SickKids | Genome Diagnostics

Simpson-Golabi-Behmel Syndrome

Simpson-Golabi-Behmel Syndrome (SGBS) is an X-linked overgrowth disorder characterized by pre- and postnatal overgrowth, minor facial anomalies, skeletal/ hand anomalies, genitourinary abnormalities and supernumerary nipples. Patients with SGBS also show an increased risk for development of embryonal tumours, especially Wilms' tumour. The main gene identified to cause SGBS is called Glypican 3 (*GPC3*) and is located on the X chromosome (Xq26). Glypican 3 appears to play an important role in embryonic growth by regulating cell proliferation and apoptosis.*GPC4* (also located at Xq26) has also been implicated in SGBS.

Genetics

Males normally have only one X chromosome in each cell. If that X chromosome carries the deletion/point mutation in the *GPC3* gene, the boy will be affected with SGBS. As a result, males are most often affected. Since females have two X chromosomes, if one X chromosome carries the mutation in the *GPC3* gene and the other one does not, the girl will be a carrier of SGBS. Female carriers may have a milder phenotype because of the effect of Lyonization.

Affected males will have carrier daughters since the X chromosome with the deletion/point mutation will be passed from the father to his daughters, and affected males will have unaffected sons, since they will inherit the father's Y chromosome. If a female is a carrier, her sons have a 50% chance of inheriting the mutation and being affected with SGBS. Her daughters have a 50% chance of inheriting the mutation and being carriers themselves, and may exhibit milder features of SGBS.

Test Methods

- Quantitative testing of the *GPC3* and *GPC4* genes to detect large deletions, using MLPA (Multiplex Ligation-dependent Probe Amplification)

- Complete sequencing of the coding region and flanking exon/intron boundaries of the *GPC3* gene to identify point mutations

Test Sensitivity

GPC3 deletions/mutations have been identified in 40% of SGBS cases.

Who Should Be Tested?

- Individuals clinically suspected of being affected with SGBS

- Women with a family history of SGBS, to determine carrier status

- Pregnancies at risk due to a family history of SGBS

Potential Outcomes & Interpretation of Test Results

Patient Sex	*GPC3* Gene Mutation	Explanation
Male	None detected	This result is unable to confirm a diagnosis of SGBS
Male	Mutation detected	This result confirms a diagnosis of SGBS
Female	None detected / none detected	Molecular analysis reduces the likelihood that this individual is a carrier of SGBS.
Female	Mutation detected / none detected	This individual is a carrier of SGBS, may exhibit a milder phenotype, and may transmit a mutation to offspring

For More Information

Online Mendelian Inheritance in Man http://www.ncbi.nlm.nih.gov/omim/ Item# 312870 Item# 300209

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

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

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1. Current molecular testing may not detect all possible mutations in the GPC3 gene. A negative test does not rule out the diagnosis of SGBS, or eliminate the possibility the individual is a carrier.

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.