MAYO CLINIC LABORATORIES

Test Definition: LAD1

Leukocyte Adhesion Deficiency Type 1, CD11a/CD18 and CD11b/CD18 Complex Immunophenotyping, Blood

Overview

Useful For

Aiding in the diagnosis of leukocyte adhesion deficiency syndrome type 1, primarily in patients younger than 18 years of age

CD11a, CD11b, and CD18 phenotyping

Genetics Test Information

ITGB2 is located on the long arm of chromosome 21(21q22.3). It encodes the common beta 2 integrin subunit (CD18), which is necessary for the expression of lymphocyte function-associated antigen 1 (CD11a/CD18), Mac-1/CR3 (CD11b/CD18), and p150/95 (CD11c/CD18).

Variants in this gene are the underlying cause for the autosomal recessive leukocyte adhesion deficiency type 1.

Method Name

Flow Cytometric Immunophenotyping

NY State Available

Yes

Specimen

Specimen Type

Whole Blood EDTA

Shipping Instructions

Specimens are required to be received in the laboratory weekdays and by 4 p.m. on Friday. Draw and package specimen as close to shipping time as possible.

It is recommended that specimens arrive within 24 hours of draw.

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

Necessary Information

Date and time of draw and physician name and phone number are required.

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 5 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
2 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
Leukocyte adhesion deficiency syndrome type 1 (LAD-1) is an autosomal recessive disorder caused by variants in the common chain (CD18) of the beta2-integrin family. LAD-1 is clinically characterized by recurrent infections, impaired wound healing, delayed umbilical cord separation, persistent leukocytosis, and recurrent soft tissue and oral infections.

Each of the beta2-integrins is a heterodimer composed of an alpha chain (CD11a, CD11b, or CD11c) noncovalently linked to a common beta2-subunit (CD18). The alpha-beta heterodimers of the beta2-integrin family include lymphocyte function-associated antigen 1 (CD11a/CD18), Mac-1/CR3 (CD11b/CD18), and p150/95 (CD11c/CD18).(1-4) The CD18 gene, *ITGB2*, and its product are required for normal expression of the alpha-beta heterodimers. Therefore, defects in CD18 expression lead to either very low or no surface membrane expression of CD11a, CD11b, and CD11c.

Severe and moderate forms of LAD-1 exist, differing in the degrees of protein deficiency, which are caused by different *ITGB2* variants. Two relatively distinct clinical phenotypes of LAD-1 have been described. Patients with the severe phenotype (<1% of normal expression of CD18 on neutrophils) characteristically have delayed umbilical stump separation (>30 days), infection of the umbilical stump (omphalitis), persistent leukocytosis (>15,000/microliter) in the absence of overt active infection, and severe destructive gingivitis with periodontitis and associated tooth loss, and alveolar bone resorption. Patients with the moderate phenotype of LAD-1 (1%-30% of normal expression of CD18 on neutrophils) tend to be diagnosed later in life. Normal umbilical separation, lower risk of life-threatening infections, and longer life expectancy are common in these patients. However, leukocytosis, periodontal disease, and delayed wound healing are still very significant clinical features.

Patients with LAD-1 (and other primary immunodeficiency diseases) are unlikely to remain undiagnosed in adulthood.

Consequently, this test should not be typically ordered in adults for LAD-1. However, it may be also used to assess immune competence by determining CD18, 11a, and 11b expression.

Reference Values

Normal (reported as normal or absent expression for each marker)

Interpretation

The report will include a summary interpretation of the presence or reduction in the level of expression of the individual markers (CD11a, CD11b, and CD18). Expression of the individual markers provides indirect information on the presence or absence of the CD11a/CD18 and CD11b/CD18 complexes.

Specimens obtained from patients with leukocyte adhesion deficiency syndrome type 1 (LAD-1) show significant reduction (moderate phenotype) or near absence (severe phenotype) of CD18 and its associated molecules, CD11a and CD11b, on neutrophils and other leukocytes.

CD11c expression also is low in LAD-1. The analytical sensitivity of the CD11c assay is insufficient to allow interpretation of CD11c surface expression. Therefore, this test is only for the expression of CD18, CD11a, and CD11b.

Cautions

This test is typically not indicated in adults. For questions about appropriate test selection, call 800-533-1710.

Patients with normal beta2-integrin expression without functional activity have been described.(5-6) Therefore, expression of CD18 alone is insufficient to exclude the diagnosis of leukocyte adhesion deficiency syndrome type 1 (LAD-1); functional assays (eg, neutrophil chemotaxis, random migration assays) must be performed if the clinical suspicion is high.

Clinical Reference

1. Anderson DC, Springer TA: Leukocyte adhesion deficiency: an inherited defect in the Mac-1, LFA-1, and p150,95 glycoproteins. Ann Rev Med. 1987;38:175-194
2. Corbi AL, Vara A, Ursa A, et al: Molecular basis for a severe case of leukocyte adhesion deficiency. Eur J Immunol. 1992;Jul:22(7):1877-1881
3. Harlan JM: Leukocyte adhesion deficiency syndrome: insights into the molecular basis of leukocyte emigration. Clin Immunol Immunopathol. 1993 June;;67(3 PT2):S16-S24
4. O'Gorman MR, McNally AC, Anderson DC, et al: A rapid whole blood lysis technique for the diagnosis of moderate or severe leukocyte adhesion deficiency (LAD). Ann NY Acad Sci. 1993 Mar 20;;677:427-430
5. Hogg N, Stewart MP, Scarth SL, et al: A novel leukocyte adhesion deficiency caused by expressed but nonfunctional beta2 integrins Mac-1 and LFA-1. J Clin Invest. 1999 Jan;103(1):97-106
6. Kuijpers TW, van Lier RAW, Hamann D, et al: Leukocyte adhesion deficiency type 1 (LAD/1) variant. J Clin Invest. 1997 Oct 1;100(7):1725-1733
7. Hanna S, Etzioni A: Leukocyte adhesion deficiencies. Ann N Y Acad Sci. 2012 Feb;1250:50-55
8. Schmidt S, Moser M, Sperandio M: The molecular basis of leukocyte recruitment and its deficiencies. Mol Immunol. 2013 Aug;55(1):49-58
9. Delmonte OM, Fleisher TA: Flow cytometry: Surface markers and beyond. J Allergy Clin Immunol. 2019 Feb;143(2):528-537

10. Knight V, Heimall JR, Chong H, et al: A toolkit and framework for optimal laboratory evaluation of individuals with suspected primary immunodeficiency. J Allergy Clin Immunol Pract. 2021 Sep;9(9):3293-3307.e6

Performance

Method Description
Flow cytometric immunophenotyping of peripheral blood is performed to evaluate the presence or absence of the CD11/CD18 complex using monoclonal antibodies directed against the CD11 isoforms, CD11a and CD11b, and CD18 antigens.(O'Gorman MR, McNally AC, Anderson DC, et al: A rapid whole blood lysis technique for the diagnosis of moderate or severe leukocyte adhesion deficiency [LAD]. Ann NY Acad Sci 1993;677:427-430)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
3 to 4 days

Specimen Retention Time
4 days

Performing Laboratory Location
Rochester

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
86356 x 3

Test Definition: LAD1

Leukocyte Adhesion Deficiency Type 1, CD11a/CD18 and CD11b/CD18 Complex Immunophenotyping, Blood

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LAD1	Leukocyte Adhesion Def. Type 1, B	94266-4

Result ID	Test Result Name	Result LOINC® Value
430	CD11a	94268-0
388	CD11b	94267-2
431	CD18	94265-6
432	LAD Interpretation	69052-9
81155	Leukocyte Adhesion Deficiency, B	No LOINC Needed