SCID Gene Sequencing Panel

Genes Tested:

ADA	*AK2*	*ATM*	*BCL11B*
CD247	*CD3D*	*CD3E*	*CDH17*
CHD7	*CIITA*	*CORO1A*	*DCLRE1C*
DOCK8	*FOXN1*	*IL2RG*	*IL7R*
JAK3	*LAT*	*LCK*	*LIG4*
MSN	*NHEJ1*	*ORAI1*	*PNP*
PRKDC	*PTPRC*	*RAC2*	*RAG1*
RAG2	*RFX5*	*RFXANK*	*RFXAP*
RMRP	*STAT5B*	*STIM1*	*STK4*
TAP1	*TAP2*	*TBX1*	*TTC7A*
ZAP70			

Disorder:

This panel detects genetic causes of Severe Combined Immune Deficiency (SCID) and selected causes of Combined Immune Deficiency (CID) and CID with associated or syndromic features.

Severe Combined Immunodeficiency is a genetically heterogeneous disorder of T lymphocyte development and adaptive immunity. The estimated prevalence of SCID is 1 in 50,000 births with a higher prevalence in males. Symptoms usually begin between three and six months of age and include severe infections, chronic diarrhea, and failure to thrive. Laboratory screening tests consistent with the diagnosis of SCID include abnormal mitogen stimulation, abnormal lymphocyte subsets, abnormal T cell phenotyping including abnormally low or absent naïve T cell populations, and abnormal TREC assay. Depending on the type of SCID, B cell and NK cell populations may also be abnormal. SCID is considered a pediatric emergency and if untreated, is often fatal by six to twelve months of age. However, many patients have a favorable prognosis with early diagnosis and bone marrow stem cell transplantation.

There can be overlap between the clinical manifestations of SCID and some CID disorders. Some patients with CID or syndromic CID disorders can also be detected by SCID newborn screening. For these reasons, selected genes that cause CID or syndromic CID are included in this panel.

Because maternal engraftment has been reported in 40% of patients with SCID (Muller et al. 2001), this may reduce the sensitivity and specificity of genetic testing. Evaluations for maternal engraftment may need to be considered in some patients.

Indications:

Confirmation of diagnosis in a patient with suspected:

- SCID diagnosis and/or abnormal newborn screening for SCID
- Omenn syndrome
- Microcephaly and immune deficiency
- Velocardiofacial syndrome in the absence of a 22q11.2 chromosome deletion
- Cartilage hair hypoplasia-anauxetic dysplasia spectrum
- T cell deficiency of unknown etiology.

Specimen:

At least 3 mLs whole blood in a lavender top (EDTA) tube or saliva in an Oragene saliva kit. Please call 513-636-4474 for a free saliva collection kit.

Note: For post-transplant patients, we accept pre-transplant samples or post-transplant skin fibroblasts ONLY (blood, saliva, and cytobrushes are not accepted). Culturing of skin fibroblasts is done at an additional charge.

Testing Methodology:

SCID panel by NGS: This test is performed by enrichment of the coding exons, flanking intronic and untranslated

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changing the outcome together

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regions (5' and 3'), as well as known pathogenic variants (HGMD 2018.4) in the promoter and deep intronic regions of the genes specified above using oligonucleotide probe hybridization followed by next-generation sequencing with >50X coverage at every target base. All pathogenic and likely pathogenic variants, as well as variants of unknown (indeterminate) significance, as determined bioinformatically, are confirmed by Sanger sequencing. Regions with <50X will be filled in by Sanger sequencing. A detailed non-coding variant list is available upon request.

Gene Specific Sequencing: PCR-based sequencing of the entire coding region and intron/exon boundaries of the specific gene.

Variant Specific Analysis: Sanger sequencing following PCR amplification of the targeted variant(s) of the specified gene.

Test Sensitivity:

Analytical Sensitivity: The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed.

Limitations: Variants in regulatory regions and non-reported variants in untranslated regions may not be detected by this test. Large deletions/ duplications, large insertions and other complex genetic events will not be identified using sequencing methodology.

Note: Single gene sequencing and targeted variant analysis is also available for all genes on the SCID panel. Deletion/duplication is available for many of the genes on this panel. For further details, visit: www.cincinnatichildrens.org/deldup.

Turn-Around Time:

- SCID Panel: up to 6 weeks
- Single gene sequencing: up to 28 days

CPT Codes:

- **Severe Combined Immunodeficiency Panel by NGS:** 81443
- **Single gene sequencing, targeted variant analysis, and deletion/duplication:** call for information.

Please call 1-866-450-4198 for current pricing, insurance preauthorization or with any billing questions.

Shipping Instructions:

Please enclose **test requisition** with sample.
All information must be completed before sample can be processed.

Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

Results:

Results will be reported to the referring physician or health care provider as specified on the requisition form.

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