PreventionGenetics

Disease Prevention Through Genetic Testing

Malignant Hyperthermia Susceptibility Testing via *RYR1* Primary 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.

Genetics: MH susceptibility is inherited in an autosomal dominant manner. Most individuals diagnosed with MH have a parent with MH susceptibility that may not have ever experienced any manifestations of the disease. Presymptomatic diagnosis of MH susceptibility allows the clinician to avoid the offending agents. There is a very real need for the screening of first degree relatives of affected individuals in order to minimize future risk to these family members.

Mutations in the *RYR1* gene are the primary known cause of MH. 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 14 *RYR1* exons that include the most common *RYR1* MH mutations (exons 2, 6, 8, 9, 11, 12, 14, 15, 17, 39, 40, 44, 45 and 46). Collectively, these exons contain about 50% of all known causative mutations in this gene. PreventionGenetics also offers sequencing of other *RYR1* exons (see test list).

Indications for Test: The ideal candidate for this test is a member of a family with a history of MH. The ideal candidate should also have had either a positive *in vitro* contracture test or a clear MH event. PreventionGenetics recommends that the hunt for the causative mutation begin in such a family member. Once the causative mutation is identified, then other family members can be screened at much reduced cost. Other, less ideal candidates for the test are those with just a family history of MH or those with a "MH-like" event and no family history.

Sensitivity of Test: This test is too new to provide a consensus value for sensitivity. However, based on literature results and our own results, we estimate that this test will detect likely causative mutations in 30-50% of ideal test candidates. Sensitivity will be lower for other 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 a minimum of 1 ml of whole blood in EDTA (purple top tube) or ACD (yellow top tube).
Whole blood collected in Na Heparin is acceptable but not preferred.
Ship whole blood specimens at ambient temperature. Do not freeze blood tube.
During hot summer months, include a frozen ice pack in the shipping container. Do not allow the ice pack to come in direct contact with the specimen tubes. In winter, 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^{o}C, 5-7 days at 4^{o}C.

Selected exon sequence analysis of the *RYR1* gene		**$790.00**
Molec Diag, Ascertainment	**83890**	
Molec Diag, Isolation	**83891**	
Molecular Diag, Amplif x 13	**83898**	
Mutat Id By Seq, Single Seg x 13	**83904**	
Molecular Diag, Separation	**83894**	
Interpretation And Report	**83912**	

(The 13 exons in this screening panel are: 2, 6, 8, 9, 11, 12, 14, 15, 17, 39, 40, 44, 45, 46)

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