



**THE UNIVERSITY of TEXAS**  
HEALTH SCIENCE CENTER AT HOUSTON

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## Genetic Basis of Aortic Aneurysm and Dissection

The thoracic aorta is the main blood vessel, which comes out of the heart and carries blood to the rest of the brain and body. The main disease that affects the thoracic aorta is aortic aneurysms (ballooning or enlargement) and dissections (a tear in the wall of the aorta) (TAAD).

Aortic aneurysms and dissections are related diseases because ascending aortic aneurysms progressively enlarge over time until they burst or tear (dissects), and in both cases can lead to death. Aortic aneurysms are a major health problem in the United States. Aortic aneurysms account for nearly 15,000 deaths yearly. Although TAAD are a symptom of some known genetic diseases, such as Marfan syndrome and Loeys-Dietz syndrome, the majority of TAADs occur with no known syndrome. Studies have found that up to 20% of aortic aneurysms tend to run in families (i.e., more than one person in the family is affected with TAAD).

### Our Research:

We have recruited over 400 families with multiple members who have TAAD for our research study. Our goal is to identify the changes/mutations in genes that cause TAAD to run in families. The majority of these families show an autosomal dominant inheritance of TAADs. This means that, if a family member has the disease, there is a 50% (1 in 2 chances) chance of passing the disease on to their children. Hereditary TAADs show inconsistency in expression (e.g., age when TAAD appears vary from person to person and sometimes aneurysms/dissections occur in vessels other than the aorta), and decreased penetrance (e.g., persons who carry the genetic marker may or may not exhibit disease) but they can still pass on the defective gene and the disease to their children and grandchildren.

By using blood, saliva, tissue, autopsy samples, and DNA, from the families with TAAD who take part in our research studies, we have mapped and identified multiple genes that cause TAAD. We have identified four genes named *TGFBR2*, *TGFBR1*, *MYH11* and *ACTA2* that when altered or mutated, lead to an increased risk for TAAD. The *ACTA2* gene is the most common cause of TAAD that has presented itself to run in families identified to date. Studies show that many genes cause familial TAAD.

We found the defective gene causing TAAD in 20% (1 in 5) of the families who take part in our research program. We are working on finding other defective genes in the remainder of families. The pace by which we can identify new defective genes that cause TAAD highly depends on the number of family members who take part in the study from each family and how fast we can get medical records to confirm the diagnosis of TAAD.

If we find the genetic cause of TAAAD in a family, we report the results back to each person in the family. We inform each family member as to whether they carry the increased likelihood for TAAAD or not due to our DNA findings. All patient information is confidential and private. Patient information is reported directly to the patient or to the patient's physician, upon request. Since premature deaths due to aortic dissections can be prevented through medical and surgical therapies, we are hoping that by identifying individuals at risk; we can prevent premature deaths from TAAAD.

Finding defective genes that cause TAAAD is the first step to understanding the underlying cause of TAAAD. We are specifically looking for what is going wrong with the aorta that causes aortic aneurysms to form and lead to aortic dissections. We hope to use this information to better medical treatment and prevent aortic aneurysms in individuals who are predisposed to this condition.

### **Participation in Study:**

If a person or family wishes to take part in our study, we will start by collecting a detailed family history. You will be asked to speak with our genetic counselor by phone (713) 500-6865 or email: van.tran.1@uth.tmc.edu. The genetic counselor will ask several questions pertaining to medical history and reproductive history of the patient and three generations of the person's family. We will also ask for medical records to confirm the information, diagnoses and ages of onset (beginning) of diseases to ensure the information is valid for the study. A signed consent will be required before collecting your biological samples or requesting medical records. We would like to obtain DNA from family members also and this can be done through the collection of saliva, (saliva can be collected in the privacy of your home in a container sent to you by our office), or the collection of blood drawn at a doctor's office or blood drawing center.

### **Who can take part in the study?**

Persons of any age can take part in our Thoracic Aortic Aneurysms and Dissections (TAAAD) study. Children (0-18) will need written permission from their parent(s). To determine if you qualify for our study you will need to speak with our genetic counselor first (see information above).

### **Potential Benefits:**

The purpose of this medical research is to find genes that lead to TAAAD running in families, and to determine which individuals are at risk for the condition. Understanding how genes work or do not work helps us to improve the management and treatment of aortic diseases. Since this research involves discovering new information, this also means it may take several years before any useful results are found for you or your family. Analyses of the known genes help us exclude or determine that you carry one of these defective genes. If you are found to carry one of the defective genes, we can predict who else in your family inherited this altered gene and their possible genetic likelihood for TAAAD. We will also identify family members who did not inherit the gene(s) and reassure them that they no longer are at an increased risk for TAAAD.

The research to be done on the samples may not help you directly because it may take years to find the cause for aortic aneurysms/dissections in you or your particular family. It is impossible to predict how many years it will take for us to find the cause for the aortic aneurysms/dissections in you or your

family. This study may help to find the cause of aortic aneurysms and dissections in you or your family.

Some potential psychological/emotional benefits may include feelings of relief to find out that they are no longer at risk in spite of their family history of TAAD. Persons may also feel relieved to know that they cannot pass a defective gene on to their children. Some persons who find out that they carry a mutation may feel motivated to take better care of themselves and start to seek out the appropriate care to improve their lives.

**Potential Risks:**

If you choose to take part by donating a blood sample then we would like to get about 20 ml (2 tablespoonfuls) of blood from you. Risks associated with taking blood samples are minimal and include pain (like a mosquito bite) or bruising.

We use strict security measures described below to protect your confidentiality and privacy; however, there is a very slight risk that, in spite of such security measures, persons outside our research team who do not have permission to have the information may find ways to get around such security measures to access your genetic information (i.e., computer hackers). Such breach of confidentiality and privacy while unlikely, could lead to some psychosocial risks, such as shame and discrimination.

Other psychological/emotional risks may be the anxiety associated with not knowing when we will or if we will find a cause for the TAAD in you or your family. Some persons may feel some anxiety about knowing their carrier status.

**CPHS STATEMENT:**

This study (HSC-01-251) has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston. For any questions about research subject's rights, or to report a research-related injury, call the CPHS at (713) 500-7942.