SickKids | Genome Diagnostics

Arrhythmogenic Right Ventricular Cardiomyopathy

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a progressive cardiac disorder caused by fatty replacement of cardiac muscle tissue that predisposes to ventricular tachycardia and sudden death. It primarily affects the right ventricle. The presentation of ARVC is highly variable within affected individuals and their families.

Genetics

ARVC is a genetically heterogeneous, autosomal dominantly inherited condition. Mutations in several different genes are known to cause ARVC:

Gene	Locus Name	Protein encoded
DSP	ARVD8	desmoplakin
PKP2	ARVD9	plakophilin-2
DSG2	ARVD10	desmoglein-2
DSC2	ARVD11	desmocollin-2
TMEM43	ARVD5	transmemebrane protein 43

Approximately 40% of ARVC patients will have mutations in the *DSP, PKP2, DSG2, DSC2 or TMEM43* gene. Many cases of ARVC are due to mutations in unknown genes. Molecular testing for ARVC consists of complete sequencing of the coding region and flanking exon/intron boundaries of the many genes listed above to detect mutations.

ARVC is present when an individual has one copy of the defective *DSP*, *PKP2*, *DSG2*, *DSC2* or *TMEM43* gene. Affected individuals have a 50% chance of transmitting the disorder to each child. There is a 50% chance that the affected individual's offspring will not be affected with ARVC.

Who Should be Tested?

- Individuals clinically suspected of being affected with ARVC
- Individuals with a family history of ARVC, to determine carrier status

Test Methods

- Complete sequencing of the coding region and flanking exon/intron boundaries of the *DSP*, *PKP2*, *DSG2*, *DSC2* and *TMEM43* genes to identify point mutations

Test Sensitivity

Approximately 40% of ARVC patients will have mutations in the *DSP, PKP2, DSG2, DSC2 or TMEM43* gene.

About 60% of ARVC cases are caused by mutations in unknown genes which will not be detected by this assay.

Potential Outcomes & Interpretation of Test Results

***DSP, PKP2, DSG2, DSC2* or *TMEM43* Gene Mutation**	**Explanation**
None detected	This result does not support a diagnosis of ARVC
Mutation detected	This result supports a diagnosis of ARVC

For More Information

Online Mendelian Inheritance in Man http://www.ncbi.nlm.nih.gov/omim/

•ARVD5#604400 •ARVD8#607450 •ARVD9#609040 •ARVD10#610193 •ARVD11#610476

GeneReviews online clinical information resource http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=arvd#arvd

The Canadian Sudden Arrhythmia Death Syndromes Foundation http://www.sads.ca/

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

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1. Current molecular testing may not detect all possible mutations for this disease. A negative test result does not rule out the possibility of ARVC.

2. The clinical course or severity of symptoms cannot be predicted by molecular analysis.

3. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.

4. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.