MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: June 3, 2025
Effective Date: July 8, 2025

Inborn Errors of Immunity Comprehensive Gene Panel, Varies

Test ID: IEICP

Useful for:

- Providing a comprehensive genetic evaluation for patients with a personal history of an inborn error of immunity (IEI)
- Establishing a diagnosis of an IEI associated with known causal genes
- Identifying variants within genes known to be associated with inherited IEI, allowing for predictive testing of at-risk family members and/or determination of targeted management (anticipatory guidance, management changes, specific therapies)

Genetics Information:

- This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 383 genes associated with inborn errors of immunity: *ACD, ACP5, ADA, ADA2, ADAM17, ADAR, AICDA, AIRE, AK2, ALPI, ANGPT1, ANKZF1, AP3B1, AP3D1, ARPC1B, ASAH1, ATM, ATP6AP1, BACH2, BCL10, BCL11B, BLM, BLNK, BLOC1S6, BTK, C1QA, C1QB, C1QC, C1R, C1S, C2, C3, C5, C6, C7, C8A, C8B, C9, CARD11, CARD14, CARD9, CARMIL2, CASP10, CASP8, CCBE1, CD19, CD247, CD27, CD28, CD3D, CD3E, CD3G, CD40, CD40LG, CD46, CD48, CD55, CD59, CD70, CD79A, CD79B, CD81, CD8A, CDC42, CDCA7, CEBPE, CFB, CFD, CFH, CFI, CFP, CFTR, CHD7, CIB1, CIITA, CLCN7, CLPB, COPA, CORO1A, CR2, CSF2RA, CSF2RB, CSF3R, CTC1, CTLA4, CTPS1, CTSC, CXCR2, CXCR4, CYBA, CYBB, CYBC1, DBR1, DCLRE1C, DDX58 (RIGI), DEF6, DGAT1, DKC1, DNAJC21, DNASE1, DNASE1L3, DNASE2, DNMT3B, DOCK2, DOCK8, DUOX2, EFL1, ELANE, EPG5, ERBIN, ERCC6L2, EXTL3, F12, FADD, FAS, FASLG, FAT4, FCHO1, FERMT1, FERMT3, FOXN1, FOXP3, G6PC (G6PC1), G6PC3, G6PD, GATA2, GFI1, GINS1, GLA, HAVCR2, HAX1, HELLS, HMOX1, HPS1, HPS3, HPS4, HPS6, ICOS, ICOSLG, IFIH1, IFNAR1, IFNAR2, IFNGR1, IFNGR2, IGHM, IGLL1, IKBKB, IKBKG, IKZF1, IKZF3, IL10, IL10RA, IL10RB, IL12B, IL12RB1, IL12RB2, IL17F, IL17RA, IL17RC, IL1RN, IL21, IL21R, IL23R, IL2RA, IL2RB, IL2RG, IL36RN, IL6R, IL6ST, IL7R, IRAK4, IRF2BP2, IRF3, IRF7, IRF8, IRF9, ISG15, ITCH, ITGB2, ITK, ITPKB, JAGN1, JAK1, JAK3, KDM6A, KMT2A, KMT2D, KNG1, LACC1, LAT, LCK, LCP2, LIG1, LIG4, LPIN2, LRBA, LSM11, LYN, LYST, MAGT1, MALT1, MAP3K14, MASP2, MCM10, MEFV, MOGS, MRTFA, MS4A1, MSN, MTHFD1, MVK, MYD88, MYSM1, NBAS, NBN, NCF1, NCF2, NCF4, NCSTN, NFE2L2, NFKB1, NFKB2, NFKBIA, NHEJ1, NHP2, NLRC4, NLRP1, NLRP12, NLRP3, NOD2, NSMCE3, OAS1, ORAI1, OSTM1, OTULIN, PARN, PAX1, PEPD, PGM3, PIK3CD, PIK3R1, PLCG2, PLG, PMM2, PNP, POLA1, POLD1, POLE, POLE2, POLR3A, POLR3C, POMP, PRF1, PRKCD, PRKDC, PSENEN, PSMA3, PSMB10, PSMB4, PSMB8, PSMB9, PSMG2, PSTPIP1, PTPRC, RAB27A, RAC2, RAG1, RAG2, RASGRP1, RBCK1, RBM8A, REL, RELA, RELB, RFX5, RFXANK, RFXAP, RHOH, RIPK1, RMRP, RNASEH2A, RNASEH2B, RNASEH2C, RNF168, RNF31, RNU4ATAC, RNU7-1, RORC, RPSA, RTEL1, SAMD9, SAMD9L, SAMHD1, SBDS, SEC61A1, SEMA3E, SERPING1, SH2D1A, SH3BP2, SH3KBP1, SKIV2L (SKIC2), SLC29A3, SLC35C1, SLC37A4, SLC39A7, SLC46A1, SLC7A7, SMARCAL1,*

SMARCD2, SNX10, SP110, SPINK5, SPPL2A, SRP54, STAT1, STAT2, STAT3, STAT5B, STIM1, STING1, STK4, STX11, STXBP2, SYK, TAP1, TAP2, TAPBP, TAZ (TAFAZZIN), TBX1, TCF3, TCIRG1, TCN2, TERC, TERT, TET2, TFRC, TGFB1, TGFBR1, TGFBR2, THBD, TINF2, TIRAP, TLR3, TLR7, TLR8, TMC6, TMC8, TNFAIP3, TNFRSF11A, TNFRSF13B, TNFRSF13C, TNFRSF1A, TNFRSF4, TNFRSF9, TNFSF11, TNFSF12, TNFSF13, TOP2B, TPP2, TRAC, TRAF3, TRAF3IP2, TREX1, TRNT1, TTC37 (SKIC3), TTC7A, TYK2, UNC13D, UNC93B1, UNG, USB1, USP18, VPS13B, VPS45, WAS, WDR1, WIPF1, WRAP53, XIAP, ZAP70, ZBTB24, ZNF341, and *ZNFX1.* See Targeted Genes and Methodology Details for Inborn Errors of Immunity Comprehensive Gene Panel and Method Description for additional details.

- Identification of a disease-causing variant may assist with diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for primary (genetic) immune disorders, also known as primary immunodeficiency disorders or as inborn errors of immunity.

Reflex Tests:

Test ID	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Testing Algorithm:

Skin biopsy:

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.

Cord blood:

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

Methods:

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

Reference Values:

An interpretive report will be provided.

Specimen Requirements:

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell 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.**
Specimen Stability Information:	Ambient (preferred) 4 days/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 is met, the required volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
Minimum Volume:	1 mL

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. Culture and 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:	**Cultured fibroblasts**
Source:	Skin
Container/Tube:	T-25 flask
Specimen Volume:	2 Flasks
Collection Instructions:	Submit confluent cultured fibroblast cells from a skin 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 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 and Molecular Testing, Tissue. 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, 2 mL with skirted conical base
Acceptable	Matrix tube, 1 mL
Collection Instructions:	1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL. 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.

Specimen Type:	**Bone marrow aspirate**
Container/Tube:	
Preferred:	Lavender top (EDTA)
Acceptable:	Yellow top (ACD)
Specimen Volume:	2 mL
Collection Instructions:	1. Invert several times to mix bone marrow. 2. Label specimen as bone marrow. 3. Send bone marrow specimen in original tube. **Do not aliquot.**
Specimen Stability Information:	Ambient 4 days/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 is met, the required volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
Minimum Volume:	1 mL

Specimen Type:	**Cord 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.**

Specimen Stability Information:	Ambient (preferred) 4 days/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 is met, the required volume must be submitted. Testing may be canceled if DNA requirements are inadequate. 3. While a properly collected cord blood sample may not be at risk for maternal cell contamination, unanticipated complications may occur during collection. Therefore, maternal cell contamination studies are recommended to ensure the test results reflect that of the patient tested and are available at an additional charge. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.
Minimum Volume:	1 mL

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.
Specimen Stability Information:	Ambient (preferred)/Refrigerated
Additional Information:	1. Blood spot specimens are acceptable but not recommended. Multiple extractions will be required to obtain sufficient yield for supplemental analysis, and there is significant risk for test failure due to insufficient DNA. 2. Due to lower concentration of DNA yielded from blood spot, 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. 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:	**Saliva**
Patient Preparation:	Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies:	Saliva Swab Collection Kit (T786)

Specimen Volume:	2 Swabs, use 2 kits for collection
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.

Additional Specimen Requirements:

For cord blood specimens: Maternal cell contamination (MCC) studies are available. **Order MATCC /** Maternal Cell Contamination, Molecular Analysis, Varies **on both the cord blood and maternal specimens under separate order numbers.** Cord blood testing will proceed without MCC studies, but results may be compromised if MCC is present.

Specimen Stability Information:

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Ordering Guidance:

- Patients who have had a previous bone marrow transplant from an allogenic donor should not have testing performed on blood, bone marrow, or saliva because any results generated will reflect the genome of the donor rather than the recipient. Testing on patients who have an active hematologic malignancy or hematologic disorder with clonal proliferation may identify both somatic mutations and germline variants, which may result in test failure or necessitate follow-up testing to determine whether the detected variant is germline or somatic. For these patients, testing a skin biopsy or cultured fibroblasts is recommended. For instructions for testing patients who have received a bone marrow transplant or have an active hematologic disorder, call 800-533-1710. For more information see Cautions.
- When the patient has a more specific phenotype, the following smaller, more targeted disease and phenotype-specific panels, which also include supplemental analysis for specific challenging genomic regions, are recommended instead of this comprehensive panel. See more targeted panels:
  -AECDP / Angioedema and Complement Disorders Gene Panel, Varies
  -AHUGP / Atypical Hemolytic Uremic Syndrome (aHUS)/Thrombotic Microangiopathy (TMA) /Complement 3 Glomerulopathy (C3G) Gene Panel, Varies
  -ALPSG / Autoimmune Lymphoproliferative Syndrome (ALPS) Gene Panel, Varies
  -AUTOG / Autoinflammatory Disorders Gene Panel, Varies
  -BCELL **/** B-Cell and Antibody Deficiency Gene Panel, Varies
  -BMFGP / Inherited Bone Marrow Failure Gene Panel, Varies
  -BTKSG / Bruton Tyrosine Kinase *BTK*, Full Gene Analysis, Varies
  -COMID / Combined Humoral and Cell-Mediated Immunodeficiency Gene Panel, Varies
  -EBLPD / Epstein Barr Virus (EBV) Susceptibility and Lymphoproliferative Disorders Gene Panel, Varies
  -EOIBD / Early Onset Monogenic Inflammatory Bowel Disease (IBD) Gene Panel, Varies

-GNANG / Hereditary Angioedema Focused Gene Panel, Next-Generation Sequencing, Varies
-GNHTC / Hereditary Thrombocytopenia Gene Panel, Next-Generation Sequencing, Varies
-HIESG / Hyper-IgE Syndrome Gene Panel, Varies
-HLHGP / Primary Hemophagocytic Lymphohistiocytosis Gene Panel, Varies
-IMMAU / Inborn Errors of Immunity with Immune Dysregulation and Autoimmunity Gene Panel, Varies
-PHCGD / Phagocytic Disorders and Chronic Granulomatous Disease Gene Panel, Varies
-SCCNP / Severe Congenital and Cyclic Neutropenia Gene Panel, Varies
-SCIDP / Severe Combined Immunodeficiency (SCID) Gene Panel, Varies
-VIRID / Viral Susceptibility, Defects in Intrinsic and Innate Immunity, Gene Panel, Varies

- Phenocopies of inborn errors of immunity exist, some of which are caused by somatic mutations (eg, autoimmune lymphoproliferative syndrome is caused by somatic mutation in *TNFRSF6*), and some of which are caused by autoantibodies (eg, chronic mucocutaneous candidiasis caused by neutralizing autoantibodies against IL-17 or IL-22 cytokines). This test is not designed to detect somatic mutations. If a phenocopy is suspected, contact the laboratory for assistance in test selection.
- Customization of this panel and single gene analysis for any gene present on this panel are available. For more information see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies. To modify this panel via CGPH, use the Inborn Errors of Immunity/Bone Marrow Failure/Telomeropathy/Pulmonary Fibrosis/Very Early Onset IBD/Pancreatitis disease state for step 1 on the Custom Gene Ordering Tool.
- 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.

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.

Deletion/Duplication Analysis:

- 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 mutations 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 the most up to date list of genes included in this test and 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 of tests performed on blood, bone marrow, or saliva specimens may be clinically inaccurate due to the presence of donor DNA. Test orders for blood, bone marrow, or saliva will be canceled by the laboratory if there is a history of an allogeneic hematopoietic stem cell transplant. Similarly, blood, bone marrow, and saliva results may be impacted by presence of active hematologic malignancy or hematologic disorder with clonal proliferation. Call Mayo Clinic Laboratories for instructions for testing a skin biopsy or fibroblast culture for patients who have received a bone marrow transplant or have an active hematologic disorder.

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 healthcare 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 judgment.
- 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.

CPT Code:

81443

Day(s) Performed: Varies

Report Available: 28 to 42 days

Questions

Contact Michelle Raths, Laboratory Resource Coordinator at 800-533-1710.