THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

AKT2 Analysis for Hypoinsulinemic Hypoglycemia with Hemihypertrophy

Clinical Features

Hypoinsulinemic hypoglycemia with hemihypertrophy (HIHGHH) [OMIM#240900] is characterized by recurrent severe fasting hypoglycemia and asymmetrical growth (1).

Molecular Genetics

AKT2 [OMIM#164731] encodes for a serine/threonine kinase (1). Hussain *et al.* (2011) identified the same *de novo* missense mutation in three patients with the HIHGHH phenotype. In one patient the mutation was identified in the mosaic state (1). The mutation identified was an activating mutation, and functional studies showed it lead to insulin-independent activation of downstream signaling.

Inheritance

AKT2 mutations associated with HIHGHH are autosomal dominant. All mutations described to date in patients with HIHGHH have been *de novo* (1). Recurrence risk for parents of a child with a confirmed *de novo* mutation is predicted to be low.

Test methods

Comprehensive sequence coverage of the coding regions and splice junctions of the *AKT2* 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 *AKT2* 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.

AKT2 sequencing

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

AKT2 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 or email.

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

References

1. Hussain K, Challis B, Rocha N et al. An activating mutation of AKT2 and human hypoglycemia. Science 2011: 334: 474.

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