SMAD3

The *SMAD3* gene is one of many genes that helps provide strength and stability to tissues in the body. The *SMAD3* gene regulates proteins that maintain the structure of the wall of the aorta and other blood vessels. When this protein doesn't work properly, the tissues can be weakened, especially the blood vessels surrounding the heart.

Impact of *SMAD3* mutations
Individuals with a mutation in the *SMAD3* gene are at an increased risk for developing hereditary cardiovascular (heart and blood vessel) disorders called arteriopathies, which can cause weakness, enlargement, and tears of the walls of the arteries. These include familial thoracic aortic aneurysm and dissection and Loeys-Dietz syndrome.

Disorders associated with the *SMAD3* gene

Mutations in the *SMAD3* gene have been associated with the following disorders:

Familial Thoracic Aortic Aneurysm and Dissection
Familial thoracic aortic aneurysm and dissection (FTAAD) is a hereditary disorder associated with problems with the large blood vessel that carries blood away from the heart to the rest of the body (aorta).

Individuals with FTAAD commonly have problems with the upper part of the aorta (thoracic aorta), which is located in the chest near the heart. The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening.

In individuals with FTAAD, the age of onset and severity of symptoms may vary, even within the same family. Some individuals with FTAAD experience no noticeable symptoms, but are still at risk for aortic dissection. Women with FTAAD are at increased risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing FTAAD typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the heart and aorta (echocardiogram). These evaluations may be combined with genetic testing to diagnose FTAAD.

Treatment for FTAAD typically includes frequent monitoring of the aorta to look for dilation and aneurysms. If an aneurysm is present, it may require surgical repair to prevent dissection. Certain medications can also be used to control blood pressure and reduce stress on the walls

of the aorta. It is generally recommended that individuals avoid strenuous exercise, contact sports, smoking, and a diet high in cholesterol.

Loeys-Dietz Syndrome
Loeys-Dietz syndrome (LDS) is a hereditary disorder associated with problems with the structure of connective tissue in many parts of the body, which can cause weakness of the blood vessel walls, skeletal problems, and abnormal bruising and scarring of the skin.

LDS is a connective tissue disorder. Connective tissue supports, binds, or connects other tissues or organs in the body. Individuals with LDS commonly have problems with the heart and the surrounding blood vessels, especially the large artery that carries blood away from the heart to the rest of the body (aorta). The walls of the aorta can become weakened and stretch (aortic dilation). This can lead to a bulge in the wall of the aorta (aortic aneurysm) or a sudden tearing of the aorta (aortic dissection). Aortic aneurysm and aortic dissection can be life threatening, and are the major cause of death in individuals with LDS. Individuals can also have aneurysms or dissections in other arteries throughout the body and have arteries with abnormal twists and turns (arterial tortuosity).

Individuals may also have skeletal problems such as an abnormal skull shape (craniosynostosis), curved spine (scoliosis) or abnormal spinal bones, a sunken chest (pectus excavatum) or a protruding chest (pectus carinatum), and long limbs whose joints have restricted movement (contractures). They often have a split in the flap of tissue that hangs down in the back of the mouth (bifid uvula) or an opening in the roof of the mouth (cleft palate). Infants and children with LDS may have trouble gaining weight (failure to thrive). Other symptoms may include easy bruising, abnormal scarring, stretch marks in the skin, and collapsed lung (pneumothorax). Symptoms and severity of the symptoms may vary between individuals. Women with LDS are at risk for serious and possibly life-threatening complications during pregnancy and may require special care.

Diagnosing LDS typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, and an imaging test used to see the blood vessels between the head and the pelvis (angiogram). These evaluations may be combined with genetic testing to diagnose LDS.

Treatment for LDS is focused on the prevention of complications and management of symptoms. Individuals are recommended to have an imaging test used to see the heart and aorta (echocardiogram) at least every year. An examination of the blood vessels (angiography) may also be performed to identify aneurysms in other areas. Medication to lower blood pressure may also be used to reduce the risk of dissection. Surgery may be required to fix any aneurysms that develop to prevent dissection. Failure to thrive can be treated with a feeding tube or high-calorie diet. Many problems with the bones, such as scoliosis and cleft palate, can be surgically repaired. In general, it is recommended that individuals with LDS avoid contact or

competitive sports, strenuous exercise, and certain medications that can affect the heart.

Useful resources

Loeys-Dietz Syndrome Foundation
Encourages education about Loeys-Dietz syndrome and provides a support network for individuals, parents, and families affected by Loeys-Dietz syndrome.
www.loeysdietz.org

The Marfan Foundation
Provides information and support to healthcare providers, caregivers, and families affected by Marfan syndrome and related disorders, including FTAAD and Loeys-Dietz syndrome.
www.marfan.org

TAD Coalition
Committed to increasing public awareness of the factors that put people at risk for aortic aneurysm and dissection, and to improving the diagnosis and management of these life-threatening conditions.
www.tadcoalition.org

Last updated April 4, 2018