TEST ID: GATA2
GATA-BINDING PROTEIN 2 (GATA2) COMPREHENSIVE GENE SEQUENCING

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 to evaluate for the genes listed on the panel.

Targeted testing for familial variants (also called site-specific or known mutation testing) is available for all genes on this panel. See KVAR1 / Known Variant Analysis-1 Variant; KVAR2 / Known Variant Analysis-2 Variants; or KVAR3 / Known Variant Analysis-3+ Variants. Contact Mayo Medical Laboratories to confirm the appropriate test code for targeted testing if testing for a gene not included on this panel, or if testing for more than 5 variants is needed.

CLINICAL INFORMATION
GATA-binding protein 2 (GATA2) deficiency is emerging as the second most common primary immunodeficiency in adults, after common variable immunodeficiency (CVID). There is a spectrum of clinical presentations associated with GATA2 deficiency, including severe viral infections (eg, human papillomavirus [HPV] warts), fungal infections, bacterial infections (eg, 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).

REFERENCE VALUES
An interpretive report will be provided.

ANALYTIC TIME
3 weeks

CONTENT AND VALUES SUBJECT TO CHANGE. SEE THE MAYO MEDICAL LABORATORIES TEST CATALOG FOR CURRENT INFORMATION.
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 mutation has a clinical phenotype) observed with GATA2 deficiency as well as variable expressivity (different clinical presentations for the same genetic mutation). 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 mutations variants, and large deletions. The latter are associated with null alleles, while regulatory mutations variants have been observed in the enhancer region of intron 5.

Somatic mutations variants in ASXL1 have been reported in GATA2 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.

INTERPRETATION

Evaluation and categorization of variants is performed using the most recent published American College of Medical Genetics and Genomics 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.

A list of common (presumed benign) GATA2 variants identified for this patient are available from the lab upon request.