SBDS Gene Analysis in Shwachman-Diamond Syndrome (SDS)

DISORDER ALSO KNOWN AS

Shwachman-Bodian Syndrome, Shwachman-Bodian-Diamond Syndrome, pancreatic insufficiency and bone marrow dysfunction, congenital lipomatosis of the pancreas

CLINICAL FEATURES

Shwachman-Diamond syndrome (SDS) is an autosomal recessive disorder that includes pancreatic exocrine insufficiency and hematological abnormalities as consistent features. Other common manifestations include skeletal abnormalities, short stature, liver dysfunction and increased risk of malignancy. Serious infections and acute myeloid leukemia are major causes of mortality and morbidity. The syndrome is caused by the partial, not complete, deficiency of the novel protein encoded by the SBDS gene, thought to be involved in RNA metabolism (PMID: 12496757).

INHERITANCE PATTERN/GENETICS

Autosomal recessive

TEST METHODS

Using genomic DNA from the submitted specimen, the coding regions and splice junctions of the requested gene are PCR amplified and capillary sequencing is performed. Bi-directional sequence is assembled, aligned to reference gene sequences based on human genome build GRCh37/UCSC hg19, and analyzed for sequence variants. Capillary sequencing or another appropriate method is used to confirm all potentially pathogenic variants. If present, apparently homozygous variants are confirmed using alternate primer pairs to significantly reduce the possibility of allele drop-out. Sequence alterations are reported according to the Human Genome Variation Society (HGVS) nomenclature guidelines. Reportable variants include pathogenic variants, likely pathogenic variants and variants of uncertain significance. Likely benign and benign variants are not routinely reported but are available upon request. The methods used by GeneDx are expected to be greater than 99% sensitive in detecting variants identifiable by sequencing.

TEST SENSITIVITY

In most studies, 75-89% of patients with Shwachman-Diamond Syndrome have at least one SBDS gene variant detected, and usually two (PMID: 12496757, 15769891). Detection of one variant is suggestive of the diagnosis, but not definitive. Detection of two variants is typically definitive but because two variants can sometimes occur in cis (on the same allele) in this gene, follow-up parental testing may be necessary. Note that this test does not evaluate, and therefore would not detect, large deletions or duplications of the SBDS gene.