

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 metabolism¹.

INHERITANCE PATTERN/GENETICS

Autosomal recessive

TEST METHODS

Analysis is performed by bi-directional sequencing of the coding regions and splice sites of exons 1-5 of the SBDS gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

TEST SENSITIVITY

In most studies, 75-89% of patients with Shwachman-Diamond Syndrome have at least one SBDS gene variant detected, and usually two^{1,2}. No other gene is known to cause this syndrome. 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.

REFERENCES:

1. Boocock, G., et al, Mutations in SBDS are associated with Shwachman-Diamond syndrome, 2003, Nature Genetics 33:97-101.
2. Kuijpers, T, et al., Hematologic abnormalities in Shwachman-Diamond syndrome: lack of genotype-phenotype relationship, 2005, Blood 106:356-361.
3. Costa E., et al, Identification of a novel AluSx-mediated deletion of exon 3 in the SBDS gene in a patient with Shwachman-Diamond syndrome, 2003, Blood Cells Mol Dis 29:96.