THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

SLC2A2 Analysis for Fanconi-Bickel Syndrome

Clinical Features

Fanconi-Bickel syndrome (FBS) [OMIM#227810] is a rare disorder characterized by hepatomegaly secondary to glycogen accumulation, glucose and galactose intolerance, fasting hypoglycemia, tubular nephropathy, rickets and growth retardation (1). Elevated glucose levels have been detected in some patients under 1 year of age and FBS should thus be considered in the differential diagnosis of neonatal diabetes when any of the other characteristic features are also present (2).

Molecular Genetics

SLC2A2 [OMIM#138160] encodes for the facilitative glucose transporter GLUT2. Mutations in *SLC2A2* associated with FBS lead to severely impaired glucose transport. Sakamoto *et al* (2000) noted glucosuria in some heterozygous carriers for *SLC2A2* missense mutations; carriers of nonsense mutations did not appear to have the same finding (3). It has been speculated that the glucosuria seen in missense mutation carriers is due to a dominant negative effect, which may not occur with nonsense mutations due to nonsense-mediated decay.

Inheritance

FBS is inherited in autosomal recessive manner. Parents of an affected child are most likely obligate carriers. Recurrence risk for carrier parents is 25%.

Test methods

Comprehensive sequence coverage of the coding regions and splice junctions of the *SLC2A2* gene is performed. Targets of interests are enriched and prepared for sequencing using the Agilent SureSelect system. The constructed genomic DNA library is sequenced using Illumina technology and reads are aligned to the reference sequence. Variants are identified and evaluated using a custom collection of bioinformatic tools and comprehensively interpreted by our team of directors and genetic counselors. All pathogenic and likely pathogenic variants are confirmed by Sanger sequencing. The technical sensitivity of this test is estimated to be >99% for single nucleotide changes and insertions and deletions of less than 20bp. Deletion/duplication analysis of the *SLC2A2* gene by oligonucleotide array-CGH identifies copy number changes involving one or more exons. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by this methodology. Array-CGH will not detect low level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

SLC2A2 sequencing

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81406
Turn-around time:	4 weeks

SLC2A2 deletion/duplication analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81405
Turn-around time:	4 weeks

Note: The sensitivity of our assay may be reduced when DNA is extracted by an outside laboratory.

Results

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References

1. Santer R, Groth S, Kinner M et al. The mutation spectrum of the facilitative glucose transporter gene SLC2A2 (GLUT2) in patients with Fanconi-Bickel syndrome. Hum Genet 2002: 110: 21-29.
2. Yoo HW, Shin YL, Seo EJ et al. Identification of a novel mutation in the GLUT2 gene in a patient with Fanconi-Bickel syndrome presenting with neonatal diabetes mellitus and galactosaemia. Eur J Pediatr 2002: 161: 351-353.
3. Sakamoto O, Ogawa E, Ohura T et al. Mutation analysis of the GLUT2 gene in patients with Fanconi-Bickel syndrome. Pediatr Res 2000: 48: 586-589.

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