

## Malignant Hyperthermia Susceptibility Testing via Single *RYR1* 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 who 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 a single, specific *RYR1* exon.

**Indications for Test:** This test is typically performed on the biological relative of a patient with a known, causative mutation in the *RYR1* gene. By sequencing only one exon rather than a panel of exons, substantial money can be saved. Alternatively, this test may also be ordered for a member of a genetically isolated population in which a specific *RYR1* mutation is found at high frequency.

**Sensitivity of Test:** Sensitivity is specified by the particular biological relationship between the patient with the known mutation and his/her relative. For example, a causative mutation will be found, on average, in 50% of the children of a parent who carries such a mutation, but in only 12.5% of the first cousins of the parent.

**MHAUS:** PreventionGenetics is working closely with the Malignant Hyperthermia Association of the U. S. ([www.mhaus.org](http://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.

Single exon sequence analysis of the <i>RYR1</i> gene		<b>\$230.00</b>
Molec Diag, Ascertainment	<b>83890</b>	
Molec Diag, Isolation	<b>83891</b>	
Molecular Diag, Amplif	<b>83898</b>	
Mutat Id By Seq, Single Seg	<b>83904</b>	
Molecular Diag, Separation	<b>83894</b>	
Interpretation And Report	<b>83912</b>	

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