Test Definition: SCDT2

SCID NBS, BS

Overview

Useful For

First-tier severe combined immunodeficiency syndrome (SCID) newborn screening

Second-tier testing of newborns with an abnormal screening result for SCID

Genetics Test Information

This test detects severe combined immunodeficiency syndrome (SCID) by measuring T-cell receptor excision circle (TREC) levels in dried-blood spots.

Highlights

This test provides absolute T-cell receptor excision circle (TREC) quantitation from dried blood spots for evaluating a potential diagnosis of severe combined immunodeficiency syndrome (SCID) or leaky SCID, or secondary conditions of T-cell lymphopenia.

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name

Droplet Digital Polymerase Chain Reaction (ddPCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Necessary Information

1. Birth weight (grams)

2. Time of birth (24 hour time)

3. Gestational age (weeks)

Specimen Required

To maximize the benefit of early identification the specimen should be collected as early as possible after 12 hours of age and before 1 week of age.

Supplies: Card-Blood Spot Collection Filter Paper (T493)

Container/Tube:

Preferred: Blood Spot Collection Card

Acceptable: Ahlstrom 226 filter paper and Whatman Protein Saver 903 Paper

Specimen Volume: 1 Blood spot

Collection Instructions:

1. Do not use device or capillary tube containing EDTA to collect specimen.

2. Do not expose specimen to heat or direct sunlight.

3. Do not stack wet specimens.

4. Keep specimen dry.

5. If collection of a new specimen is necessary, let blood dry on the Blood Spot Collection Card (T493) at ambient temperature in a horizontal position for 3 hours.

Additional Information:

1. For collection instructions, see Blood Spot Collection Instructions in Special Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

2. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521) in Special Instructions

Specimen Minimum Volume

1 completely filled circle on filter paper card

Reject Due To

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		

Specimen Type	Temperature	Time	Special Container
	Frozen		
	Refrigerated		

Clinical and Interpretive

Clinical Information

Severe combined immunodeficiency syndrome (SCID) is a heterogeneous group of genetic conditions with severe T-cell lymphopenia. Infants with SCID are often asymptomatic at birth but are at risk for recurring infections within 4 to 6 months of age. In addition to T-cell lymphopenia, patients may also have B and/or NK cell lymphopenia, depending on the underlying genetic cause. Some cases of SCID may have additional features indicative of Omenn syndrome. Typical SCID carries a high rate of mortality (100%) within the first 2 years of life unless urgently treated. Early detection of SCID is critical to enable curative therapy or to institute a bridge therapy. Hematopoietic cell significantly transplant reduces morbidity and mortality and improves long-term survival.(1,2) There are at least 16 different molecular defects associated with the SCID phenotype including the leaky SCID/Omenn syndrome.(3) Omenn syndrome is associated with a hypomorphic mutation in a gene that causes SCID, along with additional features of erythrodermia, eosinophilia, adenopathy, hepatosplenomegaly, elevated IgE, oligoclonal T cell expansion of autologous cells, lack of maternal engraftment.

Newborn screening methods for SCID detect T-cell receptor excision circles (TRECs), which are nonreplicative, extrachromosomal DNA byproducts of T-cell receptor gene rearrangements.(2,3) TREC are typically expressed only in T cells of thymic origin, and are diluted by cell division.(2,4) The TREC used for measurement in this newborn screening method is the deltaRec-psiJalpha TREC and TREC analysis provides a sensitive assessment of thymic output. Low TREC values are indicative of either SCID or another clinical condition leading to severe T-cell lymphopenia.(5,6,7) In addition to typical SCID and leaky SCID, TREC newborn screening assays can detect up other secondary conditions, including syndromic disorders associated with T-cell lymphopenia, variant SCID (where the molecular diagnosis is unknown but the immunological and clinical criteria are indicative of SCID), and secondary T-cell lymphopenia due to other genetic conditions or prematurity.

When dried blood spot TREC quantitation is below normal range for age, additional immunological follow-up testing, such as TREC analysis in enriched cells (data expressed as TREC copies relative to patient's CD3+ T cell count) (TREC / T-Cell Receptor Excision Circles [TREC] Analysis, Blood), CD4 T-cell recent thymic emigrants (CD4RT / CD4 T-Cell Recent Thymic Emigrants [RTE]) and quantitative lymphocyte subsets: T, B, and NK by flow cytometry (TBBS / Quantitative Lymphocyte Subsets: T, B, and Natural Killer [NK]) are recommended. If any of these results are abnormal, recommendations for confirmation testing will be provided as needed.

Reference Values

Negative

Interpretation

Absolute T-cell receptor excision circles (TREC) concentration and an interpretive report are provided.

Cautions

This test may not detect all cases of T-cell lymphopenia.

Carrier status (heterozygosity) for severe combined immunodeficiency syndrome (SCID) or other T-cell lymphopenia cannot be detected.

T-cell receptor excision circles (TRECs) show an inverse correlation with age, and this test is not recommended for adults.

A positive test result may suggest a diagnosis of T-cell lymphopenia, related to SCID or another condition, but requires follow-up by additional testing, such as TREC analysis (data provided relative to patient's CD3+ T cell count) in enriched cells (TREC / T-Cell Receptor Excision Circles [TREC] Analysis, Blood), CD4 T-cell recent thymic emigrants (CD4RT / CD4 T-Cell Recent Thymic Emigrants [RTE]) and quantitative lymphocyte subsets: T, B, and NK, by flow cytometry (TBBS / Quantitative Lymphocyte Subsets: T, B, and Natural Killer [NK])

Premature infants are likely to have T-cell lymphopenia; therefore, if a patient is younger than 37 weeks gestational age, or 1500 g birth weight, repeat testing at the appropriate time is recommend.

Postanalytical interpretation of results may indicate improper storage and handling of the card, or that the patient received a blood transfusion prior to specimen collection, which may require a new specimen to repeat the analysis. Leuko-reduced, irradiated packed red blood cells, should not affect TREC analysis. Blood transfusions prior to specimen collection may lead to false-positive results (see above statement).

Clinical Reference

1. CLSI (2013): Newborn Blood Spot Screening for Severe Combined Immunodeficiency by Measurement of T-cell Receptor Excision Circles; Approved Guideline. CLSI document NBS06-A. Wayne, PA: Clinical and Laboratory Standards Institute

2. Sottini A, Ghidini C, Zanotti C, et al: Simultaneous Quantification of Recent Thymic T-cell and Bone Marrow B-cell Emigrants in Patients with Primary Immunodeficiency Undergone to Stem Cell Transplantation. Clin Immunol 2010, 136:217-227. doi: 10.1016/j.clim.2010.04.005. Epub 2010 May 10

3. Picard C, Al-Herz W, Bousfiha A., et al: Primary Immunodeficiency Diseases: An Update on the Classification from the IUIS Committee for Primary Immunodeficiency. J Clin Immunol 2015, Nov;35(8):696-726. doi: 10.1007/s10875-015-0201-1. Epub 2015 Oct 19

4. Van Zelm MC, Van der Burg M, Langerak AW, et al: PID Comes Full Circle: Applications of V(D)J Recombination Excision Circles in Research, Diagnostics and Newborn Screening of Primary Immunodeficiency Disorders. Front Immunol 2011, May 4;2:12. doi: 10.3389/fimmu.2011.00012. eCollection 2011

5. Kwan A, Abraham RS, Currier R, et al: Newborn Screening for Severe Combined Immunodeficiency in 11 Screening Programs in the United States. JAMA, 2014;312(7):729-738. doi: 10.1001/jama.2014.9132

6. van der Spek J, Groenwold RH, van der Burg M, et al: TREC Based Newborn Screening for Severe Combined Immunodeficiency Disease: A Systematic Review. J Clin Immunol 2015 May, 35(4):416-430. doi: 10.1007/s10875-015-0152-6. Epub 2015 Apr 17

7. Vidal-Folch N, Milosevic D, Majumdar R, et al: A Droplet Digital PCR Method for Severe Combined Immunodeficiency Newborn Screening. J Mol Diagn 2017, Sep 19 (5): 755-765. doi: 10.1016/j.jmoldx.2017.05.011

Performance

Method Description

The droplet digital PCR (ddPCR) TREC screening assay detects severe combined immunodeficiency syndromes (SCID) by measuring absolute concentrations of T-cell receptor excision circles (TREC) and ribonuclease P (RNAseP, RPP30, a reference gene) in DBS by fluorescent droplet.(Vidal-Folch N, Milosevic D, Majumdar R, et al: A Droplet Digital PCR Method for Severe Combined Immunodeficiency Newborn Screening. J Mol Diagn 2017, Sep 19

(5): 755-765. doi: 10.1016/j.jmoldx.2017.05.011) An absolute TREC concentration is determined by applying a Poisson distribution calculation across the positive and negative droplets.(Pinheiro LB, Coleman VA, Hindson CM, et al: Evaluation of a Droplet Digital Polymerase Chain Reaction Format for DNA Copy Number Quantification. Anal Chem 2012, 84;1003-1011. doi: 10.1021/ac202578x. Epub 2011 Dec 21)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Sunday; Varies

Analytic Time

5 days

Maximum Laboratory Time

10 days

Specimen Retention Time

Minimum of 1 year

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 and its performance characteristics 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

81479

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
SCDT2	SCID NBS, BS	62333-0

Result ID	Test Result Name	Result LOINC Value
MG319	Birth Weight (grams, XXXX)	8339-4
MG320	Time of Birth (24 hr time, XX:XX)	57715-5
MG321	Gestational Age (weeks, XX.X)	76516-4
602324	Result Summary	50397-9

Test Definition: SCDT2

SCID NBS, BS

Result ID	Test Result Name	Result LOINC Value
602325	Result	62320-7
602326	Interpretation	69047-9
602327	Additional Information	48767-8
602328	Specimen	31208-2
602329	Source	31208-2
602330	Released By	18771-6