# PKP2 Gene

Subjects: Genetics & Heredity
Contributor: Lily Guo

plakophilin 2

Keywords: genes

## 1. Introduction

The *PKP2* gene provides instructions for making a protein called plakophilin 2. This protein is found primarily in cells of the myocardium, which is the muscular wall of the heart. Within these cells, plakophilin 2 is one of several proteins that make up structures called desmosomes. These structures form junctions that attach cells to one another. Desmosomes provide strength to the myocardium and are involved in signaling between neighboring cells.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Arrhythmogenic right ventricular cardiomyopathy

More than 230 mutations in the *PKP2* gene have been identified in people with arrhythmogenic right ventricular cardiomyopathy (ARVC). This condition most commonly affects the myocardium surrounding the right ventricle, one of the two lower chambers of the heart. ARVC increases the risk of an abnormal heartbeat (arrhythmia) and sudden death.

Some *PKP2* gene mutations lead to the production of an abnormally short version of plakophilin 2. Other mutations alter the structure of plakophilin 2 by adding, deleting, or changing one or more of its protein building blocks (amino acids). Studies suggest that the altered protein impairs the formation and function of desmosomes.

Without normal desmosomes, cells of the myocardium detach from one another and die, particularly when the heart muscle is placed under stress (such as during vigorous exercise). The damaged myocardium is gradually replaced by fat and scar tissue. As this abnormal tissue builds up, the walls of the right ventricle become stretched out, preventing the heart from pumping blood effectively. These changes also disrupt the electrical signals that control the heartbeat, which can lead to arrhythmia.

## 3. Other Names for This Gene

- ARVD9
- MGC177501
- plakophilin-2

### References

1. Bass-Zubek AE, Hobbs RP, Amargo EV, Garcia NJ, Hsieh SN, Chen X, Wahl JK 3rd, Denning MF, Green KJ. Plakophilin 2: a critical scaffold for PKC alpha thatregulates intercellular junction assembly. J Cell Biol. 2008 May19;181(4):605-13. doi: 10.1083/jcb.200712133.
2. Cerrone M, Montnach J, Lin X, Zhao YT, Zhang M, Agullo-Pascual E, Leo-MaciasA, Alvarado FJ, Dolgalev I, Karathanos TV, Malkani K, Van Opbergen CJM, van BavelJJA, Yang HQ, Vasquez C, Tester D, Fowler S, Liang F, Rothenberg E, Heguy A,Morley GE, Coetzee WA, Trayanova NA, Ackerman MJ, van Veen TAB, Valdivia HH,Delmar M. Plakophilin-2 is required for transcription of genes that controlcalcium cycling and cardiac rhythm. Nat Commun. 2017 Jul 24;8(1):106. doi:10.1038/s41467-017-00127-0.
3. Dalal D, Molin LH, Piccini J, Tichnell C, James C, Bomma C, Prakasa K, Towbin JA, Marcus FI, Spevak PJ, Bluemke DA, Abraham T, Russell SD, Calkins H, Judge DP.Clinical features of arrhythmogenic right ventricular

dysplasia/cardiomyopathyassociated with mutations in plakophilin-2. Circulation. 2006 Apr4;113(13):1641-9.

4. Gerull B, Heuser A, Wichter T, Paul M, Basson CT, McDermott DA, Lerman BB,Markowitz SM, Ellinor PT, MacRae CA, Peters S, Grossmann KS, Drenckhahn J,Michely B, Sasse-Klaassen S, Birchmeier W, Dietz R, Breithardt G, Schulze-Bahr E,Thierfelder L. Mutations in the desmosomal protein plakophilin-2 are common inarrhythmogenic right ventricular cardiomyopathy. Nat Genet. 2004Nov;36(11):1162-4.
5. Hall C, Li S, Li H, Creason V, Wahl JK 3rd. Arrhythmogenic right ventricularcardiomyopathy plakophilin-2 mutations disrupt desmosome assembly and stability. Cell Commun Adhes. 2009;16(1-3):15-27. doi: 10.1080/15419060903009329.
6. Joshi-Mukherjee R, Coombs W, Musa H, Oxford E, Taffet S, Delmar M.Characterization of the molecular phenotype of two arrhythmogenic rightventricular cardiomyopathy (ARVC)-related plakophilin-2 (PKP2) mutations. HeartRhythm. 2008 Dec;5(12):1715-23. doi: 10.1016/j.hrthm.2008.09.009.
7. Syrris P, Ward D, Asimaki A, Sen-Chowdhry S, Ebrahim HY, Evans A, Hitomi N,Norman M, Pantazis A, Shaw AL, Elliott PM, McKenna WJ. Clinical expression ofplakophilin-2 mutations in familial arrhythmogenic right ventricularcardiomyopathy. Circulation. 2006 Jan 24;113(3):356-64.
8. van Tintelen JP, Entius MM, Bhuiyan ZA, Jongbloed R, Wiesfeld AC, Wilde AA,van der Smagt J, Boven LG, Mannens MM, van Langen IM, Hofstra RM, Otterspoor LC, Doevendans PA, Rodriguez LM, van Gelder IC, Hauer RN. Plakophilin-2 mutations arethe major determinant of familial arrhythmogenic right ventriculardysplasia/cardiomyopathy. Circulation. 2006 Apr 4;113(13):1650-8.

---