MAYO CLINIC LABORATORIES

Test Definition: CD40

B-Cell CD40 Expression by Flow Cytometry, Blood

Overview

Useful For

Evaluating patients for hyper-IgM type 3 (HIGM3) syndrome due to defects in CD40, typically seen in patients less than 10 years

Assessing B-cell immune competence in other clinical contexts, including autoimmunity, malignancy, and transplantation

Genetics Test Information

Homozygous variants in the *CD40* gene cause autosomal recessive hyper-IgM syndrome type 3. The *CD40* gene is located on chromosome 20q12-q13.2.

Method Name

Flow Cytometry

NY State Available

Yes

Specimen

Specimen Type

Whole Blood EDTA

Ordering Guidance

This test is **not used** to detect in CD40L expression (CD154), which is responsible for X-linked hyper-IgM syndrome (HIGM1); see XHIM / X-Linked Hyper IgM Syndrome, Blood.

Shipping Instructions

Testing performed Monday through Friday. Specimens not received by 4pm (CST) on Friday may be cancelled.

Collect and package specimen as close to shipping time as possible. It is recommended that specimens arrive within 24 hours of collection.

Samples arriving on the weekend and observed holidays may be canceled.

Necessary Information

Ordering healthcare professional name and phone number are required.

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot.**
Additional Information: For serial monitoring, it is recommended that specimens are collected at the same time of day.

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood EDTA	Ambient	72 hours	PURPLE OR PINK TOP/EDTA

Clinical & Interpretive

Clinical Information

The adaptive immune response includes both cell-mediated (mediated by T cells and natural killer [NK] cells) and humoral (mediated by B cells) immunity. After antigen recognition and maturation in secondary lymphoid organs, some antigen-specific B cells terminally differentiate into antibody-secreting plasma cells. Decreased numbers or aberrant function of B cells result in humoral immune deficiency states with increased susceptibility to infections, and these may be either primary (genetic) or secondary immunodeficiencies. Secondary causes include medications, malignancies, infections, and autoimmune disorders (this does not cause immunodeficiency with increased infection).

CD40 is a member of the tumor necrosis factor receptor superfamily, expressed on a wide range of cell types including B cells, macrophages, and dendritic cells.(1) CD40 is the receptor for CD40 ligand (CD40LG), a molecule predominantly expressed by activated CD4+ T cells. CD40/CD40LG interaction is involved in the formation of memory B lymphocytes and promotes immunoglobulin (Ig) isotype switching.(1) CD40LG expression in T cells requires cellular activation, while CD40 is constitutively expressed on the surface of B cells and other antigen-presenting cells.

Hyperimmunoglobulin M (hyper-IgM or HIGM) syndrome is a rare primary immunodeficiency characterized by increased or normal levels of IgM with low IgG and/or IgA.(2) Patients with hyper-IgM syndromes may have genetic variants in 1 of several known genes. Some of these genes are *CD40LG*, *CD40*, *AICDA* (activation-induced cytidine deaminase), *UNG* (uracil DNA glycosylase), and *IKBKG* (inhibitor of kappa light polypeptide gene enhancer in B cells, kinase gamma; also known as *NEMO*).(2) Not all cases of hyper-IgM syndrome fit into these known genetic defects. Variants in *CD40LG* and *IKBKG* are inherited in an X-linked fashion, while variants in the other 3 genes are autosomal recessive in inheritance. Elevated IgM is only one of the features of NEMO deficiency and therefore, it is no longer classified exclusively with the hyper-IgM syndromes.

Distinguishing between the different forms of hyper-IgM syndrome is very important because of differing prognoses.

CD40 and CD40LG deficiency are among the more severe forms, which typically manifest in infancy or early childhood, and are characterized by an increased susceptibility to opportunistic pathogens (eg, *Pneumocystis carinii*, *Cryptosporidium*, and *Toxoplasma gondii*).(3)

CD40 deficiency, also known as hyper-IgM type 3 (HIGM3), accounts for less than 1% of hyper-IgM syndromes. Flow cytometry analysis usually shows a complete lack of CD40 expression on the B cells of these patients.(4) Intravenous injection with IgG is the treatment of choice along with immune reconstitution with hematopoietic cell transplantation. Most CD40-deficient patients have been diagnosed before age 1. Consequently, when used in the context of HIGM3, this test is only indicated in children (for diagnosis). In the case of CD40L deficiency, this test can be used for male patients or in female patients of child-bearing age (to identify carriers). A larger age spectrum has been reported with CD40L deficiency, ranging from infancy to early adulthood.

Reference Values

Present (normal)

Interpretation

This assay is qualitative; CD40 expression is reported as present (normal) or absent (abnormal). Normal B cells express surface CD40 on the majority of cells.

Hyper-IgM (HIGM3) syndrome patients typically do not express CD40 on the surface of B cells. Genotyping of *CD40* is required for a definite diagnosis of HIGM3. Call 800-533-1710 for ordering assistance.

Cautions

For questions about appropriate test selection, call 800-533-1710.

Clinical Reference

1. Bishop GA, Hostager BS. The CD40-CD154 interaction in B cell-T cell liaisons. Cytokine Growth Factor Rev. 2003;14(3-4):297-309
2. Lee WI, Torgerson TR, Schumacher MJ, et al. Molecular analysis of a large cohort of patients with hyper immunoglobulin M (IgM) syndrome. Blood. 2005;105(5):1881-1890
3. Kutukculer N, Moratto D, Aydinok Y, et al. Disseminated cryptosporidium infection in an infant with hyper-IgM syndrome caused by CD40 deficiency. J Pediatr. 2003;142(2):194-196
4.Banday AZ, Nisar R, Patra PK et al. Clinical and immunological features, genetic variants, and outcomes of patients with CD40 Deficiency J Clin Immunol. 2023;44(1):17. doi:10.1007/s10875-023-01633-1.
5. Yazdani R, Fekrvand S, Shahkarami S, et al. The hyper IgM syndromes: Epidemiology, pathogenesis, clinical manifestations, diagnosis and management. Clin Immunol. 2019;198:19-30. doi:10.1016/j.clim.2018.11.007

Performance

Method Description

The assay involves a multicolor panel of antibodies for the following markers: CD45, CD19, and CD40. After staining, the red blood cells are lysed. The remaining cells are washed and analyzed by flow cytometry. The cell surface expression of CD40 in B cells (CD19+) is determined and expressed as being present or absent.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
3 to 4 days

Specimen Retention Time
4 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
88184

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CD40	CD40 by Flow, QL, B	104694-5

Result ID	Test Result Name	Result LOINC® Value
89009	CD40 by Flow, QL, B	104694-5