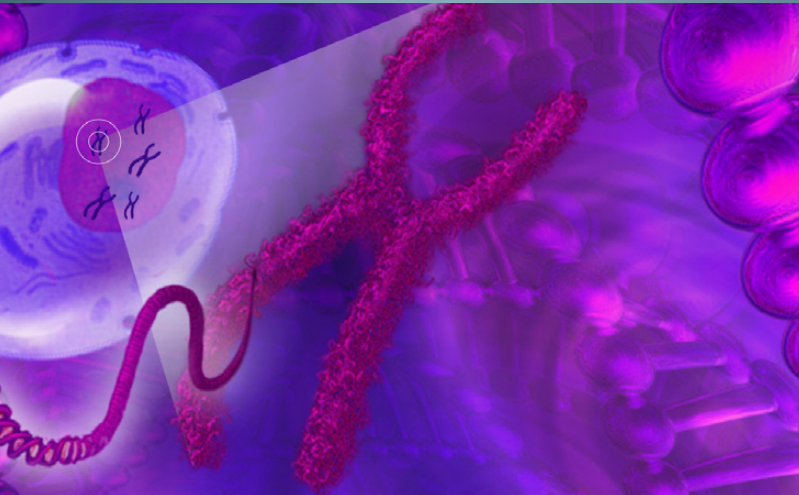




BioNews

FOR PARTICIPANTS OF THE MAYO CLINIC BIOBANK

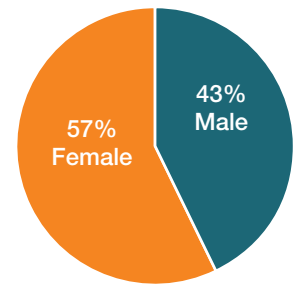
ISSUE NO. 6 | SPRING/SUMMER 2012



Recruitment Stats Update

Gender of Participants

The current total enrolled Biobank participant count is 24,872. 14,187 are female and 10,685 are male.



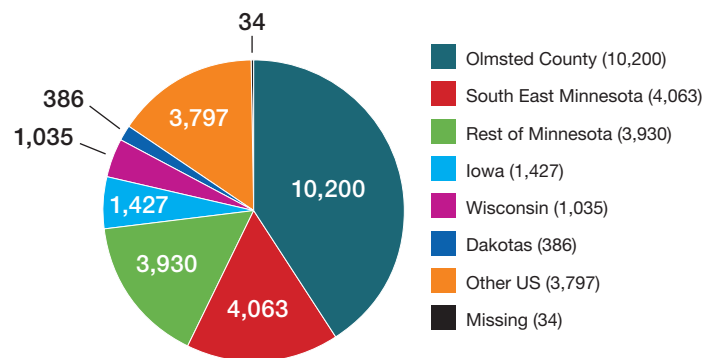
Greetings from the Mayo Clinic Biobank Staff!

We have another busy year planned. We are hoping to expand to 30,000 participants by the end of 2012, and we will also begin actively enrolling participants at Mayo Clinic in Florida. One of our larger research initiatives involves whole exome sequencing – a new approach to understanding the genetics of health and disease. In this issue, we will explain whole exome sequencing, share the Community Advisory Board’s initial discussions on this technology, and give an overview of the Center for Individualized Medicine at Mayo Clinic. We hope you enjoy this issue of BioNews, and thank you for your continued support.

Sincerely,
The Biobanking Team

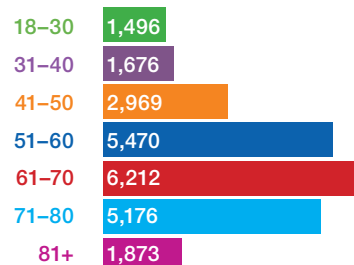
Demographic of Participants

The Biobank participants are from these areas.



Age of Participants

This graph represents different age ranges of all participants of the Mayo Clinic Biobank.



New research projects using the Biobank

The Biobank's purpose is to enable research, and we are pleased that many Mayo Clinic researchers have already made use of samples and information for studies at Mayo Clinic. Overall, we now have 41 approved projects requesting a total of approximately 31,506 samples from biobank participants. Several new projects have been approved to use samples and information from the Mayo Clinic Biobank since the last issue of BioNews.

Plasma Renalase in Heart Failure

Frank Brozovich, M.D., Ph.D., is studying a recently discovered enzyme thought to play a role in heart failure. He has requested 400 Biobank samples: 200 from participants believed to have heart failure and 200 from participants with no evidence of heart failure. Dr. Brozovich will compare blood levels of the enzyme renalase in these groups. His aim is to determine whether renalase levels can help predict outcomes of heart failure, and ultimately, to look for new drugs to treat heart disease.

Bioengineered Tissue for Pharmacogenomic Analysis of Patients Treated with Antidepressants for Major Depressive Disorder

Juan Ji, Ph.D., would like to enroll a set of Biobank participants with no personal or family history of any mental health disorders into her study. Dr. Ji's study would compare these healthy new participants to her current study participants with mental health disorders. Her research study requires obtaining a skin biopsy from her participants to make special cells that act like brain cells in the laboratory. The extension of her current study would allow her to compare response to medication of the cells from healthy individuals to those from patients with mental health disorders. Her goal is to gain a better understanding of how to determine which individuals will respond to these medications and then to use that information to match patients with the optimal drugs.

Frequency of New Genetic Variant Associated with Prostate Cancer

Stephen Thibodeau, Ph.D., is researching a new genetic variation that was recently reported to increase the risk for hereditary prostate cancer. Dr. Thibodeau has requested samples from all male Biobank participants to determine how common this genetic variation may be. Learning how common or uncommon this variation is in men will help to better understand its importance for men with prostate cancer and evaluate the risk this particular genetic variation may pose for the development of prostate cancer.

Genetic Association in Endometrial Cancer

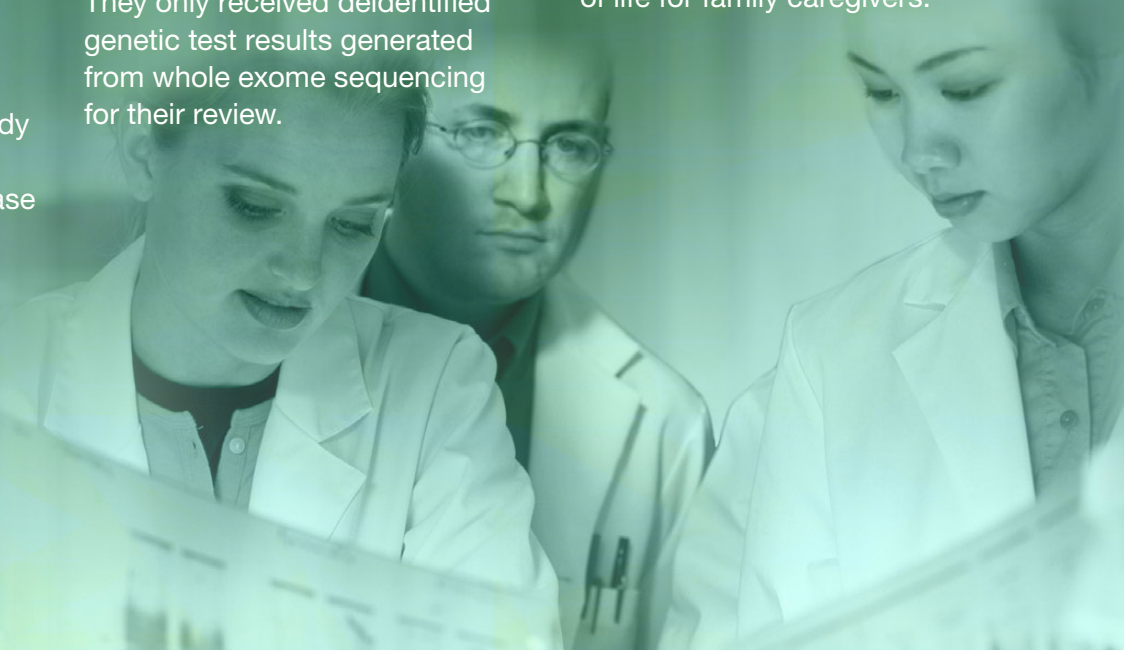
Boris Winterhoff, M.D. and Sean Dowdy, M.D., are researching genetic variants that may be associated with the development of endometrial cancer. They have requested samples from 300 Biobank participants without history of endometrial cancer. The researchers can compare these samples to patients with endometrial cancer. These patients have already been recruited through a separate study. Drs. Winterhoff and Dowdy are trying to determine whether certain genetic variations increase the risk of endometrial cancer. This study may lead to better diagnostic and screening tools, and ultimately, longer patient survival.

Requests for Review of Whole Exome Sequencing Information From Previous Study

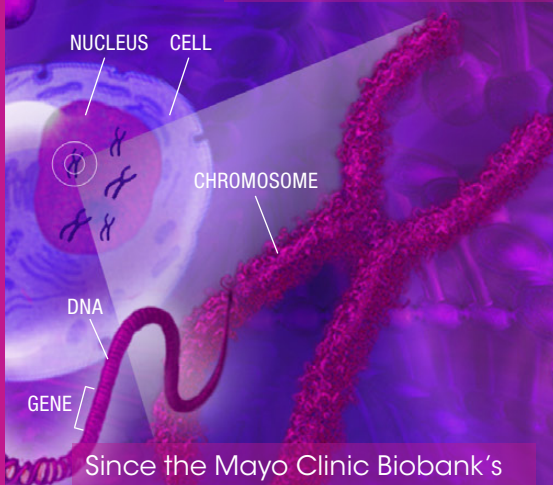
In our last issue of BioNews, we noted a study initiated by Stephen Thibodeau, Ph.D. In this study, Dr. Thibodeau and his colleagues had requested samples from 40 deceased Biobank participants (20 male and 20 female) without a history of any particular disease. The goal of his project was to perform DNA sequence analysis on all known genes (whole exome analysis) for these 40 Biobank participants. The results of the whole exome analysis will be used to help both research and clinical laboratories to compare genetic differences between health and disease. This genetic information has been generated, and 17 investigators already have requested access to the information. These investigators want to study this genetic information to better understand what the information looks like and how it may relate to the specific diseases they are studying. No additional samples were given to these investigators. They only received deidentified genetic test results generated from whole exome sequencing for their review.

Family Caregiver Burden in Home Hospice: Study of the Immune System, Quality of Life, and Risk for Disease

Judith Kaur, M.D., is researching family caregivers of end-of-life cancer patients and how this affects the caregiver's immune system, quality of life and risk for disease. She has requested samples from 30 healthy Biobank participants who have no history of disease. She will compare these to individuals, recruited through a separate study, who have been hospice caregivers. Dr. Kaur is researching whether family caregivers in home hospice may experience stress-induced immune issues. She will then determine whether other lifestyle factors, such as exercise, social support, quality of life, herbal supplements or known anti-inflammatory agents, can help to decrease immune responses for these caregivers. She also would like to determine whether caretakers who experience immune responses have increased risk for other diseases. The goal is to increase the quality of life for family caregivers.



What is Whole Exome Sequencing?



Since the Mayo Clinic Biobank's inception in April of 2009, rapid technological advances have vastly improved our ability to look at our genes. We wanted to share with you more details about one of these technologies, known as whole exome sequencing, as was shared with our Community Advisory Board.

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. These packages are known as chromosomes.

We get our chromosomes in pairs. One of each pair comes from our mother and one of each pair comes from our father. On our chromosomes are smaller structures known as our genes. We currently believe there are approximately 20,000-30,000 genes in each cell of our body. Our genes are the instructions that tell our bodies how to grow and develop properly.

Our DNA, or DeoxyriboNucleic-Acid, is the material that makes up each of our genes. Our DNA is made up of about a few billion chemical bases, which exist in pairs on the familiar DNA double helix. These chemical bases exist in pairs and consist of various arrangements of just four complex molecules called amino acids. They are: A for Adenine, G for Guanine, C for Cytosine, and T for Thymine. All of our genes are spelled out with different groupings of these four chemical letters A, T, C and G. Each gene is spelled in a certain sequence, using these letters. If there is a misspelling in the gene, we call that a genetic variation. As discussed at our Community Advisory Board meeting, you can liken our DNA to a cookbook full of recipes (genes). If there is a typo in a recipe in the cookbook (change in the letters of the gene) the end product does not turn out (gene doesn't function normally).

We all have variations in our genes. Some of those variations appear to do nothing. Others make us appear unique. Yet other variations affect how a gene works and can cause risk for disease. We 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 (called 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 Exome Sequencing (WES). Our exome refers to the portions of our genes that contain direct instructions for cells to build proteins. These regions are called exons and are thought to be the most important in determining whether there may be risk for disease. Other segments of genes known as introns are not believed to be as critical in disease risk.

It is important to know that whole exome 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. 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.

What is the Center for Individualized Medicine

The concept of using a patient's genetic material for customized diagnostic, therapeutic and preventative care is called personalized, or individualized, medicine. It represents the future of medical care. And it is at the heart of what Mayo Clinic's Center for Individualized Medicine does.

Rapid technological advances in medical and human genetics allow researchers to examine DNA and genetic interactions with more speed and precision than ever before. This enables Mayo Clinic to study the complex role that genes play in the wellness and disease of an individual patient.

For example, finding the genes that control a patient's response to different drugs may lead to simple genetic tests that help doctors make sure the drug they prescribe will deliver the maximum benefit for their patient while minimizing the risk of side effects or overdosing.

In addition, identifying cancers by genetic fingerprint (specific genetic changes in the cancer cells), rather than location in the body, will help doctors tailor treatment plans and chemotherapies that help people live longer. Such testing may ultimately lead doctors to be able to screen for genetic cancer markers (called biomarkers) before a tumor ever manifests in the body – empowering doctors and patients to prevent or slow disease before it starts.

The Center for Individualized Medicine facilitates genomic, molecular and clinical research and finds ways to deliver

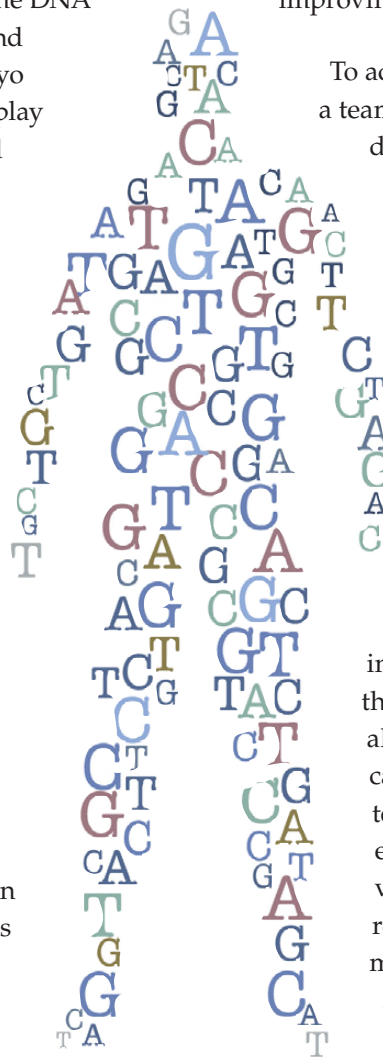
these medical innovations into the clinical practice – improving health care for every Mayo Clinic patient.

To accomplish this mission, the Center is led by a team of scientific and medical experts who help drive innovations in personalized medicine all the way from a good idea to the best medical care for Mayo patients.

The Mayo Clinic Biobank is a critical resource in this mission. Operated under the Center's Biorepository Program, the Mayo Clinic Biobank enables researchers to study a group of patients that have already donated samples and medical information to the Biobank for research.

Therefore, in less time, and for less money, than it would take each individual investigator to contact and collect samples on their own, the Biobank serves as a resource for all Mayo investigators. Therefore researchers can use these patient samples and information to study the genomics of disease much more efficiently. Armed with rapid access to the vast store of information in the Biobank, researchers at Mayo and elsewhere can conduct more high-impact studies of individualized medicine.

The Center for Individualized Medicine discovers and integrates the latest in genomic, molecular, and clinical sciences into personalized care for each Mayo Clinic patient.



For more information, please visit the Center for **Individualized Medicine** website

<http://mayoresearch.mayo.edu/center-for-individualized-medicine>



Community Advisory Board Activities

CAB activities have been off to a great start in 2012! To prepare for future discussions on issues relating to whole exome and whole genome sequencing, we were excited to get a refresher course on “Genetics 101” with Dr. Steve Thibodeau. Using a ball of string and several cookbooks, he illustrated how far we’ve come in our ability to read genetic data but also how much more we have to do before we can understand what the data means.

are facing challenges around returning results. One such institution has found that some parents of pediatric research participants say they might want all the whole genome sequencing results despite the fact that most of them cannot be interpreted. This led to a rousing group discussion about the next possible frontier of science—being able to store our genetic information on flash drives and providing these to our doctors during routine check-ups. Some felt

Using a ball of string and several cookbooks, he (Dr. Steve Thibodeau) illustrated how far we’ve come in our ability to read genetic data but also how much more we have to do before we can understand what the data means.

Kiley Johnson, M.S., C.G.C., a genetic counselor at Mayo Clinic, also gave a short presentation that summarized the different types of clinical results that come from genetic testing. While there are clear benefits to getting back certain results (where treatment is available), it definitely gets tricky when genetic test results have uncertain clinical significance. For example, if we don’t know whether gene variants are associated with certain diseases, should these results be given to research participants?

that this could potentially enhance patient care by tailoring prescription drugs and their dose to individual patients or merging genetic information into existing electronic medical records. While not yet ready for the doctor’s office, this scenario could be realized in the future. Others had concerns about what this information might mean for them in their medical care and being labeled in some way.

At the March meeting, our interim co-chair, Karen Maschke, Ph.D., in bioethics, informed us of ethical issues in genetics at a national level. All institutions involved in genetic research

As we take this opportunity in the beginning of 2012 to educate ourselves as a Community Advisory Board, we also plan for important discussions ahead. As always, the best interests of Mayo Clinic Biobank participants are at the heart of our conversations.



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