

Malignant Hyperthermia Susceptibility/Central Core Disease Testing via *RYR1* 3' Exon Sequencing

Brief Description: Malignant Hyperthermia (MH) is a severe adverse reaction to commonly used volatile anesthetics (halothane, sevoflurane, desflurane, enflurane, isoflurane) or to depolarizing muscle relaxants (succinylcholine). In susceptible patients these agents may trigger uncontrolled skeletal muscle hypermetabolism. In almost all cases, the first manifestations of MH occur in the operating room. Death can result unless the patient is promptly treated.

Central Core disease is a congenital myopathy characterized by moderate muscle weakness, musculoskeletal abnormalities and other features. Many patients with Central Core Disease are also MH Susceptible.

Genetics: MH susceptibility and Central Core Disease are inherited in an autosomal dominant manner. Mutations in the *RYR1* gene are the primary known cause of MH and the only known cause of Central Core Disease. The large *RYR1* (ryanodine receptor type I) gene with 106 exons encodes the skeletal muscle calcium release channel. This particular test involves DNA sequencing of 11 *RYR1* exons (90, 91, 95, 97, 98, 99, 100, 101, 102, 103 and 104). Collectively, these exons contain the majority (perhaps the great majority) of the known mutations causative for Central Core Disease as well as about 42% of known mutations for MH Susceptibility. This test can be ordered separately or as a continuation of initial sequencing of the *RYR1* gene.

Indications for Test: Ideal candidates for this test are patients with Central Core Disease or patients who may be MH susceptible and who have already received a negative test result for sequencing of the primary panel of 13 *RYR1* exons (see Primary MH Exon Test).

Sensitivity of Test: Based on literature results, we estimate that this test will detect likely causative mutations in 40-60% of patients with Central Core Disease and cumulatively with the Primary MH Exon Test in 45-65% of ideal MH test candidates.

MHAUS: PreventionGenetics is working closely with the Malignant Hyperthermia Association of the U. S. (www.mhaus.org). There is a 10% price discount for MHAUS members. MHAUS provides financial support for testing in some cases.

Specimen Requirements

- Collect 2-5 ml of whole blood in EDTA (purple top tube) or ACD (yellow top tube). 5 ml is the preferred volume.
- Only one blood tube is required for multiple tests.
- Ship whole blood specimens at room temperature.
- Do not freeze blood.
- During hot weather, include a frozen ice pack in the shipping container. Do not allow the ice pack to come in direct contact with the specimen tube.
- In cold weather, include an unfrozen ice pack to help moderate extremes in temperature. The DNA in whole blood is stable for at least 48 hours at 21°C, 5-7 days at 4°C.

Selected exon sequencing of the <i>RYR1</i> gene		\$740.00
Molec Diag, Ascertainment	83890	
Molec Diag, Isolation	83891	
Molecular Diag, Amplif x 11	83898	
Mutat Id By Seq, Single Seg x 11	83904	
Molecular Diag, Separation	83894	
Interpretation And Report	83912	

Single exon screening from within this screening panel for the presence previously identified mutations in the *RYR1* gene will also be provided for \$230.

Accreditation Info. CLIA ID #: 52D1027685 (expires 1/18/07) (CAP#: 7185561, AU ID: 1407125 expires 12/20/06)

Ship to:

Attn: Diagnostics Lab
PreventionGenetics LLC
3700 Downwind Drive
Marshfield, WI 54449 USA
Contact: 715-387-0484

Contact for info:

Dr. James Weber
715-387-0484
jim.weber@preventiongenetics.com
FAX: 715-384-3661