MACHAON DIAGNOSTICS

TEST SUMMARY: SOMATIC INBORN ERRORS OF IMMUNITY GENETIC PANEL

In collaboration with key opinion leaders, we designed a somatic NGS genetic panel to fill a clinical testing gap. This test 1) sequences 69 genes at ~5,000x mean read depth, 2) with 98.5% sensitivity for variant allele frequency (VAF) of 2% or greater and 100% sensitivity for VAF of 3% or greater, and 3) has a **routine turnaround time of less than 1 week**. Many patients with primary immunodeficiency or genetic errors of immunity remain undiagnosed after standard germline next-generation sequencing (NGS), including whole-exome (WES) and whole-genome (WGS) sequencing. Some of these cases will be due to somatic variants in the inborn errors of immunity (IEI) genes, increasingly recognized as an important cause of immunodeficiency (1). However, detecting somatic variants is challenging; WES/WGS does not sequence deeply enough to detect variants with low variant allele frequencies. Furthermore, the relevant immunity genes mostly do not overlap with existing cancer genetic panels. Finally, the turnaround time is generally several weeks or more and these patients are often acutely ill.

Pathogenic somatic variants in an IEI gene may cause the same disease as pathogenic germline variants, though the clinical presentation may be more variable in somatic cases. For example, as many as 20% of autoimmune lymphoproliferative disorder (ALPS) patients may have pathogenic somatic variants in the FAS gene (2). Similarly, somatic NLRP3 mutations were identified in ~70% of patients with mutation-negative NOMID/CINCA syndrome (3). Additionally, a recent and exciting finding is that some genes with no known role in immunodeficiency can cause immune disease when somatically mutated--UBA1 (causing VEXAS) and TLR8 are examples of this striking phenomenon (4, 5). VEXAS is likely the most common somatic immune disease and was only “discovered” in 2020.

Please visit MachaonDiagnostics.com for further information.

TURNAROUND TIMES
Routine TAT: <1 week
STAT TAT: Please Inquire

SPECIMEN REQUIRMENTS
3mL EDTA Whole Blood

STABILITY
Room Temp: 1 month
Refrigerated: 1 month

CPT CODES
81443

METHODOLOGY
NGS

ASSOCIATED TESTING
Soluble IL-2R alpha (CD25) Level
CXCL9 Level
Cytokine Release Syndrome (12-test) Panel
IL-18 Level
HLH Extended Genetic Panel 3.0

References: 1. Aluri J and Cooper M. (2023) Semin Immunol.67:101761. 2. Lopez-Nevado M et al. (2021) Front Immunol.12:656356. 3. Tanaka N et al. (2011) Arthritis Rheum.63(11):3625–32. 4. Beck et al (2020) N Engl J Med. 2020;383(27):2628–38. 5. Aluri et al. (2021) Blood. 2021;137(18):2450–62.

V:28APR2025

WHY CHOOSE US?
- Fastest turnaround in the US
- Clinical consultation
- Critical Results called to physician

ABOUT US:
Machaon Diagnostics is a clinical reference laboratory, specializing in coagulation, platelets, complement, genetics and rare disease.

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