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

**Test Code:** MM450
**Turnaround time:** 6 weeks
**CPT Codes:** 81405 x1, 81479 x4

### 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 IL2RG, which encodes the ? chain (?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 ?c receptors, resulting in an absence of both T cells and NK cells. B cells are present at normal levels, but have impaired function.

**T?B? SCID** is caused by autosomal recessive mutations in several genes, some of which are necessary for antigen receptor rearrangement, RAG1, RAG2, and DCLRE1C (ARTEMIS). Defects in these genes lead to impaired development of both B and T cells, while NK-cell development is normal. If the patient’s phenotype is more well-defined as either SCID B+ or SCID B-, phenotype-specific panels are available.

### References:

- OMIM.
- GeneReviews.

### Genes

ADA, CD247, CD3D, CD3E, DCLRE1C, FOXN1, IL2RG, IL7R, JAK3, LIG4, NHEJ1, ORAI1, PNP, PTPRC, RAG2, RAG1, RAG2, STAT5B, STIM1, TBX1, ZAP70

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Severe Combined Immunodeficiency (SCID) B+.
- 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: DNA, Isolated**

**Specimen Requirements:**
- Microtainer
- 8µg
- Isolation using the Perkin Elmer™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

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

**Type: Saliva**

**Specimen Requirements:**
- Orangene™ Saliva Collection Kit
- Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**
- EDTA (Purple Top)
- Infants and Young Children (2 years of age to 10 years old): 3-5 ml
- Older Children & Adults: 5-10 ml
- Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

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