Severe Combined Immunodeficiency (SCID) B+: Sequencing Panel

Test Code: MM320
Turnaround time: 6 weeks
CPT Codes: 81405 x1, 81479 x1

Condition Description

Severe combined immunodeficiency (SCID) represents a group of rare, sometimes fatal, congenital disorders characterized by little or no immune response. The defining feature of SCID, commonly known as "bubble boy" disease, is a defect in the specialized white blood cells (B- and T-lymphocytes) that defend us from infection by viruses, bacteria, and fungi. Without a functional immune system, SCID patients are susceptible to recurrent infections such as pneumonia, meningitis, and chicken pox, and can die before the first year of life. SCID occurs with an estimated incidence of 1 in 75,000 births and is considered a pediatric emergency because of the potentially lethal outcome of recurrent or persistent infections suffered by SCID patients. Several monogenic causes with different modes of inheritance have been identified for SCID. Depending on the underlying genetic defect, different primary phenotypes associated with SCID have been characterized. Genetic testing for SCID can allow distinction between the various forms of this syndrome. Knowledge of the defective gene may have implications for treatment and prognosis. This knowledge may also enable more effective genetic counseling, in addition to facilitating identification of asymptomatic carriers and timely initiation of treatment in affected descendants of carriers.

T?B+ SCID is the most common type of SCID. It is most often caused by X-linked recessive mutations in \( \text{IL2RG} \), which encodes the \( \beta \) chain \((\beta c)\) common to several cytokine receptors such as IL-2R, IL-4R, IL-7R, IL-9R, IL-15R, and IL-21R. T?B+ SCID has also been associated with autosomal recessive mutations in other autosomal genes. Mutations in these genes lead to defective signaling through the \( \beta c \) receptors, resulting in an absence of both T cells and NK cells. B cells are present at normal levels, but have impaired function.

In addition to T?B? SCID sequencing panel (see related tests), EGL Genetics offers this complementary panel that sequences the genes associated with T?B+ SCID through next generation sequencing technology. This technology is an excellent tool for obtaining gene sequences rapidly and accurately since it allows deep coverage of the genome through multiple independent sequence reads.

References:
- OMIM.
- GeneReviews.

Genes

CD247, CD3D, CD3E, FOXXN1, IL2RG, IL7R, JAK3, ORAI1, PNP, PTPRC, STAT5B, STIM1, TBX1, ZAP70

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Severe Combined Immunodeficiency (SCID) B+.

Methodology

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

Next Generation Sequencing: Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood

Specimen Requirements:
In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 60 ug

Isolation using the Qiagen\textsuperscript{TM} Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Severe Combined Immunodeficiency (SCID) B-: Sequencing Panel
- Severe Combined Immunodeficiency (SCID) B+: Deletion/Duplication Panel