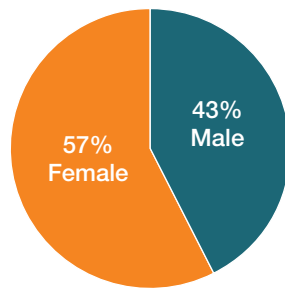


Recruitment Stats Update

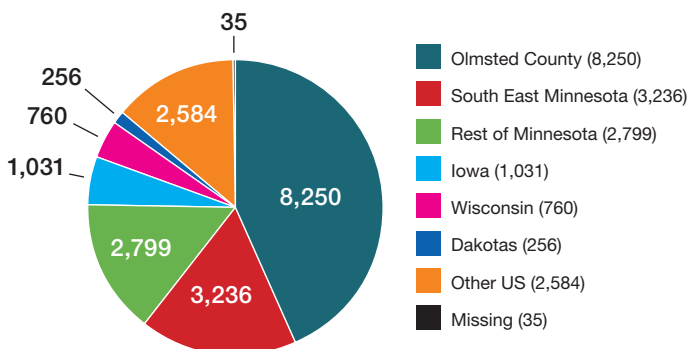
Gender of Participants

The current total enrolled biobank participant count is 18,951. 10,894 are female and 8,057 are male.



Demographic of Participants

The Biobank participants are from these areas.



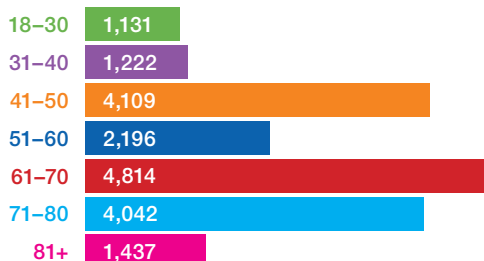
Hello Again From the Biobanking Team,

As the spring winds down and the summer begins, we mark the end of our second year of recruitment and our fourth issue of BioNews. We are excited to report that the Mayo Clinic Biobank is on target to meet our goal of 20,000 participants before the end of this year, which is ahead of schedule. We owe each of our participants a debt of gratitude for this success!

There are a lot of things to update you on inside this issue of BioNews: new data on who has participated, new studies that have been approved to use the Biobank, information on how studies are reviewed and approved, and updates coming to the website. Another major area of progress is related to our Community Advisory Board, which has met three times since our last newsletter and has named Gail Onderak as Co-Chair. Whether this is your first time receiving BioNews or your fourth, we hope you find it interesting and useful, and as always, feel free to send us suggestions for articles you would like to see in a future issue.

Age of Participants

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



Sincerely,
The Biobanking Team

NEW Research Projects

The purpose of the Biobank is to enable research. We are pleased that many Mayo Clinic researchers have already made use of samples and data for projects on important problems like cancer and heart disease. Several new projects have been approved to use samples and information from the Mayo Clinic Biobank since the last issue of BioNews.

ASSOCIATION BETWEEN HYPOTHYROIDISM (LOW THYROID LEVELS) AND CHOLANGIOCARCINOMA (LIVER CANCER)

Lewis Roberts, M.B.,Ch.B., Ph.D. is researching whether low levels of thyroid hormones are linked to risk of developing cholangiocarcinoma (a specific type of liver cancer). He has asked to review medical information on 600 Biobank participants without a history of any cancer to compare to patients who have cholangiocarcinoma that he has recruited through a separate study. He is looking to review lab results and imaging studies that may help to determine how common hypothyroidism and liver disease may be in individuals without liver cancer. He will compare Biobank participants with no history of liver cancer to his study participants. Through this study he hopes to determine whether hypothyroidism may be a risk factor for the development of cholangiocarcinoma.

PREDICTION OF CHOLANGIOCARCINOMA (LIVER CANCER)

Lewis Roberts, M.B.,Ch.B., Ph.D. has submitted a second request to the Biobank about cholangiocarcinoma (a specific type of liver cancer). In this second project, he has requested samples from 400 Biobank participants without a history of any type of cancer to compare to patients who have cholangiocarcinoma that he has recruited through a separate study. He is researching whether there are genetic variants that might predict individuals who are at risk for developing cholangiocarcinoma.

IMMUNE MARKER IN RENAL (KIDNEY) CANCER PATIENTS

Eugene Kwon, M.D. is researching immune responses to kidney (renal) cancer. He has requested samples from 172 Biobank participants without a history of any type of cancer or known immune disorder. He will compare this group to patients who have kidney cancer that he has recruited through a separate study. He is researching a particular immune marker to determine whether this marker can be detected in the blood of patients with and without kidney cancer. His goal is to better understand if this specific marker is detectable in both populations and whether it might be used to help determine the prognosis of kidney cancer in affected individuals in the future.

ANALYSIS OF GENETIC VARIATION IN POLYCYSTIC KIDNEY DISEASE GENES

Peter Harris, Ph.D. is researching a group of inherited disorders that cause cyst development in the kidney and can result in kidney failure, known as Polycystic Kidney Disease (PKD). He has requested samples from 250 Biobank participants without a history of kidney disease to compare to patients who have PKD that he has recruited through a separate study. He is researching changes within the PKD genes. His goal is to better describe genetic changes found in the PKD genes to help predict disease course and progression in patients with the diagnosis.

Using the Biobank

ASSOCIATION OF GENETIC FACTORS TO THE RISK OF BLOOD CLOTS

John Heit, M.D., Ph.D. is researching genetic factors that are associated with risk for venous thromboembolism (blood clot formation). He has requested samples from about 50 biobank participants who have a history of a blood clot to study, along with his many additional cases of patients with blood clots recruited through a separate study. He has also asked for approximately 325 Biobank participants without a history of having a blood clot to compare to his patients who have had a clot. He is researching whether there are genetic factors that may increase an individual's risk for blood clot formation. His goal is to identify these factors and individuals who are at high risk, such that healthcare providers may be able to target prevention and treatment measures in the future.

GENETIC DETERMINANTS OF PERIPHERAL ARTERIAL DISEASE

Iftikhar Kullo, M.D., is researching genetic variants that may increase an individual's risk for peripheral arterial disease. Peripheral artery disease (PAD) is a common circulatory problem in which narrowed arteries reduce blood flow to the arms and legs. He has requested samples from 1,000 Biobank participants without a history of PAD to compare to patients who have PAD that he has recruited through a separate study. He is researching genetic variations that he has identified through a separate study. His goal is to see which of these genetic factors may increase risk, such that it may be used to help predict or manage those at high risk for PAD in the future.



The Mayo Clinic Biobank Access Committee



The gatekeepers
and protectors of
Biobank samples
and information.

The Biospecimen Trust Oversight Group (BTOG) has formed a smaller group known as the Mayo Clinic Biobank Access Committee. This group makes decisions about how Biobank samples and information are used. When a researcher asks to use the Biobank for a new study, the Access Committee reviews the requests. The committee approves the request, denies it, or makes suggestions for revision of the request. As committee members make these decisions, they consider several things:

1. is the research important?
2. does the biobank have enough samples to honor the request?
3. is it necessary to contact Biobank participants for additional information or samples?
4. will there be research results that are generated that require contacting participants?

When making their decision, the Access Committee members use principles that were developed by BTOG. When the committee has a complex request, they invite the Co-Chair of the Community Advisory Board (CAB) to attend meetings to offer advice. If needed, the full CAB may review the project. This ensures that the views of the general community are included in decision making. If the research project is approved, then the researcher is sent an approval letter, and the information and samples are given to them. If the Access Committee denies the researcher's request for samples, then the researcher is sent a denial letter, and no samples or information are provided to the researcher for their project

As of this date, 21 projects have been approved for use and 2 have been denied or tabled for revisions or consideration at a later date. The Biobank Access Committee has worked feverishly to review projects and ensure that only high-quality research projects are being approved for Biobank sample use. We strive to continue this process to provide you, our valued participants, with confidence that your samples and information will not be wasted, but always put to good use, with the goal of improving health care now and in the future.

Access Principles:

- ▶ The Mayo Clinic Biobank is a resource to be used to address important research and clinical questions.
- ▶ All projects that use the Mayo Clinic Biobank require full evaluation by Mayo Clinic scientists and sometimes scientists and physicians outside of Mayo Clinic who are experts in the diseases being studied. If a project does not have a formal review prior to requesting Biobank samples, then the Access Committee will require this review, prior to approving this request.
- ▶ All research projects must be reviewed by the Mayo Institutional Review Board, which ensures high-quality, ethically sound research is being performed.
- ▶ Community Advisory Board advice will be requested as needed.
- ▶ When necessary, contact with Biobank participants will be coordinated through the Access Committee.
- ▶ A Mayo researcher must be included in any proposal submitted to the Access Committee.
- ▶ In general, patient identifiers will not be provided to investigators. Under certain circumstances, however, patient medical records may be allowed to be reviewed under strict surveillance by Biobank staff. Once records are reviewed, any identifying information (name, clinic number, date of birth, etc) will be stripped from the data that researcher was collecting from the medical records, such that no researcher would have identifying information on a biobank participant.
- ▶ The Access Committee will help determine if the study request might generate important research results and if these results should be provided to participants. Any return of research results will be coordinated and approved by the Access Committee.
- ▶ Any policies that require data to be shared with national research funding agencies must be described in the request.
- ▶ Biobank samples will be provided only for the specific uses mentioned in the access request and any change in the project must be approved by the Access Committee. Samples will not be provided for unspecified uses.
- ▶ Data generated from the use of Mayo Clinic Biobank samples will be deposited into the Mayo Clinic Biobank database to expand the information available for future use. If a researcher does not want to return data to the Biobank, then an exception would need to be made and approved by the Access Committee.
- ▶ If there is significant cost associated with the request, beyond the scope of the Biobank resources, then that cost will be the responsibility of individual investigators.



Access Committee Membership

James R. Cerhan, M.D., Ph.D., Chair
(Principal Investigator, Mayo Clinic Biobank)

Zachary S. Fredericksen
(Statistician)

W. Edward Highsmith, Jr., Ph.D.
(BAP Laboratory Director)

Scott E. Kaese
(Mayo Clinic Biobank Administrator)

Karla Kopp
(BAP Laboratory)

Barbara A. Koenig, Ph.D.
(Bioethics)

Kiley J. Johnson, MS, C.G.C.
(Genetic Counselor)

Mark Liebow, M.D.
(General Internal Medicine Physician,
Medical Director of Biobank)

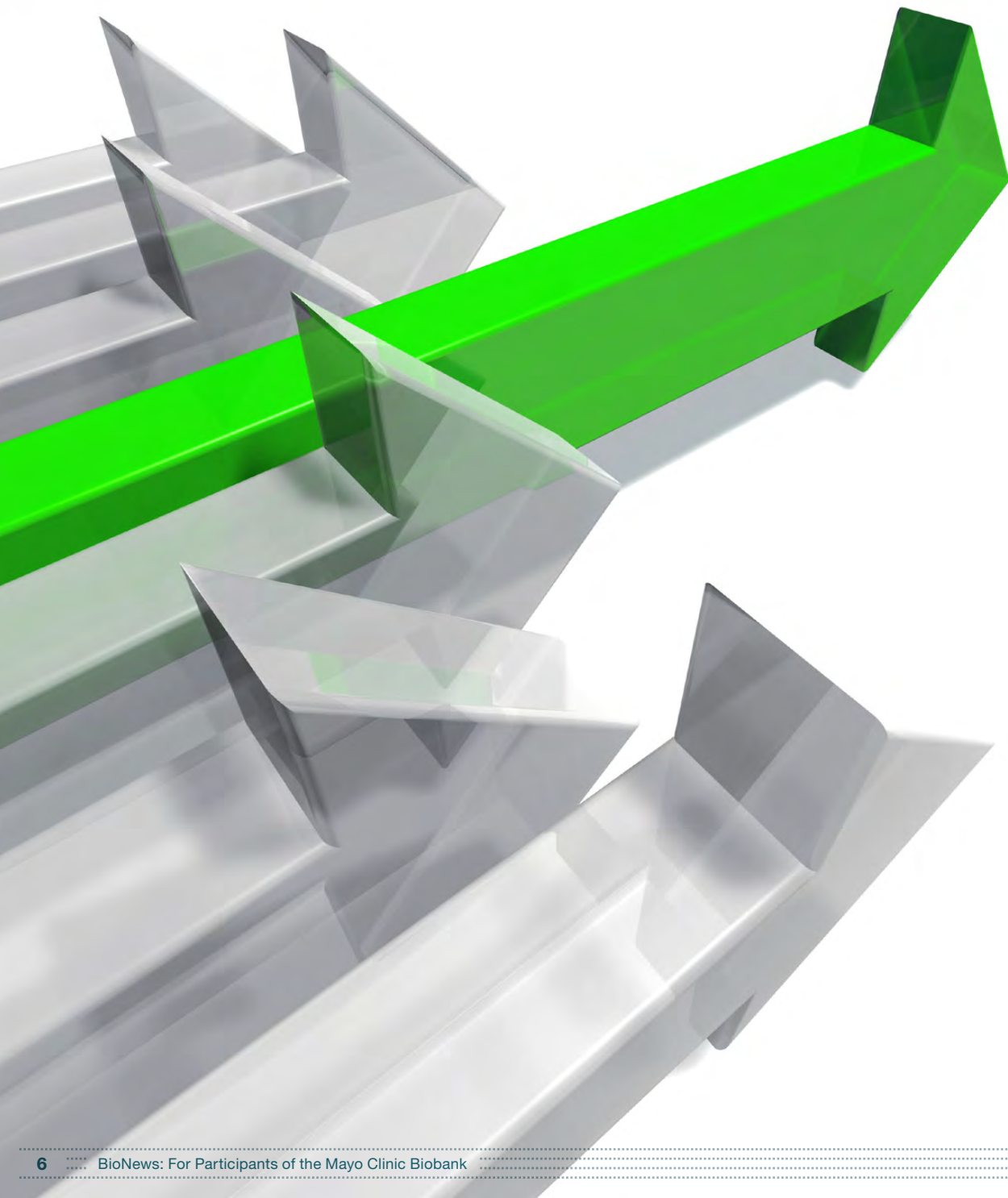
Janet E. Olson, Ph.D.
(Biobank Project Director)

Paul Y. Takahashi, M.D.
(Primary Care Internal Medicine Physician,
Medical Director of Biobank)

Stephen N. Thibodeau, Ph.D.
(BTOG Chair)

Karen Maschke, Ph.D.
(The Hastings Center)

Recent Activities of the Biobank Community Advisory Board



The Mayo Clinic Biobank Community Advisory Board (CAB) has been working hard on one issue: When should research findings be given back to Biobank donors?

The communication of research findings to individual Biobank donors is called “return of results.” As you know, the purpose of the Biobank is to encourage and support research on specific diseases or health problems. Most often, findings that are generated from that research are very preliminary. They are useful for the researcher but not shared with the Biobank donor, because there is no direct medical benefit. This means the results would not change a donor’s health care.

Return of Results

In some rare cases, however, research findings may be important to the health of an individual Biobank donor. The CAB is trying to help sort out exactly when the Mayo Clinic Biobank will offer such information to donors. Helping make such “judgment calls” is a major role of the CAB. It might seem at first glance that more information is always good. Our experience so far suggests that making these decisions is hard. Experts often disagree. It is very hard to determine when returning a research finding is the right thing to do.

The CAB started by holding several educational sessions where the issue of return of results was discussed, including a review of laws and national policy. Next, the CAB decided to have a discussion using an actual example. The Biobank Access Committee (see related article, p. 4) received a request from a Mayo Clinic researcher who studies a disease called polycystic kidney disease (abbreviated as PKD). That proposed use of the Biobank raised the question of whether in some cases genetic findings should be returned to individual donors.

The PKD Study:

The study compares the DNA of patients with polycystic kidney disease (PKD) to the DNA of Biobank donors who do not have PKD. There are specific genes that are known to be associated with PKD. In this project, researchers wish to study the meaning of certain alterations within these genes, alterations which are not understood. We are using the word “alteration” to describe changes in the DNA. We are not using the word “mutation” because we do not yet know if these gene changes cause disease.

What is PKD?

Mayo Clinic researchers study a group of genetic disorders that result in cyst development in the kidney known as polycystic kidney disease. They study three kinds of PKD:

- 1 a form of the disease that begins in adulthood,
- 2 a form that begins in early infancy, and,
- 3 a more complex form of the disease that includes problems outside the kidney, such as problems with the brain and spinal cord as well as defects in fingers and toes, which also occurs in infancy.

For these three disorders, the researchers have collected large numbers of patients with PKD and have screened them for alterations in the genes responsible for disease. This analysis has revealed a significant

number of genetic alterations that are of uncertain significance. This means researchers are not yet certain if these alterations actually cause polycystic kidney disease or if they are simply harmless gene changes. Testing for these gene alterations in a large group of normal individuals who are not known to have PKD will help the researchers to evaluate whether the alterations are linked to disease.

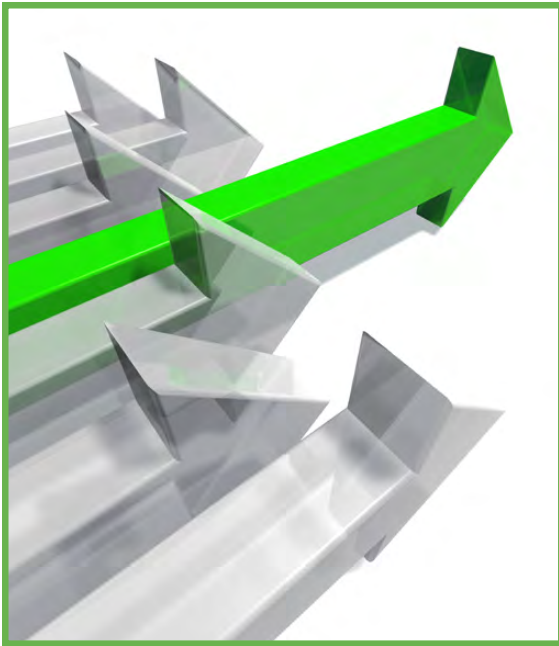
Why use the Biobank?

The Mayo Clinic Biobank population is a good control group for this research. A large group of samples from the Biobank that match the researchers’ samples will be a valuable resource for evaluating new genetic alterations.

Why is Return of Results an Issue in this Study?

As the research progresses, which gene alterations are truly associated with PKD will become better understood. There may be Biobank donors who have these gene alterations but do not know it. Since PKD is a disease where early treatment may be beneficial, Biobank donors could benefit from knowing they have a gene alteration. In addition, because PKD is an inherited disorder, family members may be at risk for PKD as well. Some people might want to know this information while others might not.

Continued >



How We Discussed the Case

Thinking about return of results ahead of time is one of the Biobank's ground rules. We discussed this "case" to help clarify these complex issues. The CAB members read background material provided ahead of time. One of the leading experts on PKD attended the meeting. He gave a presentation about the disease and was available to answer questions.

Next the CAB members divided up into two groups. Each group was lead by a facilitator. Members spent about an hour thinking about the case example, each imagining that he or she were the biobank donor who might be offered results. (Note that the Biobank already has an established policy that donors will never be required to get results.) They wrote out their hopes and concerns on colored paper and shared them with the group. We then discussed the CAB members "hopes" and "concerns" for receiving an offer of research results.

Hopes and Concerns

The conversation was rich and detailed. The CAB members understood the potential benefit. One CAB member noted: *"If I was informed I had a gene, I could watch*

my symptoms and possibly be diagnosed and receive treatment earlier." This idea of taking preventative steps or getting available treatment early on in the disease progression was also noted by two other CAB members: *"If manageable through drugs, [or] diet it would be good to know,"* and *"Can help patient provide information to their primary care provider."*

Many comments focused on an individual's family and how knowledge of PKD genetic research results might benefit them and their families. Such statements included: *"Can help family*

members be aware of disease so they can be checked," "It would allow me to know if my children should be tested," and *"An individual's offspring can be notified that their parent was a carrier."* One individual mentioned that if one has a *"bucket lister"* personality, knowing the results would bring focus to that person's life. CAB members also raised the hope that knowing in advance would aid mental and spiritual preparation with comments such as, *"Can help person prepare spiritually,"* and *"make peace w/ yourself."*

While discussion of "hopes" generated thoughts about the benefits of returning PKD results to donors or their families, considering "concerns" caused some CAB members to pause and think about negative consequences. Many CAB members were worried about what kinds of psychological harms might be caused by the return of a genetic finding. Comments focused on undue stress and anxiety for both the individuals themselves and for their families. For example, one CAB member stated: *"May cause personal or family panic."* Another talked about how over-reacting to learning about her risk

to PKD could lead to a lower quality of life: *"People might (some would) overreact and overestimate the risk and obsess over it, and it could lower their quality of life even if they don't have or may never get disease."*

Potential impact on quality of life was discussed. CAB members imagined what it might be like to learn about a condition that couldn't be prevented or treated. One member stated: *"If there is no treatment, or guarantees that I have it, why tell me? Why scare me?"*

Next Steps

The CAB members worked hard to master the complex technical details about the genetics of PKD. Following the meeting, the Biobank Co-Chairs conveyed details of the discussion back to the Mayo Clinic Biobank Access Committee and to the Biospecimen Trust Oversight Group. Because Biobank research is new, there is very little guidance about when to return results. The CAB discussions are of critical importance as we learn what kinds of results donors might wish to learn about. The discussion will continue! Return of results is a very hard issue. We are fortunate to have the CAB's involvement in helping to guide our policies. If you have thoughts or ideas, please mail or email.

CONTACT INFORMATION

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UPDATES ON THE WEB

... COMING SOON

We anticipate new and exciting updates by mid to late summer on our web site, so please visit us at:

mayoresearch.mayo.edu/biobank



A picture gallery showcasing some of our activities.



Videos further explaining the biobank and our overall missions and visions.



Additional new studies that are using Biobank Samples.



Posting of this newsletter in a printable format.



A page devoted to our Community Advisory Board activities and updates.

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



A Letter from the Community Advisory Board Co-Chair

Hello, my name is Gail Onderak. I am the newly elected co-chair of the Mayo Clinic Biobank Community Advisory Board (CAB). I would like to take this opportunity to communicate to you who the CAB is, what we as a group have been doing, and what my duties are as CAB co-chair.

The Community Advisory Board is made up of twenty members. Nine of these members were selected because of their participation in the Olmsted County Deliberative Democracy event. This event was an interactive discussion that took place over two weekends in September of 2007. Olmsted County community members engaged in an open dialogue about their hopes and concerns for a biobank. At the end of this event, participants agreed upon key recommendations for governance of an ideal biobank. The additional eleven members of the Community Advisory Board have been specifically chosen to reflect the diversity of community interests and backgrounds. Each of these members brings to the group a unique perspective and opinion that is valued.

“As a group, our goal at each of these meetings is to protect the rights of all Biobank participants.”

The CAB has met five times as of yet, and we plan to convene every two months moving forward. During these meetings, our members actively debate and reflect on the issues raised by biobanking. Most recently, we spent one meeting focused on the legal and ethical issues surrounding returning research results to participants. At another, we considered the consequences of data sharing in genetic research. As a group, our goal at each of these meetings is to protect the rights of all Biobank participants.

co-chair along with Barbara Koenig, Ph.D., a member of the Mayo Clinic Biomedical Ethics Research Unit. In this role, I have been attending the executive group meetings of the Biospecimen Trust Oversight Group (BTOG). BTOG is a committee of scientists, physicians, and ethicists charged with overseeing the operation of the Mayo Clinic Biobank, as well as other biospecimen collections at Mayo Clinic. In addition, I have participated in several Access Committee meetings, whose responsibility it is to review, prioritize, approve, and coordinate requests for use of the Mayo Clinic Biobank. As CAB co-chair at these meetings, I hope to represent the Community Advisory Board and be a voice for our community.

At the September 2010 Community Advisory Board meeting, I was elected to serve as CAB

In reading this, I hope that you have gained a better understanding of who the CAB is and what we are trying to accomplish. As always, you can find more information about the Biobank by visiting the website:

<http://mayoresearch.mayo.edu/biobank>.

Sincerely,

Gail Onderak
Community Advisory Board Co-Chair

Contact Us

If you have questions or need more information about the Mayo Clinic Biobank, please contact one of our staff members at:

507-293-0203 (local)

1-866-613-2386 (toll free)

biobank@mayo.edu (e-mail)

<http://mayoresearch.mayo.edu/biobank>



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