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:

<table>
<thead>
<tr>
<th>Gene</th>
<th>Locus Name</th>
<th>Protein encoded</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSP</td>
<td>ARVD8</td>
<td>desmoplakin</td>
</tr>
<tr>
<td>PKP2</td>
<td>ARVD9</td>
<td>plakophilin-2</td>
</tr>
<tr>
<td>DSG2</td>
<td>ARVD10</td>
<td>desmoglein-2</td>
</tr>
<tr>
<td>DSC2</td>
<td>ARVD11</td>
<td>desmocollin-2</td>
</tr>
<tr>
<td>TMEM43</td>
<td>ARVD5</td>
<td>transmembrane protein 43</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>DSP, PKP2, DSG2, DSC2 or TMEM43 Gene Mutation</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>None detected</td>
<td>This result does not support a diagnosis of ARVC</td>
</tr>
<tr>
<td>Mutation detected</td>
<td>This result supports a diagnosis of ARVC</td>
</tr>
</tbody>
</table>

For More Information

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


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](http://www.cagc-accg.ca) or the National Society of Genetic Counsellors website at [www.nsgc.org](http://www.nsgc.org)

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.