SickKids | Genome Diagnostics

# Shwachman-Diamond Syndrome

Shwachman-Diamond Syndrome (SDS) affects many organs in the body and the symptoms may vary between individuals. The primary features of SDS include: bone marrow dysfunction (leading to inadequate production of some types of blood cells), pancreatic defects (leading to difficulties in digesting food), skeletal abnormalities, and short stature. Other secondary features may affect some but not all people affected with SDS. People with SDS are at risk for serious, sometimes fatal, complications such as severe infections, bone marrow failure and acute myelogenous leukemia.

## Genetics

The *SBDS* gene, located on chromosome 7 (7q11), has been found to be the causative gene for SDS. A pseudogene, *SBDS-P,* exists within a distally duplicated region and shares 97% nucleotide sequence identity with the *SBDS* gene. The majority of SDS patients have mutations resulting from gene conversion between the *SBDS* and *SBDS-P* genes. Two common conversion mutations account for ~80% of all SDS disease alleles.

SDS is an autosomal recessive disorder and the disease is present when a child receives two copies of a defective *SBDS* gene, one from each parent. Any person with one copy of the defective *SBDS* gene is a SDS carrier. Carriers do not have, and will never develop, SDS. However, if two carriers wish to have children, there is a 25% chance that their baby will be born with SDS. There is a 75% chance that their baby will not have SDS.

## Who Should Be Tested?

- Individuals clinically suspected of being affected with SDS
- Individuals with a family history of SDS, to determine carrier status
- Pregnancies at risk due to a family history of SDS

## Test Methods

- Direct sequencing to test proband samples for two recurrent mutations in exon 2 of the *SBDS* gene: c.183_184delinsCT (p.Lys62X) and c.258+2T>C (p.Cys84Tyrfs).
- Direct sequencing of the remaining exons may be required to identify rare mutations in the *SBDS* gene.

## Potential Outcomes & Interpretation of Test Results

| Reason for referral | *SBDS* Gene Mutations Allele 1 / allele 2 | Explanation |
|---|---|---|
| Diagnosis | None detected / none detected | This result does not support a diagnosis of SDS |
| Diagnosis | Mutation detected / none detected | This result is unable to confirm a diagnosis of SDS |
| Diagnosis | Mutation detected / mutation detected | This result confirms a diagnosis of SDS |
| Carrier testing | None detected / none detected | This individual is unlikely to be a carrier of SDS |
| Carrier testing | Mutation detected / none detected | This individual is a carrier of SDS and may transmit a mutation to offspring |

*For More Information*

Online Mendelian Inheritance in Man http://www.ncbi.nlm.nih.gov/omim/ Item # 260400

GeneReviews online clinical information resource http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=sds

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

SickKids

*1. Current molecular testing may not detect all possible mutations in this gene. A negative result does not rule out the possibility that the individual carries a rare mutation not detected in the assay.*

*2. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.*

*3. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.*