

## PKP2

The *PKP2* gene is one of many genes that helps provide strength and stability to tissues in the body. The *PKP2* gene makes a protein which is found in the heart muscle. When this protein doesn't work properly, the heart can be weakened.

### Impact of *PKP2* mutations

Individuals with a mutation in the *PKP2* gene are at an increased risk for developing different hereditary cardiovascular (heart and blood vessel) disorders called cardiomyopathies, which can affect the heart's ability to pump blood. These include arrhythmogenic cardiomyopathy and dilated cardiomyopathy.

### Disorders associated with the *PKP2* gene

Mutations in the *PKP2* gene have been associated with the following disorders:

#### Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is associated with a replacement of heart tissue with fat and/or fibrous tissue, which can make it hard for the heart to pump blood.

AC, also referred to as arrhythmogenic right ventricular cardiomyopathy or dysplasia (ARVC or ARVD), is associated with a replacement of the muscle with fat and/or fibrous tissue in the minor pumping chamber of the heart, called the right ventricle. As a result, the right ventricle is enlarged (dilated) and the heart has a difficult time pumping blood, which can cause heart failure. In some cases, the major pumping chamber of the heart, called the left ventricle, can also be affected. The most common symptoms are strong or irregular heartbeats (heart palpitations), light-headedness, chest pain or fainting due to a fall in blood pressure (syncope). People with AC can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmia), which can increase the risk of sudden cardiac death. Sudden cardiac death can occur, even in individuals who have no other symptoms. Most people are diagnosed between their 20s and 40s.

Diagnosing AC typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with AC are advised to make certain lifestyle changes, such as avoiding strenuous exercise. Depending on whether AC symptoms are present, medications may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart

failure, a heart transplantation may be considered.

Regular visits to a cardiologist specializing in AC are recommended in order to check that treatment is effective.

### **Dilated Cardiomyopathy**

Dilated cardiomyopathy (DCM) is associated with an enlargement of the heart, which can make it hard for the heart to pump blood.

DCM is associated with the enlargement (dilation) of the major pumping chamber of the heart, called the left ventricle. When this happens, the heart has a difficult time pumping blood. People with DCM may not have any symptoms until they experience heart failure as the heart gets weaker. Common symptoms of heart failure include shortness of breath, fatigue, and buildup of fluid in the body (edema). In advanced stages of disease, people with HCM can have a problem with the electrical system of the heart that controls the heartbeat's regular rhythm (arrhythmias), which can increase the risk of sudden cardiac death. Blood clotting disorders (thromboembolism) including stroke can occur.

Diagnosing DCM typically involves evaluating an individual's medical and family histories, as well as a regular physical exam, an imaging test used to see whether the heart muscle is abnormally thick (echocardiogram), and a test of the heart's electrical system called an electrocardiogram (EKG or ECG). Additional screening and diagnostic tests may be ordered, including an MRI.

Individuals with DCM are advised to make certain lifestyle changes, such as avoiding strenuous exercise and reducing salt intake if symptoms are present. Depending on whether DCM symptoms are present, medications that help control blood pressure may be prescribed. Some individuals may also need a device that detects a dangerously fast heart rhythm and delivers a shock to correct it called an implantable cardioverter defibrillator (ICD) or other surgical procedures. If medications and surgical procedures are not working to manage heart failure, a heart transplantation may be considered. Regular visits to a cardiologist specializing in DCM are recommended in order to check that treatment is effective.

## Useful resources

### **American Heart Association**

Focused on building lives free of heart disease by providing accessible education and funding innovative research.

[www.heart.org](http://www.heart.org)

### **ARVD/C Patient Registry (The Johns Hopkins Hospital)**

The goal of the registry is to clinically characterize AC patients and learn more about the natural history of the disorder, range of severity and the genes that cause AC.

<https://www.hopkinsmedicine.org>

### **SHARE Registry**

Advancing the understanding of cardiomyopathy by increasing community awareness and supporting research.

<https://theshareregistry.org>

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