Cincinnati Children's
Heart Institute

Heart Institute Diagnostic Lab
CAP#: 1667801
CLIA#: 36D0656333
Phone: (513) 803-1751
Fax: (513) 803-1748
Email: HeartDx@cchmc.org

SKI– Shprintzen-Goldberg Syndrome

The *SKI* gene codes for a protein which is involved in the signaling pathway for transforming growth factor beta (TGF-β). This pathway helps regulate cell growth, proliferation, differentiation, motility, and apoptosis. The TGF-β pathway is also involved in activating the SMAD complex. Mutations in the *SKI* gene block the SMAD complex from entering the nucleus, thus targeted gene activation does not occur. Mutations in the *SKI* gene (all in exon 1) have been reported to be associated with Shprintzen-Goldberg syndrome (SGS). SGS is characterized by distinctive facial features, skeletal abnormalities, and intellectual disability. Cardiovascular findings associated with SGS include mitral valve prolapse and aortic root dilation. Mutations in the *SKI* gene are inherited in an autosomal dominant manner. *SKI* is a 7 exon gene located at 1p36.33.

Indication

SKI gene testing is utilized to confirm a diagnosis of SGS in patients with clinically evident disease.

Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship To:

Cincinnati Children's
Hospital Medical Center
Attn: Heart Institute Diagnostic Lab
240 Albert Sabin Way,
Room S4.381
Cincinnati, OH 45229-3039

Methodology:

All 7 exons of the *SKI* gene, as well as the exon/intron boundaries and portion of untranslated regions of the gene are amplified by PCR. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an *ABI PRISM® 3730 DNA Analyzer*. Sequence variants different from National Center for Biotechnology Information GenBank references are further evaluated for genetic significance. If a mutation is identified, a known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 99% of the mutations in exons 1-7 of *SKI* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

References:

1. Carmignac V, Thevenon J, Ades L, Callewaert B, Julia S, Thauvin-Robinet C, Gueneau L, Courcet JB, Lopez E, Holman K, Renard M, Plauchu H, Plessis G, De Backer J, Child A, Arno G, Duplomb L, Callier P, Aral B, Vabres P, Gigot N, Arbustini E, Grasso M, Robinson PN, Goizet C, Baumann C, Di Rocco M, Sanchez Del Pozo J, Huet F, Jondeau G, Collod-Beroud G, Beroud C, Amiel J, Cormier-Daire V, Riviere JB, Boileau C, De Paepe A, Faivre L. In-frame mutations in exon 1 of *SKI* cause dominant Shprintzen-Goldberg syndrome. *American Journal of Human Genetics*. 2012;91:950-957.

2. Doyle AJ, Doyle JJ, Bessling SL, Maragh S, Lindsay ME, Schepers D, Gillis E, Mortier G, Homfray T, Sauls K, Norris RA, Huso ND, Leahy D, Mohr DW, Caulfield MJ, Scott AF, Destree A, Hennekam RC, Arn PH, Curry CJ, Van Laer L, McCallion AS, Loeys BL, Dietz HC. Mutations in the TGF-Beta repressor *SKI* cause Shprintzen-Goldberg syndrome with aortic aneurysm. *Nature Genetics*. 2012;44:1249-1254.

Specimen:

Peripheral blood in EDTA tube
Adult: 3-5mL
Child: 3-5mL
Infant: 1-3mL
For other specimen types, please contact Amy Shikany at 513-803-3317

Turnaround Time:

Full Mutation Analysis 2-4 weeks
Known Mutation Analysis 1-2 weeks

CPT Codes:

Full Gene Sequencing	81479
Additional Family Members	81403