Test Definition: DOCK8

Dedicator of Cytokinesis 8 (DOCK8) Deficiency, Blood

Overview

Useful For

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

This test **is not useful for** assessing *DOCK8* carrier status.

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 disease-causing missense variant (point alteration) or a small deletion/insertion (delin)
-Compound heterozygous disease-causing missense variants plus small deletions/insertions

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, natural killer 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 disease-causing alteration in *DOCK8* at the protein level; to examine a reported variant of undetermined significance; 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

Ordering Guidance
This flow cytometry test is complementary to genetic testing.

Shipping Instructions
Testing is not performed on Saturday, Sunday, or observed holidays. Only collect and ship specimen for arrival on days when testing is performed.

Specimens received on days when testing is not performed or after 5 p.m. Central on Friday will be canceled if specimen is outside of stability when testing is next performed.

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

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.**

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 & 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.

Dedicator of cytokinesis 8 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.

Dedicator of cytokinesis 8 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, natural killer (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 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(6):1289-302 e4. doi:10.1016/j.jaci.2009.10.038
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(6):1667-1675. doi:10.1016/j.jaci.2014.03.025
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(1):221-223. doi:10.1016/j.jaci.2014.02.023
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(2):402-412. doi:10.1016/j.jaci.2014.12.1945
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(1):9-19. doi:10.1111/imr.12723
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(3):848-855. doi:10.1016/j.jaip.2018.10.035

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+), natural killer-cells (CD45+CD14[neg]CD3[neg]CD56+), Monocytes (CD45+CD14+).(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
2 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
86356 x 4

LOINC® Information

Test Definition: DOCK8

Dedicator of Cytokinesis 8 (DOCK8) Deficiency, Blood

Test ID	Test Order Name	Order LOINC® Value
DOCK8	DOCK8 Deficiency, B	96415-5

Result ID	Test Result Name	Result LOINC® Value
608496	%CD3+DOCK8+	96416-3
608497	%CD19+DOCK8+	96417-1
608498	%CD56+DOCK8+	96418-9
608499	%CD14+DOCK8+	96419-7
608513	DOCK8 Interpretation	69052-9