University of Maryland
School of Medicine
Amish Research Clinic
921 Village Road
Lancaster, Pa 17602

Our Mission

The Amish Research Clinic contributes to improvements in healthcare through research. We serve as a resource for health information and knowledge to the Amish Community.

Phone #: (717) 392-4948

2018 Annual Newsletter

Amish Research Clinic

Greetings from the Amish Research Clinic

We hope you and your family are healthy and happy. The purpose of this newsletter is to keep you informed about our medical research and what we have learned from the studies you have made possible by donating your precious time as a research participant.

I like to reflect back on our humble beginnings exactly 25 years ago when our medical research with the Amish began on a shoestring budget in 1993. I traveled door to door with Sadie Beiler performing tests for diabetes in the homes of Amish research volunteers. Working from the trunk of a Honda Accord, we administered sugar drinks and drew blood samples. Once the two-hour test was completed, we fired up a portable generator which powered a small centrifuge to process the blood samples before returning to Baltimore each day where the sugar levels were measured in the laboratory. We performed over 100 glucose tolerance tests in virtually every corner of Lancaster County. We found many families in which diabetes was common. In addition to diagnosing diabetes in many unsuspecting Amish, we provided education about diet and lifestyle, home blood glucose monitors and strips, and medical follow-up for further treatment when necessary. This work led to a grant that enabled the opening of the Amish Research Clinic in February 1995. For about 10 years, the Amish Research Clinic was located on the first floor of the Clinic for Special Children in Strasburg. Our next 10 years were in a leased building in the Greenfield Business Park. Thanks to Davy Stoltzfus and the Amish Research Clinic Advisory Committee, the ARC now has a permanent home in Lampeter where we conduct our medical research.

Over the years we have studied many different conditions at the ARC, including diabetes, heart disease, high blood pressure, cholesterol abnormalities, osteoporosis (weak bones), breast density, celiac disease, mental health and illness, obesity, and longevity and wellness. We are also interested in understanding how certain medications work and why some people respond well to them while others do not. To date, more than 8000 Amish have participated in one or more of our studies. Our largest study is the Wellness Study, which has recruited over 5500 volunteers. This study provides participants with screenings for heart disease, anemia, thyroid problems, liver disease, kidney disease, diabetes, abdominal aneurisms, and osteoporosis. None of this work would be possible without our compassionate Amish volunteers and the Amish Community, who have provided their partnership and support. Together, our research has resulted in new discoveries that has had an impact on health in the Amish as well as for people around the world.

As many of you know, I now work for Regeneron, a large drug company whose goal is to use genetic discoveries to develop new medicines. I still maintain my appointment at the University of Maryland and am at the ARC regularly. The University of Maryland - Regeneron collaboration has created a very exciting opportunity to fast-track some of the discoveries made in the Amish into new medicines.

We currently have 10 active studies and continue to need volunteers. Participating in research may provide a number of health benefits including free medical evaluations and screenings for a number of common disorders. It also provides the opportunity to contribute to new knowledge, which may help millions of people with the diseases that we study. Some of the studies are conducted at our clinic in Lancaster and free transportation to and from the clinic is provided. Other studies are conducted right in your own home. Not only do you gain lots of knowledge about your health but with most studies, we even pay you for your time and effort. If you have any questions or you are interested in participating in any of our studies, please call 717-392-4948. You can also write us a note. Please make sure you include your address and phone number so we can get back to you.

Amish Liaisons

Anna Esh (New)
Naomi Esh
Susie Fisher
Hanna King
Sylvia King
Verna Petersheim
Barbie Ann Stoltzfus
Barbie B Stoltzfus
Fannie Stoltzfus
Mary Stoltzfus
Susie Stoltzfus
Lydia Zook

Patrick Donnelly, RDCS, Sonographer

Maryann Drolet, BSMT, ASCP, Research Specialist

Nancy Fisher, (New) Research Nurse

Mary McLane, CNM, MSN, Research Nurse

Sylvia Newcomer, BSMT, ASCP, Research Specialist

Yvonne Rohrer, RN, Research Nurse

Susan Shaub, RN, BSN, Nurse Coordinator

Donna Trubiano, RN, Research Nurse

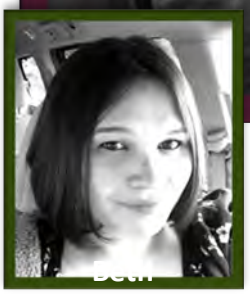
Nancy Weitzel, Research Nurse

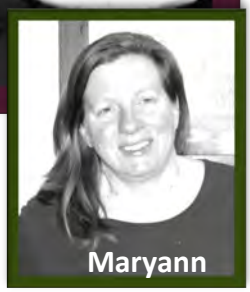
Regina Guaraldi, Driver (New)

Grace Redcay, Driver

Fred Young, Driver (New)

Elizabeth Zehr, Administrative Assistant





Lancaster Research Team

Braxton Mitchell, PhD, MPH

We hope you enjoy this issue of the newsletter!

Alan Shuldiner and the ARC team

Alan Shuldiner, MD

Maryland Research Team

Amber Beitelshees, Pharm. D., MPH
Carole Sztalryd-Woodle, PhD
Christy Chang, PhD
Coleen Damcott, PhD
Michael Miller, MD
Joshua Lewis, PhD
Mao Fu, MBBS, PhD
Elizabeth Streeten, MD
Nanette Steinle, MD

Pamela Lambert
Simeon Taylor, MD
Teodor Postolache, MD
Toni Pollin, PhD
Julie Douglas, PhD
Norann Zaghloul, PhD
May Montasser, PhD
Robert Reed, MD
Elliot Hong, MD

Kavita Thanglavelu, MSW
Samantha Lightner, BS
Feven Fisseha, BA
Krissa Jackson
Judy Liu RN, MS
Beth Steger, LCSW-C
Caroline Silva, LCPC
Melanie Daue

Amish Wellness Study

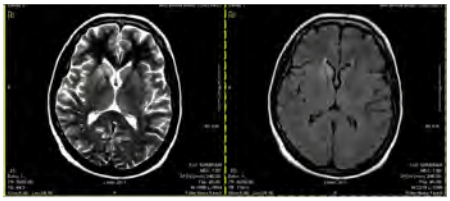
The Amish Wellness Study continues to recruit participants. This study offers all Amish adults basic wellness screening including tests of cholesterol, blood sugar, thyroid, bone strength, and heart health. We have found that high cholesterol and hypothyroidism (low thyroid function) are quite common in the Amish. Blood is also being collected and stored at the University of Maryland for research on genetic and non-genetic factors in health and disease. The research team hopes to visit all Amish households. Testing takes place in our "Wellmobile" housed in a large motor vehicle which visits each Church district. If we haven't visited your Church district yet, we will be there in the future. To date, over 5000 Amish individuals ages 18 and older have enrolled in the Wellness Study, which is funded by our partnership with Regeneron Genetics Center LLC. Thank you!

Brain Body Connection

The Brain Body Connection is a study of behavioral health and wellness. The purpose of the research is to find out more about brain differences that make it more likely someone will have mental health problems. This is a study for families where one or more family members participate in the study; both those who struggle with issues and those who do not. Amish adults and children aged 12 and above are eligible to participate.

The study has two parts that require full days to complete and study participants are compensated for their time and effort. The first part takes place at the Amish Research Clinic. It includes a clinical assessment and interviews. The second part takes place in Catonsville, MD and involves magnetic resonance imaging (MRI) of the brain. We use these pictures to understand the brain circuits, or wirings, which are related to mental health. These brain wirings often run in families.

If you would like to learn more about this study, please contact the Amish Research Clinic at 717-392-4948.



Ongoing Studies

Donation Message

The Amish Research Clinic is a non-profit organization. Freewill donations, to help with operating expenses are appreciated. Checks can be made payable to the University of Maryland Baltimore Foundation (or UMBF), which administers gifts to the University of Maryland Amish Research Clinic and sent to:

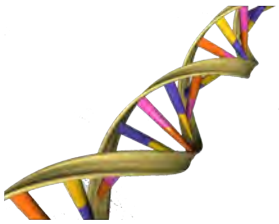
University of Maryland School of Medicine
Office of Development
Attn: Amish Research Clinic
31 South Greene Street
Baltimore, MD 21201

We want to thank those of you who have provided us support in the past. With your help, we have been able to purchase two new transport vans and cover expenses associated with our new clinic. If you have any questions, please call Pamela Lambert at 410-706-0419 or 717-512-6013.

All Publications can be viewed on this website…

https://www.ncbi.nlm.nih.gov/myncbi/collections/47782571/

Until recently, medications have been made with the idea that each drug works pretty much the same in everybody. We now know that the "one size fits all" approach does not work for everybody. We have two studies that are looking at the effects of certain gene variations on medications that are currently being used to treat type 2 diabetes. The information from these studies may help doctors know how to choose the best medication or best dosage for people with type 2 diabetes.



Pharmacogenetics of GLP1R Inhibitors

This study looks at how well exenatide and sitagliptin, FDA approved drugs that are used to treat type 2 diabetes, work in different people. We are recruiting healthy people that have participated in an Amish Research Clinic study before and carry certain gene variations that may affect how well exenatide or sitagliptin lower blood sugar.

Genetics of Response to Canagliflozin

This study measures the effect of canagliflozin, an FDA approved drug that is used to treat type 2 diabetes, on healthy, non-diabetic people to see if a person's genes influence how well the canagliflozin removes sugar from the body. We also want to see if a person's genes influence whether they are at risk for side effects from the drug. This study involves taking canagliflozin for 5 days.

Chromosome 9 Study

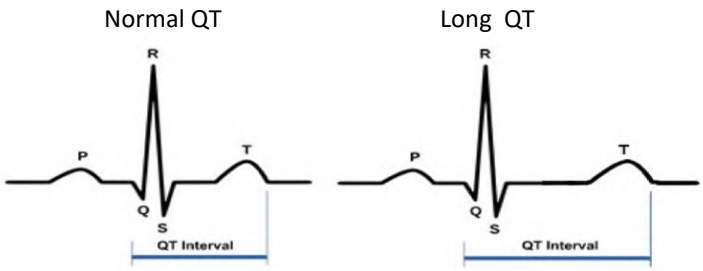
A New Gene associated with LDL Cholesterol

Elevated low density lipoprotein cholesterol (LDL) is a major risk factor for cardiovascular disease (CVD), the leading cause of death worldwide. LDL is governed by genetics and environmental factors, as well as the interplay between them. While environmental risk factors for LDL are very well established, most of the LDL genetic risk factors are still unknown. Identifying the genes related to LDL can help in better understanding the role of LDL in CVD leading to improved prediction, prevention and treatment of CVD.

We recently identified a variation in the *B4GALT1* gene that appears to be strongly associated with LDL. The rare variant is found in 6% of the Amish while extremely rare in the general population. It seems to be associated with lower levels of LDL. The overall goal of this project is to confirm this association and learn more about other effects of this variant. We hope to gain key insights into LDL metabolism by researching carriers of this genetic variant.

KCQN1

Through our genetic analyses, we identified a variation (mutation) in the gene *KCNQ1*, which is associated with Long QT Syndrome (LQTS). LQTS is associated with an increased risk for fainting and sudden death, throughout the lifespan. LQTS causes at least 10% of crib deaths and can cause sudden death in children and adults, generally during physical activity. Mutations in *KCNQ1* are present in about 1/2000 in the general population but are present in 1/40 in the Amish. Beta blocker medications are very effective in LQTS, preventing fainting and sudden death by 70-90%. In this study, we are gathering information on how common fainting and sudden death are in LQTS in Amish individuals who have this gene mutation, assessing risk in individuals and recommending beta blocker medications to those who are at high risk. We havae not finished analyses yet but so far, we have found that fainting is common in Amish individuals with the mutation and 13% have an immediate family member who has died suddenly below age 30. People who have been involved in our previous studies who carry this mutation have been mailed a letter indicating that they have the mutation and asking if they are interested in evaluation.



Studies in Analysis

Breast Density Study

Breast density refers to the amount of dense glandular tissue in the breast. It is measured by a routine mammogram or x-ray of the breast to detect unsuspected cancer. Dozens of studies over the past quarter of a century have suggested that dense breasts are more cancer prone. But no one knows exactly why. With the help of nearly 1,500 Amish women, we've been trying to answer that question by searching for the genes that affect density. We recently published an article, together with our colleagues in the US and abroad, describing over half a dozen genes that influence breast density in the Amish and other populations of European descent. Several of these genes are also associated with the risk of breast cancer.

Over the coming year, we plan to continue searching for new genes that influence breast density and studying the link between breast density and breast cancer. Meanwhile, we would like to remind all Amish women of the importance of getting a routine mammogram. The National Cancer Institute recommends that women over the age of 40 years have a mammogram every 1-2 years coupled with a breast exam by a doctor to improve the early detection of breast cancer. By doing so, a woman may reduce her risk of dying from breast cancer by about 17% (if she is 40 to 49 years old) and by about 30% (if she is 50 years or older). If you need assistance scheduling a mammogram, please call us at 717-392-4948.

Zinc Study

Based on increasing knowledge of genes that affect diabetes, we enrolled 60 participants in a study to evaluate the effect of a zinc supplement on blood sugar and insulin levels. The participants spent two mornings in the clinic and took a zinc supplement for 14 days in between. We found that some people improve their insulin levels in response to zinc while others do not. This work was recently published in a scientific journal.

Genetics of Pain Study

Pain is the primary reason that patients seek medical attention. Recent medical advances have dramatically increased life expectancy and, therefore, the number of people living with chronic diseases and chronic pain. More than 116 million Americans are chronically in pain, and they make more than 70 million visits to healthcare providers at a cost of more than $600 billion every year. Most of the patients have their pain for five or more years, causing decreased quality of life and increased stress for the entire family. Scientists believe that there is a link between our genes and how we sense pain, which is why some people require more pain medication than others after the same injury, or develop chronic pain after recovering from an illness. However, exactly which genes are involved in determining these differences are not known. The goal of this research project is to gain a better understanding of how our genes control pain sensing and why some people feel more pain than others. We recruited over 100 participants and measured their response to pain from heat, cold and pressure. While the participants experienced some temporary pain from heat, cold and pressure produced by an instrument placed on their arms, they were not injured in any way and all subjects tolerated the testings very well. We are now in the data analysis phase of this study. Thank you so much for supporting this effort and to our participants, for giving your time so generously.

PPAR Study

The purpose of the *PPAR Study* is to determine why some people do not respond to pioglitazone, an approved drug commonly used to treat diabetes. We thank the around 30 Amish participants who participated in the study. We are in the process of analyzing the samples to find the genes responsible for individual differences in response. Once we finish the analyses we will return with more information in this newsletter. It is possible that we may resume recruitment in the future to study groups of people that are either very responsive or very non-responsive to pioglitazone.

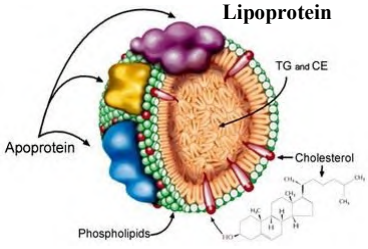
Ongoing Studies

CES1 Study (New Study)

When a person suffers from a heart attack or needs to get a stent placed, doctors usually prescribe aspirin and a drug called clopidogrel (also known as Plavix) in order to prevent blood clots. While these drugs work well in most patients, some people do not respond adequately to clopidogrel. One of the reasons why people don't respond well to the drug is because of their genetics. Luckily, doctors have different options of the medications they can prescribe if they believe that clopidogrel will not work well. One of those drugs is called ticagrelor. Ticagrelor does the same thing as clopidogrel but in a slightly different way. In this study, we will evaluate how differences in a gene called CES1 affects how people respond to clopidogrel. In addition, those same people will also take ticagrelor and we will study how well this drug works in them. The purpose of this study is to help doctors prescribe the right medication to people based on their genetic background. These results could be very important in preventing heart attacks and complications during heart surgery by making sure the right people get the right medicine.

The Lipoprotein Turnover Study

Lipoproteins are special types of packages in the blood that help carry and deliver dietary fats and cholesterol to parts of our body that need them. This study will help us learn more about how certain genetic changes affect the way the body makes or uses lipoproteins. We will compare someone who has a genetic change with a sibling who does not have that change. Our study will look at the way these fat and cholesterol packages are made and broken down. This information might help in developing new ways to prevent or treat disorders of fat and cholesterol metabolism.



Perfect Pitch (New Study)

Some of you may have heard about, or even participated in, the Perfect Pitch study. This study was inspired by one of our neurologist colleagues, who has an interest in how the brain works to process music. Some people have the rare ability to precisely recreate musical notes after hearing them only once. Moreover, ability to do this may run in families. In the Perfect Pitch Study, we are testing participants to see if they have this trait, and we will then see if we can map perfect pitch to particular genes to understand how the brain processes this type of information.

Sulfate Survey

Sulfate helps to regulate the function of many cells in our body. It helps the body make hormones; it modifies other nutrients and chemicals needed for brain function; and it affects how we break down and use medications. Regarding the effects of sulfate in the brain, there has been some speculation that sulfate deficiency could even be related to developmental problems in social behavior that affect the ways we socialize with other people. However, little is known about how sulfate regulation in the human body may alter development or brain function.

The Sulfate Study is a family-based research study that explores the impact of circulating sulfate levels on human communication, social interaction, and behavior. The study uses surveys and questionnaires to obtain information about how genes and other variables affect these factors. Two of the genes we want to study are related to the processing of sulfate in the body and can significantly change the levels of sulfate.

We are currently asking some of the participants in the Wellness study to complete the questionnaires. So far 311 people have agreed to participate. We have begun preliminary analyses on these and hope to complete the analysis in the coming months. The results obtained from this study may help us better identify factors that increase or decrease the risk of developing behavioral or social abnormalities, such as Autism Spectrum Disorder.

Ongoing Studies

Studies in Analysis

Seasonal Affective Disorder Study (SAD)

Seasonal Affective Disorder (SAD) affects millions of Americans. People with SAD have low mood, low energy, gain weight, and feel sleepy through the winter. Decreased day length triggers SAD in some individuals and light therapy treats SAD. Some patients need medications or talk therapy for a full improvement. This is the first study of SAD in the Amish. Our findings, published in the Journal of Affective Disorders, show that the frequency of SAD and the heritability of the disorder are lower than expected. We have also published an article in the Journal of Clinical Psychiatry on Australian twins and Old Order Amish, suggesting that in Australian twins, but not in the Amish, seasonal affective disorder overlaps with bipolar disorder and schizophrenia. We are also finalizing an article on a link between seasonality of mood and lower adiponectin, a hormone implicated in weight regulation, previously associated with depression. We are also finalizing a publication on measuring light in the Amish homes.

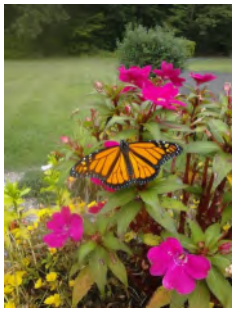
Omega-3/Fish Oil Study

This study is designed to learn whether omega-3 fish oil can help to reduce the type of fat that causes health problems. Fat that accumulates in the gut appears to promote inflammation more than fat that accumulates in other areas of your body and this may put you at increased risk of heart disease. Omega-3 fish oil lowers blood fats (triglycerides) but we are not sure whether it also reduces inflammation of fat. To be eligible for this study, Amish men and women older than 18 years needed to have a fasting triglyceride levels above 150 with an increased waistline (35 inches or more in women and 40 inches or more in men). Participants were assigned to take either omega-3 or placebo capsules (4 each day). At the beginning and end of the 9 month study, pictures of their fat were taken using a technique called magnetic resonance imaging (MRI). We removed a small amount of fat from the belly by aspiration and blood and urine collection were performed at the beginning and end of the study. We are currently not recruiting for this study. We will be analyzing the data in the near future.

Toxoplasma gondii Exposure Questionnaire

Toxoplasma gondii (T. gondii) is a microscopic organism found in about 10-20% of people in the US. In the Old Order Amish in Lancaster, we found it in approximately 50% of individuals. Most people with T. gondii are healthy. However, T. gondii can occasionally cause disease, mainly in people with a weakened immune system and babies born to women first exposed during pregnancy. In addition, some research suggests that T. gondii may be associated with depression.

Questionnaires asking about factors that have been shown to contribute to being exposed to T. gondii were mailed the beginning of January 2016; to people that participated in the Wellness Study. Thank you to all who have participated in this study. We have further analyzed the risk factors and we are now working on writing manuscripts. The main result is that eating undercooked or raw meat, drinking unpasteurized milk and working with animals is linked with being positive for T. gondii. We are also investigating links between different types of T. gondii and immune responses that may affect other organs, and genetic links with T. gondii exposure. We recently published an article accepted on the heritability of neopterin, a marker of inflammation previously found elevated in T. gondii positivity. The heritability appeared to be small, and thus neopterin levels in the blood might be more a reflection of a "state" under the influence of changes in the environment rather than stable traits. We also found a weak association with mood states. We plan to also study in collaboration with Dr. Hong, the connection between T. gondii and changes in brain functional connectivity and white matter integrity. We are also in the process of analyzing samples of settled dust from Amish homes and air conditioning filters near Amish fields as well as air samples collected during field work to investigate a completely new way of transmission, i.e. airborne. The analysis of these samples for T. gondii includes genetic and biological approaches. This project, if the airborne presence of T. gondii is confirmed, may lead to new guidelines for pregnant women in areas with high prevalence, given that becoming infected during pregnancy may very adversely affect the brain of the newborn.



Pharmacogenetics of SGLT2 Inhibitors

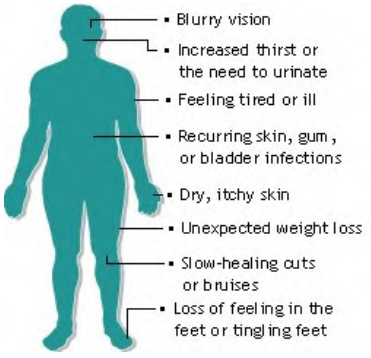
This study, which began the summer of 2015, will help us have a better understanding of the effect of canagliflozin on healthy, non-diabetic people to see if a particular gene variation influences how well canagliflozin works in the kidneys to remove sugar from the body. People who participated in an Amish Research Clinic study before and carry certain gene variations participated in this study.

Osteoporosis Study

This study was started in March 1997 and thanks to our many wonderful Amish participants, we are making great progress in studying genes that are important for bone health. In collaboration with many other groups around the world, we have found 64 genes that are important for bone health. Bone strength (at its "peak" in the early 20s in women and mid 20s in men) is 85% determined by genes. Bone loss, starting around age 50 is at least 30% due to genetic causes. This study which includes a free DXA bone density scan, remains open for recruitment to Wellness participants age 50 and above, who receive an abnormal heel ultrasound. The study also offers a rescan every two years to previous Osteoporosis study participants who had abnormal results.

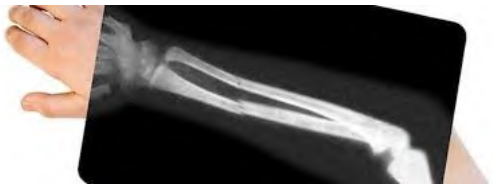
The Amish Family Diabetes Study (AFDS)

The Diabetes Study was the very first study done by the Amish Research Clinic, 25 years ago! The goal of this project is to identify genes involved in the adult-onset form of diabetes, also called Type 2 diabetes. Identifying these genes may lead to new understandings of the disease and better ways to prevent or treat it. Thanks to many of the Lancaster Amish, we have recruited over 1300 volunteers. The search for diabetes risk genes is ongoing. Symptoms of diabetes may include fatigue, increased thirst, hunger and urination. If left untreated, diabetes can lead to eye, liver, kidney, nerve and blood vessel problems. If you or someone in your family is experiencing these symptoms and would like to be tested for diabetes, please call the clinic at 717 -392-4948. All testing is free and usually done in your home.



OPPG Study

Osteoporosis pseudoglioma syndrome (OPPG) is a rare genetic disorder of weak bones (osteoporosis), blindness (from birth) and sometimes behavioral problems. Although OPPG is extremely rare in the general population (about 60 people with OPPG are known worldwide), many children with OPPG have been diagnosed in the Old Order Mennonite community in PA (15 children so far). OPPG can lead to multiple broken bones (fractures) of the upper and lower leg bones and back. Dr Streeten has been studying OPPG for many years, trying to find a new treatment that will help strengthen the bones in people with OPPG. Traditional medications used to treat osteoporosis can help in OPPG but do not totally prevent fractures. Currently, this protocol is not active.



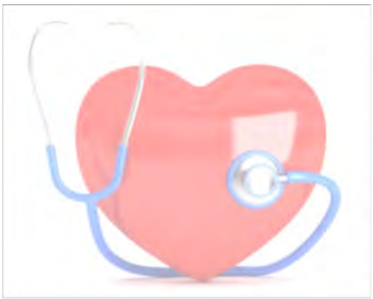
Studies in Analysis

Pear 1 Study

Cardiovascular disease is the leading cause of death in the United States with heart attacks (also known as myocardial infarction) being the most common form of this disease. When a person has a heart attack, aspirin is the most commonly given drug in order to help patients get better. Aspirin works by preventing blood clots, which is a common reason why people have heart attacks. While aspirin prevents the formation of blood clots in many people, some patients do not benefit (or get a reduced benefit) from taking this drug. This is known as aspirin resistance. The reason why some people have aspirin resistance may be due to differences in their genes. In this study, we will evaluate how differences in the gene PEAR1 and other factors determine how well people respond to 3 different doses of aspirin. So far; we have enrolled 67 participants in this study. The results of this study may be very important in helping doctors prescribe the best dose of aspirin based on the patient's genetic make up to prevent or treat a heart attack.

Lp(a) Study

Heart disease (CVD) is a leading cause of human morbidity and mortality in the world. A high cholesterol level in the blood is an important risk factor for heart disease. Recent evidence from large cohorts suggest that a particular protein that is associated with cholesterol, called Lipoprotein (a) [Lp(a)] is an important determinant of heart disease and stroke. However, no practical method for pharmacologic lowering of Lp(a) levels is currently available. The objective of this study is to define how genes influence Lp(a). We are particularly interested in two regions on chromosomes 6 & 11. Participants of this study were asked to provide a blood sample and also undergo other tests to look at blood vessels in the neck and brain using ultrasound and MRI. We enrolled 90 Amish subjects in this study. Identifiction of the genes that influence Lp(a) levels may lead to the design of novel therapeutic strategies to lower Lp(a) levels to prevent or treat heart disease in patients with diabetes.



Metabolic Impact of ApoC-III (MiACT)

Based on our exciting finding that about 1 in 20 Amish people carry a gene change that helps them to clear dietary fat from their blood faster and may help prevent heart disease, we are conducting a study to learn more about this gene change called APOC3 R19X.

People with this gene change make less of a substance in the body called ApoC-III. The new study is helping us to learn how ApoC-III works and whether lowering it in other people might be a useful way to prevent heart disease. We are comparing people with and without the gene change for how their fat is distributed in their bodies, how their bodies process dietary fat, cholesterol and sugar, and how fat and cholesterol move around in their bloodstream. Over 100 people have enrolled in the study, which is funded by the National Institutes of Health. Some of these participants graciously gave 16 hours of their time in one day for a special part of the study that is allowing us to learn up close how apoC-III controls the travel of fat in the body. Our work on apoC-III was discussed in the Philadelphia Inquirer.