

Using Genetic Testing to Diagnose SCID (including SCID/OS and Zap-70 deficiency)

Indications:

- Severe, persistent, or recurrent infections, often with low-virulence opportunistic organisms, typically leading to sinopulmonary problems, diarrhea, thrush and/or failure to thrive
- T-cell lymphopenia with exclusion of AIDS, if at risk
- Family history of SCID or of death in infancy due to infection

Benefits:

- Genetic testing can confirm a diagnosis of SCID in the proband and allow early diagnosis in family members.
- Early diagnosis of SCID and related SCID subtypes is critical, since survival rate is highest if bone marrow transplantation is performed before serious infections develop.¹

Background:

- SCID, or Severe Combined Immunodeficiency Syndrome, is a fatal disorder characterized by absence of adaptive immunity due to severe T-cell lymphopenia. While T-cell lymphopenia is common to all forms of SCID, levels of B and natural killer (NK) cells may vary depending on the underlying genetic defect.
- Several monogenic causes with different modes of inheritance have been identified for SCID and SCID/OS. The most common form of SCID, *IL2RG*-related XSCID, is an X-linked recessive disorder and accounts for ~46% of all SCID cases. All other known causes of SCID are inherited in an autosomal recessive manner.¹
- Omenn Syndrome (OS) and Zap-70 deficiency are distinct SCID subtypes distinguished by the presence of non-functional T cells.
 - OS results from a leaky mutation in one of the genes that causes classical SCID that allows development of some T cells. In addition to the presence of oligoclonal T cells, symptoms of OS include elevated levels of IgE, eosinophilia, and erythema, lymphadenopathy, and hepatosplenomegaly.²
 - Zap-70 deficiency is clinically very similar to classic SCID, but is distinguished by the selective absence of CD8⁺ T cells in the presence of normal or elevated CD4⁺ T cells levels.³
- Both SCID and its subtypes are considered pediatric emergencies because of the potentially lethal outcome of recurrent or persistent infections suffered by these patients. However, bone-marrow transplantation offers the prospect of a cure.

References: 1. Buckley RH (2004) *Annu Rev Immunol* 22:625-55. 2. Santagata et al (2000) *Immunol Rev* 178:64-74. 3. Elder ME (1998) *Semin Hematol* 35:310-320. 4. Müller et al (2001) *Blood* 98: 1847-1851. 5. Aureli et al (2006) *Pediatr Transplant* 10: 744-746.

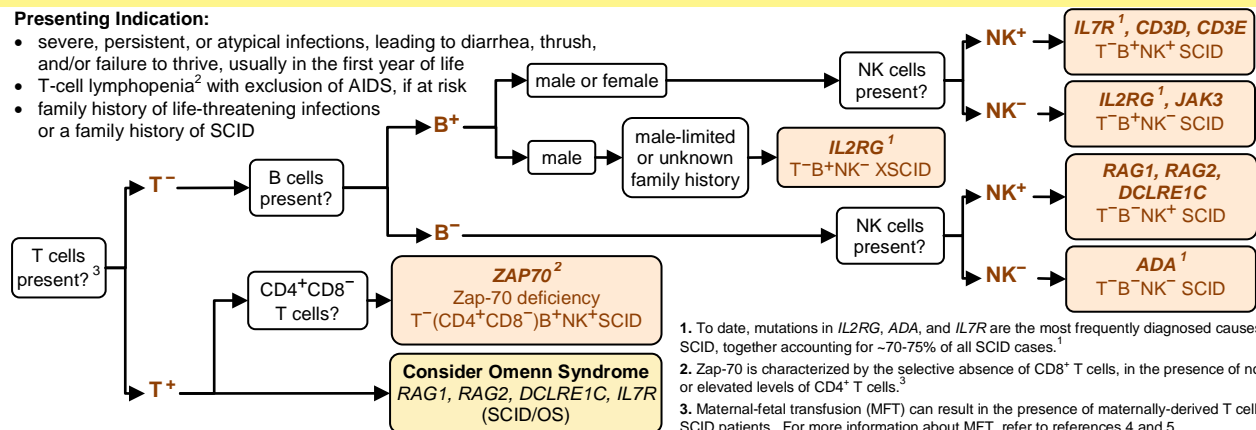
Ordering Information: Please see other side.

Ordering Information for Severe Combined Immunodeficiency Syndrome (SCID) Testing

Guidelines for Test Selection

Presenting Indication:

- severe, persistent, or atypical infections, leading to diarrhea, thrush, and/or failure to thrive, usually in the first year of life
- T-cell lymphopenia² with exclusion of AIDS, if at risk
- family history of life-threatening infections or a family history of SCID



1. To date, mutations in *IL2RG*, *ADA*, and *IL7R* are the most frequently diagnosed causes of SCID, together accounting for ~70-75% of all SCID cases.¹

2. Zap-70 is characterized by the selective absence of CD8⁺ T cells, in the presence of normal or elevated levels of CD4⁺ T cells.³

3. Maternal-fetal transfusion (MFT) can result in the presence of maternally-derived T cells in SCID patients. For more information about MFT, refer to references 4 and 5.

Ordering Information for Single Gene Tests

| Indicated Test (Indication) | Test Code |
|---|-----------|
| <i>IL2RG</i> (T-B+NK- SCID, XSCID) | 100401 |
| <i>JAK3</i> (T-B+NK- SCID) | 100402 |
| <i>RAG1</i> (T-B-NK+ SCID or SCID/OS) | 100403 |
| <i>RAG2</i> (T-B-NK+ SCID or SCID/OS) | 100404 |
| <i>DCLRE1C</i> (<i>ARTEMIS</i>) [T-B-NK+ SCID (RS-SCID) or SCID/OS] | 100410 |
| <i>ADA</i> (T-B-NK-SCID) | 100405 |
| <i>IL7R</i> (T-B+NK+ SCID or SCID/OS) | 100406 |
| <i>CD3D</i> (T-B+NK+ SCID) | 100407 |
| <i>CD3E</i> (T-B+NK+ SCID) | 100408 |
| <i>ZAP70</i> [Zap-70 deficiency; T+(CD4+CD8-)B+NK+ SCID] | 100409 |

Ordering Information for Multi-Gene Panels*

| | |
|---|--------|
| <i>IL2RG, JAK3</i> (T-B+NK-SCID) | 100499 |
| <i>RAG1, RAG2</i> (T-B-NK+ SCID or SCID/OS) | 100498 |
| <i>RAG1, RAG2, DCLRE1C</i> (T-B-NK+ SCID or SCID/OS) | 100492 |
| <i>IL7R, CD3D, CD3E</i> (T-B+NK+ SCID) | 100496 |
| <i>IL2RG, ADA, IL7R</i> (SCID) | 100495 |
| <i>IL2RG, JAK3, RAG1, RAG2, DCLRE1C, ADA, IL7R, CD3D, CD3E</i> (SCID) | 100493 |

*For multi-gene panels, a summary report will be issued in addition to an abbreviated report for each individual gene.

Family Testing (single amplicon)

Family Testing is available for all genes. Please contact Client Services at 1-866-647-0735 for requirements.

Test Methodology

- Amplification by polymerase chain reaction (PCR); sequencing of entire protein-coding region

NOTE: Specimens must be accompanied by a completed consent form. In the case of family tests (ie, known mutations), a copy of the result of the first patient tested in the family (the index case) must be submitted unless that test was performed at Correlagen. Other family members are subsequently tested for the specific mutation found in the first patient tested.

For test information, sample requirements, or to request a sample shipping kit, please contact Client Services at 1-866-647-0735 or visit us on the web at www.correlagen.com.