**

The biobank has been successful in supporting research in part because of its size. Regeneron will sequence the DNA of biobank participants plus the DNA of patients that have provided samples to several smaller biobanks of various research groups at Mayo Clinic. In total, about 100,000 individual samples will be sequenced. We anticipate positive results on approximately 2,000-3,000 Mayo Clinic research participants.

YOUR TRUST IN THE BIOBANK IS OUR GUIDING VALUE. Many people who gave their blood to the biobank did so because they trust in Mayo Clinic. We know how hard we have to work to continue to earn that trust. We recognize that people feel differently about receiving genetic information. Some people do not want to know about genetic risks that might take place far in the future. Most people do want to learn more about health risks they can take action on. Some people have questions about privacy. If a positive genetic result is found by sequencing your biobank sample, you will be asked about whether you want to learn more about it. A positive result would only be placed in your electronic health record with your permission and only if this result is confirmed by another test done in a clinical lab.

WHAT WOULD A POSITIVE GENETIC RESULT MEAN FOR YOU? If you were to receive a positive genetic result, the biobank will cover the costs of a genetic counseling session and help connect you to appropriate clinical care. A positive genetic test result is not enough information to diagnose a new illness. A clinical care team would need to learn more. This might require additional testing or monitoring and could lead to different recommended treatments. For

example, a biobank contributor might need to see a heart specialist if he or she learned about the genetic result which increases risk for high cholesterol. A heart doctor would discuss tests and medications that can help monitor or reduce heart health risk.

WHAT WOULD A POSITIVE GENETIC RESULT MEAN FOR YOUR FAMILY? Genetic disease can pass — or be inherited — from one generation to the next. A positive genetic result in a biobank contributor can have health implications for blood relatives. If a biobank contributor finds out about increased risk, he or she might have inherited that risk from a biological parent. He or she might have passed that increased risk on to children. If a positive result is returned to you, you will speak to a genetic counselor about your personal and family health history, which can help you to better understand what the genetic result means for you and your family. If you have questions about how to best communicate genetic information with family members, a genetic counselor can also help.

WHAT WILL PROJECT GENERATION MEAN FOR THE FUTURE? In spite of recent advances in technology and our knowledge of genetics, there is so much more to learn about genetics and health. Project Generation will help us understand the genetics of all the biobank contributors, but it also has implications for their children, their children's children, and so on.

Keep reading future issues of BioNews to get updates on Project Generation.

COMMUNITY ADVISORY BOARD (CAB): AN UPDATE!

THEN

Community views on biobanking have been part of the story of Mayo Clinic Biobank even before the first blood sample was collected. We began working with community members in 2007, with a "deliberative community engagement event". Twenty citizens drawn from the population of Olmsted County, Minnesota, took part in conversations about biobanking and issues surrounding genetic and genomic research. This event involved the community members coming together, prepared by reading materials that brought them up them up to speed on scientific and policy questions. Community members shared their values and opinions on biobanking with each other, researchers, and biobanking leaders over several days. One recommendation voiced by the participants was the need for ongoing community guidance and involvement in Biobank governance. The Community Advisory Board (CAB) was created to ensure that the voice of the community continues to be heard. Over the years, the CAB network has expanded and now includes three distinct boards of 15-20 people from the surrounding local communities. CABs meet 4-6 times per year in Rochester, Minnesota; Jacksonville, Florida; and Phoenix, Arizona.

AND NOW

This year, all three CABs met the new CAB network facilitator Karen M. Meagher, PhD. Dr. Meagher is Assistant Professor and Associate Director of Public Engagement in the Biomedical Ethics Research Program at Mayo Clinic. Trained in moral philosophy, her research interests focus on public health ethics and social implications of advances in genomic science and technology. She hails from Rochester, NY (the other Rochester!) and in her free time she enjoys hiking with her husband and drinking tea.

Dr. Meagher led strategic planning sessions at all three CAB sites in the first half of 2019 to learn about CAB past successes and develop a plan for the CABs over the next five years. For example, in January the Jacksonville area

CAB shared their local views on building CAB membership, meeting with researchers, and reaching out to the surrounding communities. In March, the Rochester area CAB met with Dr. Matthew J. Ferber, PhD creator of Mayo Clinic GeneGuide to ask questions about this direct-to-consumer product. In June, the Phoenix, Arizona area CAB played a Lego game that explained the concept of sharing data for research and helped identify community concerns and perceived benefits of the movement of their information between different "players" involved in research. Their discussion will be used to modify the process of fielding requests by researchers to access the Sangre Por Salud (SPS) biobank collection of samples from the local Latinx population. The SPS biobank collection was developed as a partnership between Mayo Clinic, Mountain Park Health Center, and Arizona State University.

PHARMACOGENOMICS 101

Pharmacogenomics (PGx) (also called pharmacogenetics) is the study of how your genes may affect your response to drugs. The word "pharmacogenomics" comes from the combination of the words pharmacology and genomics.

- Pharmacology deals with the uses and effects of medications
- Genomics deals with understanding genes and their roles

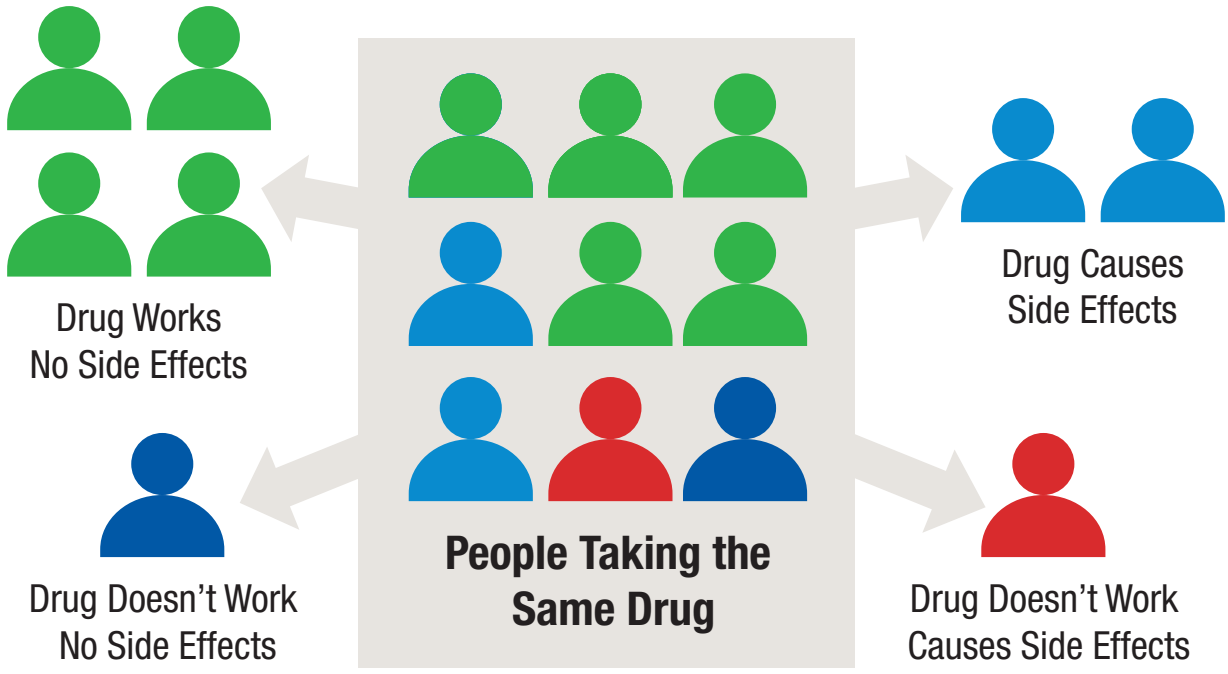
Genes carry information that you inherit from your parents. Different versions of genes result in individual traits such as eye color. Genes can also influence how your body handles drugs. Versions of these genes may increase the risk of side effects or cause the drug not to work for you.

Chemotherapy drugs are more effective when treating certain types of cancers. Codeine offers no pain relief in some patients and in others causes life-threatening reactions, such as respiratory depression. Other individuals experience harmful side effects from statin drugs designed to lower cholesterol levels. Finding the right dose of blood-thinning agents, such as warfarin, can involve a long process of trial and error.

Some Food and Drug Administration-approved drug labels contain warnings or information about potential adverse event risks, variable responses, drug-action mechanisms or genotype-based drug dosing. Recommendations are based on genomic information about the drug. Pharmacogenomics drives greater drug effectiveness, with increased safety and reduced side effects.

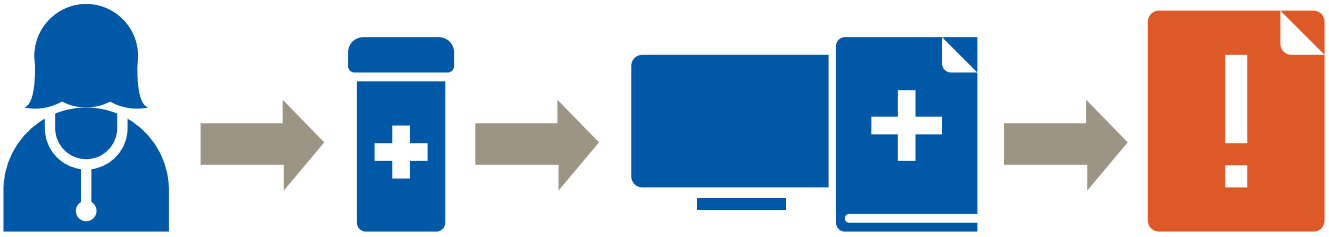
Pharmacogenomic testing is one tool your healthcare provider can use to help identify the right drug for you. Many factors impact how a person responds to medication including:

- Genetic factors
- Sex
- Smoking/alcohol
- Food interactions
- Age
- Race/ethnicity
- Illness or organ dysfunction, especially kidney or liver function
- Food interactions
- Other medications



The right drug…at the right dose…at the right time. Those goals drive pharmacogenomics.

THE RIGHT 10K STUDY



Provider | Prescription | Electronic Medical Record PGx Result | Alert: Patient Likely Needs a Higher Dose

The Right Drug, Right Dose, Right Time Using Genomic Data to Individualize Treatment Protocol (RIGHT) study completed recruitment of 11,098 Mayo Clinic Biobank participants. The RIGHT study was designed to determine if putting PGx information into the electronic medical record improves patient care. The RIGHT study is the largest study of PGx in the world.

For RIGHT participants, when their clinician prescribes a drug, he/she will see an alert if they have a gene version that affects the drug. The alert may suggest a change in dose (either higher or lower) or suggest an alternative drug.

Research investigating the impact of PGx information in the electronic medical record is ongoing. Our goal is to determine if having this type of information in the electronic medical records benefits patients.

Q: CAN I JOIN THE RIGHT 10K STUDY?

A: At this time, the RIGHT 10K Study is complete and no longer accepting new participants.

Q: HOW DO I GET PHARMACOGENOMICS TESTING?

A: Pharmacogenomic testing can be ordered by your primary care provider. If you are interested in pharmacogenomics testing, please discuss with your primary care provider whether this type of testing may be right for you.

SAVE A TREE

Biobank staff is currently working on the next version of the follow up questionnaire. Please help us save a tree and fill out the questionnaire electronically! If you have set up your Mayo Clinic patient portal, you provided an email address at that time. We will use that address. If you have never set up your Mayo Clinic patient portal or would like to provide a new email address, please send your email address to Biobank@mayo.edu.

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As always, if you have any suggestions or feedback on our website, please contact us!

CONTACT US

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

507-293-0203 (local)
1-866-613-2386 (toll free)
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http://mayoresearch.mayo.edu/biobank

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