

Mannan-Binding Lectin Testing

Background: When the adaptive immune response is either immature or compromised, the innate immune system constitutes the principal defense against infections. Mannan-binding lectin (MBL), also referred to as mannose-binding lectin or protein, is an acute-phase, carbohydrate-binding protein that is synthesized in the liver and secreted into the circulatory system. Structurally MBL is a C1q-like molecule that in association with MBL-associated serine proteases (MASPs) bind to surface carbohydrates on bacteria, fungi, viruses and protozoa making them accessible for phagocytosis through MBL receptors or by activating the complement cascade via the recently elucidated lectin. Functional MBL is a multimeric protein that consists of three-six MBL oligomers that are derived from a single functional gene (*mbi2*) on chromosome 10. Interindividual serum MBL concentrations differ 1000-fold (<10 to 10000 ng/mL) and are determined mainly by allelic variances within the *mbi2* gene.

Genetics: There are seven known allelic variants: three located in exon 1 (A/D, A/B and A/C), three located in the promoter region (H/L, Y/X and nt C/T), and one located in the 5' untranslated region (P/Q). Deficiency of oligomeric MBL (<100 ng/mL) is relatively common in the general population and is mainly due to allelic variants in both exon 1 and the promoter.

Clinical Utility: Deficiency of oligomeric MBL appears to predispose individuals to serious infections (e.g. pneumonitis, sepsis, osteomyelitis, gastroenteritis and meningitis) when the adaptive immune system is immature such as in early childhood or when suppressed such as during chemotherapy or after organ transplantation. The determination of MBL protein concentration within individuals especially those suffering from recurrent infections may be useful for the elucidation of suspected immune defects and as a prognostic indicator alerting to the need for heightened therapeutic or prophylactic measures. Furthermore, clinical studies support that determining MBL protein concentration should be used for the initial screening, but in order to gain the most complete diagnostic information it is also necessary to determine both MBL function and MBL and MASP-2 genotypes for the following reasons:

- 1) MBL activation of the MBL complement pathway can be inhibited by reduced or deficient levels of MASP-2 which is found in approximately 10% of the population due to a single allelic variant within the MASP-2 gene.
- 2) Most MBL disease associations are found with homozygosity or compound heterozygosity for variant structural alleles which can only be determined by MBL genotyping.

IBT offers a comprehensive test list for the full evaluation of a patient's MBL status

Mannan-Binding Lectin Protein

Test Code: 0033 CPT Code: 86160 or 86849
Test Method: EIA
Specimen: 1 mL Serum

Mannan-Binding Lectin Pathway Function Test

Test Code: 0034 CPT Code: 86161
Test Method: EIA-C4b Deposition Assay
Specimen: 2 mL Serum

ProGenotyper[®] Mannan-Binding Lectin

Test Code: 402857 CPT Codes: 83891, 83898,
83896 x 8, 83903 x 7, 83912
Test Method: Real-Time PCR Melting Curve Analysis
Specimen: 2 mL Heparinized Blood

ProGenotyper[®] MASP-2 Polymorphism (D120G)

Test Code: 402856 CPT Codes: 83891, 83898,
83896 x 2, 83903, 83912
Test Method: Real-Time PCR Melting Curve Analysis
Specimen: 2 mL Heparinized Blood

References:

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- [4] Kilpatrick, D.C. Mannan-binding lectin and its role in innate immunity. *Transfus. Med.* 2002; 12(6):335-352.
- [5] Kilpatrick, D.C. Mannan-binding lectin: clinical significance and applications. *Biochim. Biophys. Acta* 2002; 1572:401-413.
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- [7] Steffensen, R. et al. Detection of structural gene mutations and promoter polymorphisms in the mannan-binding lectin (MBL) gene by polymerase chain reaction with sequence-specific primers. *J. Immunol. Methods* 2000; 241:33-42.

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