Test Definition: DOCK8

DOCK8 Deficiency, B

Overview

Useful For

Aids in the diagnosis of dedicator of cytokinesis 8 (DOCK8) deficiency

Genetics Test Information

The human *DOCK8* gene is on chromosome 9.

Autosomal recessive germline pathogenic variants observed in dedicator of cytokinesis 8 (DOCK8) deficiency fall into the following main categories:

-Large homozygous deletions

-Compound heterozygous large deletion plus pathogenic missense variant (point mutation) or a small insertion/deletion (indel)

-Compound heterozygous pathogenic missense variants plus small insertions/deletions

A study of 34 patients with DOCK8 deficiency has shown variable degrees of somatic reversion in half of the cohort, mainly in memory T cells and NK cells. The extent of somatic reversion is inversely correlated with cumulative disease burden. This type of repair cannot happen in cases with large homozygous deletions.

Highlights

The test detects the expression of dedicator of cytokinesis 8 (DOCK8) in T cells, B cells, NK cells, and monocytes in the peripheral blood.

It can be used as a screening step prior to genetic testing for *DOCK8*; to confirm the finding of an established pathogenic alteration in *DOCK8* at the protein level; to examine a reported variant of undetermined significance (VUS); and to evaluate the potential presence of somatic reversion in a patient with DOCK8 deficiency.

It can help distinguish DOCK8 deficiency from conditions with overlapping clinical manifestations, including Job syndrome (AD-HIES), ZNF341 deficiency, and severe atopic dermatitis.

Method Name

Flow Cytometry

NY State Available

Yes

Specimen

Specimen Type

Whole Blood EDTA

Advisory Information

This flow cytometry test is complementary to genetic testing.

Shipping Instructions

Specimens are required to be received in the laboratory weekdays and by 4 p.m. on Friday. 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 physician name and phone number are required.

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions: Send specimen in original tube. **Do not aliquot.**

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood EDTA	Ambient	48 hours	PURPLE OR PINK TOP/EDTA

Clinical and Interpretive

Clinical Information

Dedicator of cytokinesis 8 (DOCK8) is an atypical guanine exchange factor that plays a role in regulating actin polymerization and cytoskeletal rearrangement. DOCK8 is important in both innate and adaptive immunity by contributing to cellular migration, cytotoxicity, antibody production, and immunological memory.

DOCK8 deficiency is a rare, combined immunodeficiency with an autosomal recessive inheritance that typically presents in childhood. Its clinical features include atopic disease, recurrent sinopulmonary infections, cutaneous viral infection, *Staphylococcus aureus* skin infections, and cancer.

DOCK8 deficiency is diagnosed based on clinical phenotype, immunologic findings, and molecular analysis.

Diseases in the differential diagnosis include Job syndrome (AD-HIES), ZNF341 deficiency, and severe atopic dermatitis.

Assessment of DOCK8 expression on immune cells is an important component and facilitates the diagnosis of this

condition and the timely treatment of the patient.

Reference Values

The appropriate reference values will be provided on the report.

Interpretation

The results will be reported as the percentage of dedicator of cytokinesis 8 (DOCK8) expression on T cells, B cells, NK cells, and monocytes.

The absence of DOCK8 expression on all cell types will be consistent with DOCK8 deficiency. In this case, genetic analysis of *DOCK8* to confirm the diagnosis and to identify the underlying alteration will be recommended.

The expression of DOCK8 on a subset of T cells and/or NK cells could suggest somatic reversion in a patient with DOCK8 deficiency, which can modulate disease phenotype over time.

Cautions

This test cannot be relied upon for identifying carrier status for Dedicator of Cytokinesis 8 (DOCK8) deficiency.

Clinical Reference

1. Engelhardt KR, McGhee S, Winkler S, et al: Large deletions and point mutations involving the dedicator of cytokinesis 8 (DOCK8) in the autosomal-recessive form of hyper-IgE syndrome. J Allergy Clin Immunol 2009; 124:1289-302 e4

2. Jing H, Zhang Q, Zhang Y, et al: Somatic reversion in dedicator of cytokinesis 8 immunodeficiency modulates disease phenotype. J Allergy Clin Immunol 2014;133:1667-1675

3. Pai SY, de Boer H, Massaad MJ, et al: Flow cytometry diagnosis of dedicator of cytokinesis 8 (DOCK8) deficiency. J Allergy Clin Immunol 2014;134:221-223

4. Engelhardt KR, Gertz ME, Keles S, et al: The extended clinical phenotype of 64 patients with dedicator of cytokinesis 8 deficiency. J Allergy Clin Immunol 2015;136:402-412

5. Su HC, Jing H, Angelus P, Freeman AF: Insights into immunity from clinical and basic science studies of DOCK8 immunodeficiency syndrome. Immunol Rev 2019; 287:9-19

6. Aydin SE, Freeman AF, Al-Herz W, et al: Hematopoietic Stem Cell Transplantation as Treatment for Patients with DOCK8 Deficiency. J Allergy Clin Immunol Pract 2019; 7:848-855

Performance

Method Description

The dedicator of cytokinesis 8 (DOCK8) protein expression assay is performed on whole blood. Samples are fixed, permeabilized and stained with antibodies specific for CD45, CD14, CD19, CD3, and CD56 along with either the DOCK8 antibody (unconjugated) or isotype control (unconjugated). A secondary mouse anti-rabbit reporter antibody is added to allow the assessment of DOCK8 and isotype control expression. Samples are then analyzed on a flow cytometer. DOCK8 expression is evaluated on the following populations: T-cells: (CD45+CD14[neg]CD3+), B-cells: (CD45+CD14[neg]CD3[neg]CD19+), NK-cells (CD45+CD14[neg]CD3[neg]CD56+), Monocytes (CD45+CD14+).(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday

Specimen must be received by 4p.m. on Friday.

Analytic Time

2 days

Maximum Laboratory Time

4 days

Specimen Retention Time

4 days

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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 U.S. Food and Drug Administration.

CPT Code Information

86356 x 4

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
DOCK8	DOCK8 Deficiency, B	In Process

Result ID	Test Result Name	Result LOINC Value
608496	%CD3+DOCK8+	In Process
608497	%CD19+DOCK8+	In Process
608498	%CD56+DOCK8+	In Process
608499	%CD14+DOCK8+	In Process
608513	DOCK8 Interpretation	69052-9