Overview

Useful For
A comprehensive evaluation of the GATA2 gene in patients with clinical or immunological symptoms suggestive of GATA-binding protein 2 (GATA2) deficiency

Screening family members of patients with confirmed GATA2 deficiency

Genetics Test Information
This test includes next-generation sequencing and supplemental Sanger sequencing.

Identification of a pathogenic variant may assist with prognosis, clinical management, familial screening, and genetic counseling.

Highlights
This test may aid in the diagnosis of GATA2 deficiency.

Reflex Tests

<table>
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<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
<tr>
<td>FIBR</td>
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<tr>
<td>CRYOB</td>
<td>Cryopreserve for Biochem Studies</td>
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</table>

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

Special Instructions
- Informed Consent for Genetic Testing
- GATA2 Gene Sequencing Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name
Custom Sequence Capture and Targeted Next-Generation Sequencing

NY State Available
Yes

Specimen

Specimen Type
Varies

Advisory Information
Targeted testing for familial variants (also called site-specific or known mutation testing) is available for this gene.
See:

- **KVAR1 / Known Variant Analysis-1 Variant, Varies**
- **KVAR2 / Known Variant Analysis-2 Variants, Varies**
- **KVAR3 / Known Variant Analysis-3+ Variants, Varies**

Call 800-533-1710 to confirm the appropriate test for targeted testing.

**Necessary Information**

1. **GATA2 Gene Sequencing Patient Information** is **required**. See Special Instructions Testing may proceed without the Patient Information however it aids in providing a more thorough interpretation. Ordering physicians are strongly encouraged to fill out the form.

2. Include physician name and phone number with the specimen.

**Specimen Required**

Submit only 1 of the following specimens:

**Preferred:**

**Specimen Type:** Whole blood

**Container/Tube:** Lavender top (EDTA)

**Specimen Volume:** 3 mL

**Collection Instructions:**

1. Invert several times to mix blood.
2. Send specimen in original tube.

**Specimen Stability Information:** Ambient (preferred) 4 days/Refrigerated 14 days

**Specimen Type:** Peripheral blood mononuclear cells (PBMCs)

**Container/Tube:** Cell pellet

**Collection Instructions:** Send as a suspension in freezing medium or cell pellet frozen on dry ice.

**Specimen Stability Information:** Frozen

**Specimen Type:** Cultured fibroblasts

**Container/Tube:** T-75 or T-25 flask

**Specimen Volume:** 1 Full T-75 or 2 full T-25 flasks

**Additional Information:** Indicate the tests to be performed on the fibroblast culture cells.
**Specimen Stability Information:** Ambient (preferred)/Refrigerated <24 hours

**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. Tubes of culture media can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin).

**Specimen Volume:** 4-mm punch

**Additional Information:** A separate culture charge will be assessed under FIBR / Fibroblast Culture. An additional 4 weeks is required to culture fibroblasts before genetic testing can occur.

**Specimen Stability Information:** Refrigerated (preferred)/Ambient

**Specimen Type:** DNA

**Container/Tube:** 2 mL screw top tube

**Specimen Volume:** 100 mcL (microliters)

**Collection Instructions:**

1. The preferred volume is 100 mcL at a concentration of 250 ng/mcL
2. Include concentration and volume on tube.

**Specimen Stability Information:** Frozen (preferred)/Ambient/Refrigerated

**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 Special Instructions:

- [Informed Consent for Genetic Testing](#) (T576)
- [Informed Consent for Genetic Testing-Spanish](#) (T826)

**Specimen Minimum Volume**

Whole blood: 1 mL

**Reject Due To**

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

**Specimen Stability Information**

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<tr>
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<th>Temperature</th>
<th>Time</th>
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<tbody>
<tr>
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Clinical and Interpretive

Clinical Information

GATA-binding protein 2 (GATA2) deficiency is emerging as the second most common primary immunodeficiency disorder (PIDD) or inborn error of immunity in adults, after common variable immunodeficiency (CVID). There is a spectrum of clinical presentations associated with GATA2 deficiency, including severe viral infections (e.g., human papillomavirus [HPV]), warts, fungal infections, bacterial infections (e.g., atypical mycobacterial infections such as nontuberculous mycobacterial infections [NTM] or mycobacterium avium complex [MAC]), myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), and Emberger syndrome (primary lymphedema with MDS). Other clinical phenotypes of GATA2 deficiency may include aplastic anemia, pulmonary alveolar proteinosis (PAP), sensorineural hearing loss, neutropenia, and congenital lymphedema without MDS at diagnosis. Immunological phenotypes include dendritic cell, monocyte, CD4+ T cell, B and natural killer (NK) cell deficiencies. Also, the loss of a specific NK-cell subset, CD56 bright NK cells, has been reported in these patients. GATA2 deficiency was first described in 2011 as being associated with either MonoMAC (monocytopenia and mycobacterial infection) syndrome or DCML deficiency (dendritic cell, monocyte, B and NK cell lymphocyte deficiency).

GATA2 is a zinc finger transcription factor, involved in the generation and function of hematopoietic stem cell progenitors and, therefore, affects several of the subsequent cell lineages.

GATA2 deficiency is a disease of haploinsufficiency, and most germline variants appear to arise de novo (spontaneously) but are then transmitted in an autosomal dominant manner. Standard genotype-phenotype correlations are difficult to make, as there is considerable clinical heterogeneity and the age of presentation varies from early childhood to late in adult life. Additionally, there may be a role for environmental factors triggering certain infectious manifestations. There has been incomplete penetrance (not every individual with a variant has a clinical phenotype) observed with GATA2 deficiency as well as variable expressivity (different clinical presentations for the same genetic variant). The genetic alterations observed in GATA2 are heterogeneous, and include missense variants, nonsense variants, and variants in the regulatory region of intron 5, in-frame deletions involving the C-terminal zinc finger domain, frameshift variants, and large deletions. The latter are associated with null alleles, while regulatory variants have been observed in the enhancer region of intron 5.

Somatic variants in ASXL1 have been reported in GATA2 deficiency patients and have been postulated to be associated with transformation to myeloid leukemia. The definitive treatment for GATA2 deficiency is hematopoietic cell transplantation (HCT). Additionally, systemic use of interferon-alpha may be helpful in patients with NK cell deficiency who have recurrent or severe HPV or herpes virus infections. Also, prophylactic antibiotics may be needed or mandated in the nontransplanted patient. The pulmonary alveolar proteinosis observed in GATA2 deficiency is in the context of negative results for anti-GM-CSF autoantibodies has been shown to improve after HCT and suggests correction of alveolar macrophage function.

Early genetic diagnosis of GATA2 deficiency is critical in determining strategies for managing the disease considering the broad clinical spectrum. Genetic diagnosis by confirmation of a pathogenic GATA2 variant may also aid in family counseling and screening.

Reference Values

An interpretive report will be provided.

Interpretation

Evaluation and categorization of variants is performed using the most recent published American College of Medical Genetics and Genomics (ACMG) recommendations. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.
Unless reported or predicted to cause disease, alterations found deep in the intron or alterations that do not result in an amino acid substitution are not reported.

**Cautions**

The nomenclature of variants identified in the GATA2 gene may vary depending on the reference transcript used. When comparing the result to published literature this fact should be kept in mind.

**CLINICAL CORRELATIONS:**

Some individuals who have involvement of one or more of the genes on the panel may have a variant that is not identified by the methods performed (eg, promoter variants, deep intronic variants). The absence of a variant, therefore, does not eliminate the possibility of disease. Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

For predictive testing of asymptomatic individuals, it is often useful to first test an affected family member. Identification of a pathogenic variant in an affected individual allows for more informative testing of at-risk individuals.

**TECHNICAL LIMITATIONS:**

Next-generation sequencing may not detect all types of genetic variants. Additionally, rare variants may be present that could lead to false-negative or false-positive results. If results do not match clinical findings, consider alternative methods for analyzing these genes, such as Sanger sequencing or large deletion/duplication analysis.

If the patient has had an allogeneic blood or bone marrow transplant or a recent (ie, <6 weeks from time of sample collection) heterologous blood transfusion, results may be inaccurate due to the presence of donor DNA.

**EVALUATION TOOLS:**

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 predictions made by these tools may change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.

Reclassification of Variants-Policy:

At this time, it is not standard practice for the laboratory to systematically review likely pathogenic variants or variants of uncertain significance that are detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time. Consultation with a healthcare provider, or team of healthcare providers, with expertise in genetics and primary immunodeficiencies, is recommended for interpretation of this result.

A list of benign and likely benign variants detected is available from the lab upon request.

**Clinical Reference**


2. Dickinson RE, Griffin H, Bigley V, et al: Exome sequencing identifies GATA-2 mutation as the cause of dendritic
cells, monocyte, B and NK lymphoid deficiency. Blood 2011;118:2656-2658


### Performance

**Method Description**

Next-generation sequencing (NGS) is performed using an Illumina instrument with paired-end reads. The DNA is prepared for NGS using a custom Agilent SureSelect Target Enrichment System. Data is analyzed with a bioinformatics software pipeline. (Unpublished Mayo method)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Varies

**Analytic Time**

2 weeks

**Maximum Laboratory Time**

4 weeks

**Specimen Retention Time**

Extracted DNA: 2 months

**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**

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