The TMEM43 gene encodes a highly conserved nuclear envelope protein transmembrane protein 43. The TMEM43 gene contains 12 exons and spans around 18.7 kb genomic distance that was mapped to chromosome 3p25.1. Defects in this gene are the cause of familial arrhythmogenic right ventricular dysplasia/cardiomyopathy type 5 (ARVD/C5). ARVD/C is an autosomal dominant disease characterized by partial degeneration of the myocardium of the right ventricle, electrical instability and sudden death. Mutations in TMEM43 are also associated with Emery-Dreifuss muscular dystrophy 7 (EDMD7), which is an autosomal dominant genetically heterogeneous muscular disease that presents with muscular dystrophy, joint contractures, and cardiomyopathy with conduction defects. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for TMEM43 mutations. Individuals are tested by DNA sequencing of the coding exons of the TMEM43 gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

Molecular confirmation of familial arrhythmogenic right ventricular dysplasia/cardiomyopathy type 5 (ARVD/C5) and Emery-Dreifuss muscular dystrophy 7 (EDMD7).

Genomic DNA is analyzed for TMEM43 mutations by DNA sequencing of the coding exons of the TMEM43 gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated regions. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-12 of TMEM43.