MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: May 2, 2022
Effective Date: June 2, 2022

Tuberous Sclerosis Gene Panel, Varies

Test ID: TSCP

Useful for:

- Establishing a molecular diagnosis in individuals with features of tuberous sclerosis complex (TSC).
- Identifying pathogenic variants within the *TSC1* and *TSC2* genes known to be associated with TSC, allowing for predictive testing of at-risk family members.
- Prenatal diagnosis in a fetus with ultrasound findings of TSC (eg, cardiac rhabdomyomas)

Reflex Tests:

Test ID	Reporting Name	Available Separately	Always Performed
FIBR	Fibroblast Culture	Yes	No
CRYOB	Cryopreserve for Biochem Studies	No	No
MATCC	Maternal Cell Contamination, B	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No

Methods:

Sequence Capture and Targeted Next-Generation Sequencing followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing.

Reference Values:

An interpretive report will be provided.

Specimen Requirements:

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Submit only 1 of the following specimens:

Specimen Type:	**Whole blood**
Container/Tube:	Lavender top (EDTA) or yellow top (ACD)
Acceptable:	Any anticoagulant
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)/Refrigerated
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:	Refrigerated (preferred)/Ambient
Additional Information:	A separate culture charge will be assessed under FIBR / Fibroblast Culture for Biochemical and Molecular Testing, Tissue. An additional 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type:	**Cultured fibroblasts**
Container/Tube:	T-25 flask
Specimen Volume:	2 Flasks
Collection instructions:	Submit confluent cultured fibroblast cells from a skin biopsy from another laboratory.
Specimen Stability Information:	Ambient (preferred)/Refrigerated (<24hours)
Additional Information:	A separate culture charge will be assessed under FIBR / Fibroblast Culture for Biochemical and Molecular Testing, Tissue. An additional 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type:	**Blood spot**
Supplies:	Card-Blood Spot Collection (Filtration Paper) (T493)
Preferred:	Collection card (Whatman Protein Saver 903 Paper)
Acceptable:	PerkinElmer 226 (formerly Ahlstrom 226) filter paper, or Blood Spot Collection Card (T493)
Specimen Volume:	5 Blood spots
Collection instructions:	1. An alternative blood collection option for a patient 1 year of age or older is a fingerstick. For infants younger than 1 year, a heel stick should be used. See Dried Blood Spot Collection Tutorial for how to collect blood spots via fingerstick.

	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. For collection instructions, see Blood Spot Collection Instructions 2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) 3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) 4. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing.
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:	1 Swab
Collection instructions:	Collect and send specimen per kit instructions.
Additional Information:	Due to lower concentration of DNA yielded from saliva, it is possible that additional specimen may be required to complete testing.
Specimen Stability Information:	Ambient 30 days
Specimen Type:	**Amniotic fluid**
Container/Tube:	Amniotic fluid container
Specimen Volume:	20 mL
Specimen Stability Information:	Refrigerated (preferred)/Ambient
Additional Information:	A separate culture charge will be assessed under CULFB / Fibroblast Culture for Molecular Testing, Chorionic Villi/Products of Conception.
Specimen Type:	**Chorionic villi**
Container/Tube:	15-mL tube containing 15 mL of transport media
Specimen Volume:	20 mg
Specimen Stability Information:	Refrigerated
Additional Information:	A separate culture charge will be assessed under CULFB / Fibroblast Culture for Molecular Testing, Chorionic Villi/Products of Conception.
Specimen Type:	**Confluent cultured cells**
Container/Tube:	T-25 flask
Specimen Volume:	2 flasks

Collection Instructions: Submit confluent cultured cells from another laboratory.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Note:

Due to the complexity of prenatal testing, consultation with the laboratory is required for all prenatal testing. Prenatal specimens can be sent Monday through Thursday and **must be received by 5 p.m. CT on Friday** in order to be processed appropriately. All prenatal specimens must be accompanied by a maternal blood specimen. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Stability Information:

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

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 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 heterologous 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:

- At this time, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages health care providers 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 findings or secondary findings may implicate another predisposition or presence of active disease. These findings will be carefully reviewed to determine whether or not they will be reported.

CPT Code:

81406
81407
81265-Maternal cell contamination (if appropriate)
88233-Tissue culture, skin, solid tissue biopsy (if appropriate)
88235-Amniotic Fluid culture (if appropriate)
88240-Cryopreservation (if appropriate)

Day(s) Performed: Varies

Report Available: 28 to 42 days

Questions

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