

CD40 Ligand *ProGenotyper*[®] Test

Test Name: CD40 Ligand *ProGenotyper*[®] Test

Alternative Names: X-linked HIGM 1, CD40L

Test Code: 30000

CPT Code: 83890, 83898 x 5, 83891 x 5, 83904 x 10,
83912

Clinical Utility:

This test is intended for the detection of CD40 ligand (CD40L) mutations associated with X linked hyper-IgM syndrome (XHIGM). An immunodeficiency with most early reports showing patients had elevated serum immunoglobulin (IgM) levels but markedly reduced IgG, IgA, and IgE levels. However, according to the US XHIGM Registry report in 2003, elevated IgM levels were found in less than one third of patients. All patients had reduced levels of IgG and more than three fourths of patients had reduced levels of IgA. Patients with XHIGM have profound susceptibility to bacterial infections and an increased susceptibility to opportunistic infections.

Background:

In the processes of B cell proliferation, differentiation, and immunoglobulin class switch recombination, CD40L on activated T cells is necessary for interaction with B cells expressing CD40. Defective expression of CD40L on CD4+ helper T cells causes an important reduction or absence of isotype-switched memory B cells and abnormal immunoglobulin levels.

Frequency:

U.S. registry reports a minimum incidence rate for XHIGM was approximately 1 in 1,000,000 live births from 1984-1993. This may be an underestimation because not all U.S. physicians participated in the registry.

Physical Manifestations:

- Chronic diarrhea with failure to thrive
- Pulmonary infections may have cough, tachypnea, dyspnea, retraction, accessory muscle use, hypoxia, or abnormal breath sound on auscultation
- Lymphadenopathy
- Jaundice, pruritus, and hepatomegaly
- Oral mucosal and perirectal ulcerations, especially with concomitant neutropenia
- Approximately one fourth of patients with XHIGM have bronchiectasis; higher if the initiation of intravenous immunoglobulin (IVIG) therapy is delayed.

Related Tests:

Humoral Immune Status Panel I (401744)

T-B-NK Immunophenotyping (403106)

Specimen Requirements:

- 2mL whole blood (EDTA or sodium heparin)
- Ship **overnight** at ambient temperature

Units and Normal Reference Range:

All 5 exons in CD40L are sequenced and compared to reference sequence NG_007280.1. Results are reported as no mutation, heterozygous (HET) mutation, homozygous (HOMO) mutation, or unknown (UKN) mutation. A mutation that has not previously been reported in the literature is considered unknown. Normal individuals have no mutation.

Method:

1. Patient DNA is extracted from whole blood.
2. Regions of the CD40L gene are amplified by PCR from the genomic DNA and the products of each fragment are purified.
3. Cycle sequencing is performed with one or two sequencing primers per CD40L fragment.
4. These products are purified and run on the ABI3730 Genetic Analyzer.
5. The resulting sequence is compared to the reference sequence.

References:

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4. Milner JD, Brenchley JM, Laurence A, et al. 2008. Impaired T(H)17 cell differentiation in subjects with autosomal dominant hyper-IgE syndrome. *Nature* 452(7188):773-6.
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For more information, contact

IBT Laboratories

11274 Renner Boulevard, Lenexa, Kansas 66219

913.492.2224 800.637.0370

www.ibtlabs.com