

Overview

Useful For

Establishing a diagnosis of a severe combined immunodeficiency (SCID) associated with known causal genes

Identifying variants within genes known to be associated with SCID, allowing for predictive testing of at-risk family members and/or determination of targeted management (anticipatory guidance, management changes, specific therapies)

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 50 genes associated with severe combined immunodeficiency (SCID): *ADA, AK2, ATM, BCL11B, CARD11, CD247, CD3D, CD3E, CD3G, CD8A, CHD7, CIITA, CORO1A, DCLRE1C, DOCK2, DOCK8, EXTL3, FOXN1, IKZF1, IL2RA, IL2RG, IL7R, JAK3, LAT, LCP2, LIG4, MTHFD1, NBN, NHEJ1, ORAI1, PAX1, PNP, POLE2, PRKDC, PTPRC, RAC2, RAG1, RAG2, RFX5, RFXANK, RFXAP, RMRP, SEMA3E, SMARCA11, STIM1, TBX1, TTC7A, WAS, WIPF1, and ZAP70*. See [Targeted Genes and Methodology Details for Severe Combined Immunodeficiency \(SCID\) Gene Panel](#) for details regarding the targeted gene regions evaluated by this test.

Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for SCID.

Testing Algorithm

For skin biopsy or cultured fibroblast specimens, a fibroblast culture will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

For postnatal umbilical cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Combined Immunodeficiency, Severe Combined Immunodeficiency, and B-Cell/Antibody Deficiency Patient Information](#)
- [Targeted Genes and Methodology Details for Severe Combined Immunodeficiency \(SCID\) Gene Panel](#)

Method Name

Sequence Capture and Amplicon-Based Next-Generation Sequencing (NGS)/Quantitative Real-Time Polymerase Chain Reaction (qPCR) and Sanger Sequencing as needed

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Targeted testing for familial variants (also called site-specific or known variants testing) is available for the genes on this panel. See FMTT / Familial Variant, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogeneic donor will interfere with testing. For information about testing patients who have received a bone marrow transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Green top (sodium heparin)

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information

Specimen Stability Information: Ambient 4 days (preferred)/Refrigerated 4 days/Frozen 4 days

Additional Information:

1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens

received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.

2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.

3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

Specimen Type: Saliva

Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

Supplies:

DNA Saliva Kit High Yield (T1007)

Saliva Swab Collection Kit (T786)

Container/Tube:

Preferred: High-yield DNA saliva kit

Acceptable: Saliva swab

Specimen Volume: 1 Tube if using T1007 or 2 swabs if using T786

Collection Instructions: Collect and send specimen per kit instructions.

Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days

Additional Information: Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Specimen Type: Blood spot

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

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: PerkinElmer 226 filter paper or blood spot collection card

Specimen Volume: 2 to 5 Blood spots

Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see [How to Collect a Dried Blood Spot Sample](#).

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.

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

4. Do not stack wet specimens.

5. Keep specimen dry.

Send: Ambient (preferred)/Refrigerated

Additional Information:

1. Blood spot specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from blood spots, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

2. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to

complete testing.

3. For collection instructions, see [Blood Spot Collection Instructions](#)

4. For collection instructions in Spanish, see [Blood Spot Collection Card-Spanish Instructions](#) (T777)

5. For collection instructions in Chinese, see [Blood Spot Collection Card-Chinese Instructions](#) (T800)

Specimen Type: Skin biopsy

Supplies: Fibroblast Biopsy Transport Media (T115)

Container/Tube: Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.

Specimen Volume: 4-mm Punch

Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours

Additional Information:

1. Specimens are preferred to be received within 24 hours of collection.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Cultured fibroblasts

Source: Skin or tissue

Container/Tube: T-25 flask

Specimen Volume: 2 Flasks

Collection Instructions: Submit confluent cultured fibroblast cells from a biopsy. Cultured cells from a prenatal specimen will not be accepted.

Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours

Additional Information:

1. Specimens are preferred to be received within 24 hours of collection. Culture and/or extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Extracted DNA

Container/Tube:

Preferred: Screw Cap Micro Tube, 2mL with skirted conical base

Acceptable: Matrix tube, 1mL

Collection Instructions:

1. The preferred volume is at least 100 µL at a concentration of 75 ng/µL.
2. Include concentration and volume on tube.

Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated

Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

Forms

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:

- [Informed Consent for Genetic Testing](#) (T576)
- [Informed Consent for Genetic Testing \(Spanish\)](#) (T826)
- 2. [Combined Immunodeficiency, Severe Combined Immunodeficiency, and B-Cell/Antibody Deficiency Patient Information](#)

Specimen Minimum Volume

See Specimen Required

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Severe combined immunodeficiency (SCID) is characterized by the absence or dysfunction of T lymphocytes, which affects both cellular and humoral adaptive immunity. This absence or dysfunction of T cells results in a severe form of inherited primary immunodeficiency that may be life-threatening. SCID typically presents in infancy with persistent respiratory and gastrointestinal infections, failure to thrive, or graft-versus-host disease (due to engraftment of maternal T cells). The absence of lymphoid tissue, immunoglobulins, and B lymphocytes may also be noted.

Critically, having low T-cell numbers is not sufficient on its own for a diagnosis of SCID because other non-SCID disorders, such as thymic defects, may also present with significant T-cell lymphopenia. SCID results from genetic causes of hematopoietic stem cell intrinsic defects in T-lymphocyte development. Primary thymic function defects should be differentiated from SCID because hematopoietic stem cell transplantation is unlikely to be curative for thymic function defects, as the defect is in thymic stromal cell development, not in hematopoietic stem cells.

Severe combined immunodeficiency is suspected when the patient has fewer than 300 autologous CD3 T cells per microliter and additional suggestive features, such as having less than 20% of CD4+ cells with naive cell surface markers, an abnormal SCID newborn screen, a family history of SCID, recurrent or opportunistic infections, or features of Omenn syndrome. An important diagnostic criterion for typical SCID is having less than 50 autologous CD3 T cells per microliter in blood, which requires immediate medical intervention. Other diagnostic criteria may include the identification of a disease-causing variant or variants in a gene whose product is known to be essential for T-cell development and having no alternate explanation for low T-cell count and low to undetectable TREC (T cell receptor excision circles) or <20% of CD4 T cells with naive cell surface marker CD45RA. Alternatively, the presence of maternal T cells in peripheral blood due to failure to reject transplacentally transferred cells is a pathognomonic finding.

Atypical or "leaky" SCID is the term used for patients with partial defects in T-cell number and function. Leaky SCID tends to present in patients older than 12 months of age with recurrent, severe, and prolonged viral infections, bronchiectasis, failure to thrive, and autoimmune manifestations, including cytopenias. Patients may display partial or restricted antigen-specific antibody responses. Leaky SCID is often caused by hypomorphic variants in genes normally associated with typical SCID. Leaky SCID can be diagnosed based on the following: low T-cell number for age; oligoclonal T cells; abnormal TREC or <20% of CD4+ T cells that are naive; the identification of disease-causing variants identified in a gene whose product is known to be essential for T-cell development; reduced T-cell proliferation tests (defined as a proliferative response to phytohemagglutinin, anti-CD3, or anti-CD3/CD28); and the exclusion of other SCID or combined immunodeficiency conditions with a known genotype, thymic disorder, and other disorders associated with low T-cell numbers.

Omenn syndrome, a form of leaky SCID that typically presents in infancy, is characterized by erythroderma, alopecia, hepatosplenomegaly, and lymphadenopathy. Laboratory findings may include elevated IgE, eosinophilia, and lymphocytosis. While *RAG1* and *RAG2* hypomorphic variants are most often associated with leaky SCID or Omenn syndrome, patients may have variants affecting other genes and the proteins they produce, such as Artemis or interleukin-7 receptor (IL-7R) alpha. There are forms of leaky SCID with hypomorphic variants in these genes that do not have the associated Omenn syndrome phenotype.

Severe combined immunodeficiency can be classified as T-B- or T-B+ SCID, with further subdivision possible based on the presence or absence of natural killer (NK) cells. T-B- SCID is typically caused by a defect in V(D)J recombination, the process that creates the antigen receptor diversity critical to the adaptive immune system. However, T-B- SCID may also be caused by certain enzyme deficiencies, such as adenosine deaminase deficiency, which results in accumulation of metabolic by-products that are toxic to lymphocytes. Reticular dysgenesis-the most severe form of combined immunodeficiency-is caused by a deficiency of the enzyme adenylate kinase 2 and genetic variants in the *AK2* gene. Reticular dysgenesis is characterized by a T-B-NK- phenotype, congenital agranulocytosis, lymphopenia, lymphoid and thymic hypoplasia, and bilateral sensorineural deafness.

T-B+ SCID is characterized by impaired development of mature T-cells and the presence of nonfunctional B cells. It is most often caused by genetic variants that affect cytokine-mediated signaling. X-linked T-B+ SCID is due to variants in the *IL2RG* gene, which encodes the common gamma chain that is a part of the IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21 receptors. Autosomal recessive forms of T-B+ SCID due to variants in *JAK3* or *IL7R* also disrupt cytokine signaling. Genetic variants in one of the four CD3 genes (*CD3G*, *CD3D*, *CD3E*, and *CD247[CD3Z]*) inhibit CD3 signaling and cause T-B+ SCID.

The T-B+ cellular phenotype may also be caused by thymic defects that must be differentiated from T-B+ SCID to guide treatment decisions as stated above. Causes of these thymic defects include coronin-1A deficiency, which causes disruption of thymic egress of T cells and defective T-cell locomotion, and CD45 deficiency caused by variants in the *PTPRC* gene. Thymic defects with additional congenital anomalies may be observed in DiGeorge syndrome (represented on this panel by *TBX1*), CHARGE (coloboma, heart defects, atresia choanae [also known as choanal atresia], growth retardation, genital abnormalities, and ear abnormalities) syndrome (due to variants in *CHD7* or *SEMA3E*), and patients with genetic variants in *FOXP1*.

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.⁽¹⁾ Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

This analysis targets single and multi-exon deletions/duplications; however, in some instances, single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.

This test is not designed to detect low levels of mosaicism or to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Genes may be added or removed based on updated clinical relevance. For detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent non-leukocyte reduced blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants:

Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages health care professionals to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time. Due to broadening genetic knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

Variant Evaluation:

Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.⁽¹⁾ Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgement.

Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. These findings will be carefully reviewed to determine whether they will be reported.

Clinical Reference

1. Tangye SG, Al-Herz W, Bousfiha A, et al. Human inborn errors of immunity: 2022 update on the classification from the International Union of Immunological Societies Expert Committee. *J Clin Immunol*. 2022;42(7):1473-1507. doi:10.1007/s10875-022-01289-3
2. Dvorak CC, Haddad E, Heimall J, et al. The diagnosis of severe combined immunodeficiency (SCID): The Primary Immune Deficiency Treatment Consortium (PIDTC) 2022 definitions. *J Allergy Clin Immunol*. 2023;151(2):539-546. doi:10.1016/j.jaci.2022.10.022
3. Bousfiha A, Moundir A, Tangye SG, et al. The 2022 update of IUIS Phenotypical Classification for human inborn errors of immunity. *J Clin Immunol*. 2022;42(7):1508-1520. doi:10.1007/s10875-022-01352-z
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6. Walkovich K, Vander Lugt M. ZAP70-related combined immunodeficiency. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. *GeneReviews* [Internet]. University of Washington, Seattle; 2009. Updated September 23, 2021. Accessed November 13, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK20221/
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[Internet]. University of Washington, Seattle; 2006. Updated March 7, 2024. Accessed November 13, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1483/

8. Allenspach E, Rawlings DJ, Scharenberg AM. X-linked severe combined immunodeficiency. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2003. Updated August 5, 2021. Accessed November . Available at www.ncbi.nlm.nih.gov/books/NBK1410/

9. 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

Performance

Method Description

Next-generation sequencing (NGS) and/or Sanger sequencing is performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed, as well as some other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletions/insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS and/or a polymerase chain reaction-based quantitative method is performed to test for the presence of deletions and duplications in the genes analyzed.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. See [Targeted Genes and Methodology Details for Severe Combined Immunodeficiency \(SCID\) Gene Panel](#) for details regarding the targeted gene regions identified by this test (Unpublished Mayo methods)

Genes Analyzed: *ADA*, *AK2*, *ATM*, *BCL11B*, *CARD11*, *CD247*, *CD3D*, *CD3E*, *CD3G*, *CD8A*, *CHD7*, *CIITA*, *CORO1A*, *DCLRE1C*, *DOCK2*, *DOCK8*, *EXTL3*, *FOXN1*, *IKZF1*, *IL2RA*, *IL2RG*, *IL7R*, *JAK3*, *LAT*, *LCP2*, *LIG4*, *MTHFD1*, *NBN*, *NHEJ1*, *ORAI1*, *PAX1*, *PNP*, *POLE2*, *PRKDC*, *PTPRC*, *RAC2*, *RAG1*, *RAG2*, *RFX5*, *RFXANK*, *RFXAP*, *RMRP*, *SEMA3E*, *SMARCA11*, *STIM1*, *TBX1*, *TTC7A*, *WAS*, *WIPF1*, and *ZAP70*

PDF Report

Supplemental

Day(s) Performed

Varies

Report Available

28 to 42 days

Specimen Retention Time

Whole blood: 28 days (if available); Extracted DNA: 3 months, Saliva: 30 days (if available); Blood spots: 1 year (if available)

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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 and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

- 81443
- 88233- Tissue culture, skin, solid tissue biopsy (if appropriate)
- 88240- Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SCIDP	SCID Gene Panel	107540-7

Result ID	Test Result Name	Result LOINC® Value
620135	Test Description	62364-5
620136	Specimen	31208-2
620137	Source	31208-2
620138	Result Summary	50397-9
620139	Result	82939-0
620140	Interpretation	69047-9
620141	Additional Results	48767-8
620142	Resources	99622-3
620143	Additional Information	48767-8
620144	Method	85069-3
620145	Genes Analyzed	82939-0
620146	Disclaimer	62364-5
620147	Released By	18771-6