PARTNERS BIOBANK NEWSLETTER

PARTNERS HEALTHCARE | BIOBANK

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Biobank by the Numbers

67,000
participants

125
supported studies

15,000
genotyped samples

640,000
stored samples

Thank you again for your continued participation in the Partners Biobank.

Elizabeth Karlson, MD
Co-Director
of the Biobank

The mission of the Partners Biobank is to drive the medical discoveries that will help improve healthcare for generations to come. Your participation, and the participation of more than 60,000 people in our communities, is at the heart of this mission.

To date, the Partners Biobank has provided samples and data to more than 125 researchers at Massachusetts General, Brigham and Women's, and McLean hospitals. Your engagement in the Partners Biobank fuels their research into new ways to understand, treat, and even prevent disease.

This newsletter includes:
- A summary of our return of research results program
- Descriptions of a few of the research studies that are using Biobank samples and data

As always, we rely on our community of participants to help support research at our hospitals. We thank you for your continued support!

Coming soon: The Biobank has collected blood samples for 75% of participants. We try to make blood collection as easy as possible. As such, we have been working to automate the Biobank order for a blood sample. This means that if the Biobank has not yet collected your sample, we will be able to add this to your next blood draw when you see your doctor or healthcare provider.

Returning Research Results to Biobank Participants

The Partners Biobank has started returning research results to Biobank participants. These results are genetic variants, also called mutations, that indicate a high risk of developing certain conditions and diseases if the research result is validated by a clinical test. The purpose of returning research results is to provide Biobank participants with information that could positively impact their clinical care.

Results being returned are genetic variants that the American College of Medical Genetics (ACMG) defines as being actionable. This means that there are screening tests and/or preventative measures for people who have these variants.

Examples include variants that are associated with higher risks of developing breast and ovarian cancer, colon cancer, or cardiomyopathy. As genetic knowledge increases, the list of variants that are considered medically actionable will change. Biobank staff will regularly review all the DNA we have analyzed to ensure we are contacting all participants with actionable variants as this list evolves.

"We believe that this program exemplifies one way in which the Biobank can positively impact participants' health" said Scott T. Weiss MD, Principal Investigator of the Biobank and Head of Personalized Medicine at Partners HealthCare.

Scott T. Weiss, MD,
Principal Investigator
of the Biobank

The Biobank is funded to analyze DNA, through a process called genotyping, for 50,000 of its participants. Altogether, only about 500 (1%) of these people are expected to have a genetic mutation considered to be medically actionable. The Biobank will return results to these 500 participants on an ongoing basis for the next few years.

Biobank staff will send letters and make phone calls to schedule a free consultation with a Genetic Counselor. This is a research result that needs to be repeated to confirm that it is a medically actionable result.

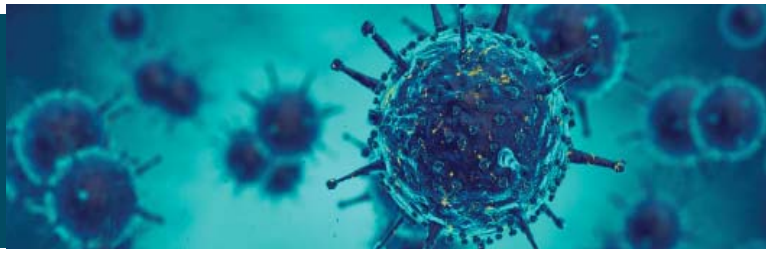
The Genetic Counselor is a resource to help participants decide whether to get the research result validated in a clinical laboratory. The decision to pursue clinical validation and receive the result is up to each participant. The Biobank will cover the cost of the test to validate the result, if done at clinical laboratory affiliated with the Biobank. The consultation to learn and discuss the result of this clinical test will be billed to the participant or the participant's insurance per standard clinical processes.

The Biobank is a research program and does not replace clinical care. The vast majority of Biobank participants will never be contacted with research results. This does not mean a Biobank participant doesn't have or won't develop an important health problem.

The return of research results program is in its early stages and will likely evolve with feedback from researchers and participants alike. Your opinion matters and if you have any thoughts on the return of results program please contact us by email (biobank@partners.org) or by phone (617-525-6700).

For more detailed information about the return of results process, including the list of medically actionable variants, please visit our website at www.partners.org/biobank.

New Approach to Disease Detection



Cells are the basic building blocks of all living things. The death of cells is an indication of tissue damage, and plays a key role in disease development and the understanding of overall health. The accurate detection of cell death holds the potential to transform medicine through earlier detection of disease, assessment of disease progression, and real-time evaluation of treatment.

Raul Mostoslavsky, MD, PhD, a researcher at the Mass General Cancer Center, and his lab are investigating the connection between cell death and disease progression through the study of DNA. For this project, Dr. Mostoslavsky has teamed up with Yuval Dor, PhD, and Benjamin Glaser, MD, both at the Hadassah Medical Center at the Hebrew University of Jerusalem.

When a cell dies, it releases fragmented DNA that circulates freely in the blood. This circulating DNA has unique "fingerprints," characteristics that indicate the origin of the dying cell. This means that analysis of circulating DNA holds the promise to indicate where tissue damage is occurring potentially before it impacts someone's health.

The primary focus of this research project is to develop a novel technology for the monitoring of cell death in specific tissues through a simple blood test. This new test would be among the first to be able to measure specific cell death in a non-invasive way, and to enable researchers to both identify that cell death occurred and also the site from which it originated.

This method has the potential to be applied to earlier detection of multiple types of cancer, type 1 diabetes, and neurodegenerative diseases. It could also be utilized to evaluate tissue damage following a traumatic brain injury or stroke.

Samples from the Partners Biobank are being used in two ways for this research. The first is the examination of cell death events within specific populations to determine patterns of tissue DNA across groups. For example, in a group of aged individuals, a common pattern of tissue DNA might predict biological aging.

The second, longer-term goal is to utilize the uniqueness of the Biobank to track patients who develop cancer after they provided their Biobank sample, to determine whether tissue-specific DNA predictors were present before disease presented. The Partners Biobank is integral to this research because it provides the possibility for both retrospective and prospective research.

Recent Research Studies: We have distributed samples and data to more than 125 studies, including the three below. For more detail, please go to https://biobank.partners.org/research-initiatives.

Improved Treatment of Kidney Cancer, Vladimir Valtchinov, PhD and Atul Shinagare, MD, Center for Evidence Based Imaging, Department of Radiology at BWH.

Renal Cell Carcinoma (RCC), the most common type of kidney cancer, accounts for close to 90 percent of all cancers of the kidneys. A substantial number of well-established gene variants are associated with the development of RCC. The goal of this research is to establish and assess clinical relevance of correlations between diagnostic imaging (MRI and CT scans) and established gene variants (both hereditary and sporadic) in RCC, and further assess their predictive relevance with outcomes and treatment options.

Health Impact of Working the Night Shift (SHIFT Study), Richa Saxena, PhD, Department of Anesthesia, Critical Care and Pain Medicine at MGH.

The Partners Biobank has provided Dr. Richa Saxena and her team a unique opportunity to advance their research on understanding the link between sleep, genetics and common chronic diseases. Dr. Saxena has started a new study called SHIFT, which is seeking to better understand how sleep and diet patterns of night-shift workers may influence the development of type 2 diabetes. The researchers are using Biobank genetic data and Health Information Survey data to identify and recruit day- and night-shift workers who might be interested in participating in the SHIFT study.

New Technology for Diagnosing Cancer, Alarice Lowe, MD, Director of Circulating Tumor Cell Laboratory, Department of Pathology at BWH.

Patients with early and late stage cancers have been found to have rare tumor cells in their blood, known as Circulating Tumor Cells (CTCs). Dr. Alarice Lowe is researching how to develop better systems to identify these CTCs and test them with standard pathology protocols. Her research has allowed her to recently publish a paper confirming the use of routine methods used in a cytology laboratory to process CTC samples. Dr. Lowe is currently using Biobank samples to test new CTC systems and protocols, with the potential to replace invasive biopsy tests that are currently used to diagnose cancer.

List of Research Results that are being Returned and Confirmed by Clinical Validation

This list was adapted from the American College of Medical Genetics and Genomics (ACMG) list of medically actionable genes. This list is regularly updated.

Phenotype/Associated Condition	Gene	Description
Hereditary Breast and Ovarian Cancer	BRCA1	An increased risk for the development of breast, ovarian, prostate and other cancers.
	BRCA2	
Li-Fraumeni Syndrome	TP53	A rare disorder that greatly increases the risk of developing several types of cancer, particularly in children and young adults.
Peutz-Jeghers Syndrome	STK11	A syndrome that causes the development of noncancerous growths, called hamatomatous polyps, in the gastrointestinal tract (stomach and intestines).
Lynch Syndrome	MLH1	A disorder characterized by an increased risk of many types of cancers, particularly colon cancer.
	MSH2	
	MSH6	
	PMS2	
Familial Adenomatous Polyposis	APC	A syndrome marked by an increased risk for the development of colon cancer.
MYH-Associated Polyposis; Adenomas, multiple colorectal, FAP type 2; Colorectal adenomatous polyposis, autosomal recessive, with pilomatricomas	MUTYH	A disorder characterized by an increased risk of colon cancer.
Juvenile Polyposis	BMRP1	A disorder characterized by the development of noncancerous (benign) growths, specifically in the gastrointestinal tract, before the age of twenty.
	SMAD4	
Von Hippel Lindau Syndrome	VHL	A disorder characterized by the formation of tumors and cysts in many parts of the body, including the brain, spinal cord, and retina.
Multiple Endocrine Neoplasia Type 1	MEN1	A syndrome associated with tumors of the endocrine (hormone-producing) glands.
Mulitple Endocrine Neoplasia Type 2	RET	A syndrome associated with a high risk of developing thyroid cancer and other tumors of the endocrine glands.
Familial Medullary Thyroid Cancer	RET	A syndrome associated with an increased risk of developing thyroid cancer.
PTEN Hamartoma Tumor Syndrome	PTEN	A disorder that causes a high risk for the development of benign and malignant **tumors** of the thyroid, breast, and uterus.
Retinoblastoma	RB1	An eye cancer that begins in the back of the eye (retina) in children.
Hereditary Paraganglioma-Pheochromcytoma Syndrome	SDHD	Syndromes characterized by the growth of paragangliomas, which are tumors that come from neuroendocrine tissues. The paragangliomas develop in the skull base and neck.
	SDHAF2	
	SDHC	
	SDHB	
Tuberous Sclerosis Complex	TSC1	A multisystem disorder characterized by the growth of noncancerous (benign) tumors in many parts of the body, most commonly skin, brain, and kidneys.
	TSC2	
WT1- related Wilms tumor	WT1	Most common kidney tumor that is developed in childhood, and can often leads to kidney cancer.

Neurofibromatosis type 2	NF2	A disorder most commonly associated with noncancerous tumors in the nervous system. These growths develop along the nerve that carries information from the inner ear to the brain.
Ehlers-Danlos Syndrome-vascular type	COL3A1	Disorders that affect the connective tissues that support the skin, bones, blood vessels, and many other organs and tissues. Most commonly affects the joints and skin.
Marfan Syndrome, Loeys-Dietz Syndromes, and Familial Thoracic Aortic Aneurysms and Dissections	FBN1	Disorders characterized by the enlargement of the aorta which increases risk of aneurysm.
	TGFBR1	
	TGFBR2	
	SMAD3	
	ACTA2	
	MYH11	
Hypertrophic cardiomyopathy, Dilated cardiomyopathy	MYBPC3	An increased risk of heart disease that can cause sudden cardiac arrest young, seemingly healthy individuals.
	MYH7	
	TNNT2	
	TNNI3	
	TPM1	
	MYL3	
	ACTC1	
	PRKAG2	
	GLA	
	MYL2	
	LMNA	
Catecholaminergic polymorphic ventricular tracycardia	RYR2	A condition characterized by abnormal heart rhythm (arrhythmia).
Arrythmogenic right ventricular cadriomyopathy	PKP2	An increased risk of heart disease that appears in adulthood, can cause sudden death during strenuous exercise.
	DSP	
	DSC2	
	TMEM43	
	DSG2	
Romano-Ward Long QT Syndromes Types 1,2, and 3, Brugada Syndrome	KCNQ1	Condition associated with irregular heartbeats that can cause fainting, seizures, or sudden death.
	KCNH2	
	SCN5A	
Wilson Disease	ATP7B	A disorder that causes too much copper to accumulate in the organs, particularly the liver, brain, and eyes.
Orinthine transcarbamylase deficiency	OTC	A disorder that causes ammonia to accumulate in the blood. This can cause developmental delay, intellectual disability, and liver damage.
Malignant hyperthermia susceptibility	RYR1	A rare life-threatening condition that is usually triggered by exposure to certain drugs used for general anesthesia
	CACNA1S	