

Brugada Syndrome 1 via *SCN5A* Gene Sequencing – Test #492

Brief Description of Clinical Features: Brugada syndrome 1 (OMIM 601144) is a cardiac channelopathy characterized by arrhythmia, syncope, nocturnal agonal respiration, sudden death, and abnormal electrocardiographic findings consisting of right precordial ST-segment elevation, in the absence of structural cardiac abnormalities. Several drugs have been reported to cause these electrocardiographic abnormalities in patients with Brugada syndrome (see www.brugadadrugs.org). Symptoms usually manifest during adulthood, but they may appear any time between two days and 80 years of age (Antzelevitch, *Circ Res* 91:1114-1118, 2002). The prevalence of Brugada syndrome varies among ethnic groups and is highest in populations from Southeast Asia. See also the Sudden Arrhythmia Death Syndromes Foundation at (www.sads.org) and Brugada et al. (*GeneReviews*, 2009, www.genetests.org).

Genetics: Brugada syndrome is a genetically heterogeneous disease that is usually inherited in an autosomal dominant manner. Mutations in the gene *SCN5A* represent the most common cause of Brugada syndrome (Chen et al. *Nature* 392: 293–296, 1998; Kapplinger et al. *Heart Rhythm* 7:33-46, 2010). Over 300 *SCN5A* causative mutations have been reported in patients from various ethnic groups. *SCN5A* mutations are distributed along the entire coding region of the gene and include missense, nonsense, frameshift, and splicing mutations. Most mutations occurred in familial cases, although *de novo* mutations were also reported (Rook et al. *Cardiovasc Res* 44:507-517, 1999; Brugada et al., 2009). In addition to Brugada syndrome, heterozygous *SCN5A* mutations were identified in patients with Long QT syndrome 3 (LQT3) (Wang et al. *Cell* 80:805-811, 1995) and patients with Progressive Familial Heart Block, Type 1A (PFHB1A) (Schott et al. *Nat Genet* 23: 20–21, 1999). Also, several compound heterozygous *SCN5A* mutations were reported in patients with autosomal recessive Sick Sinus Syndrome 1 (SSS1) (Benson et al. *J Clin Invest* 112:1019-1028, 2003).

Description of This Particular Test: The *SCN5A* gene encodes the alpha-subunit of human cardiac sodium channel, which is responsible for the generation of cardiac action potential and for rapid impulse conduction through the myocardium. This test involves bidirectional DNA sequencing of all 27 coding exons and splice sites of the *SCN5A* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. As indicated, we will also perform sequencing of any single exon (Test #100) or pair of exons-for SSS1 only (Test #200) for family members of patients with known mutations and to confirm previous research results (\$190-\$340 charge).

Reference Sequences: Genomic: NC_000003.11 mRNA: NM_001099404.1 Protein: NP_001092874.1 (CCDS 46799.1)

Indications for Test: All patients with symptoms suggestive of Brugada syndrome, patients with LQT3 syndrome (OMIM 603830) and no mutations in the most common LQT genes; patients with PFHB1A (OMIM 113900); and patients with autosomal recessive, congenital SSS1 (OMIM 608567).

Sensitivity of Test: This test will detect mutations in ~ 21% of patients with Brugada syndrome (Kapplinger et al. *Heart Rhythm* 7:33-46, 2010).

Turnaround Time: Maximum of 40 days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Price: Sequencing of *SCN5A* Gene, Exons 2- 6 and 9-29 **\$1460**

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x31	83898 \$ 450	Sequencing x31	83904 \$ 680
Separation x1	83894 \$ 130	Interpretation/Report x1	83912 \$ 130

Accreditation Info: CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

Contact: Dr. Khemissa Bejaoui, khemissa@preventiongenetics.com, www.preventiongenetics.com