THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

Woodhouse-Sakati Syndrome: *DCAF17* Mutation Analysis

Clinical Features

Woodhouse-Sakati syndrome (WSS) [OMIM#241080] is a rare disorder characterized by hypogonadism, alopecia, cognitive impairment, diabetes mellitus and progressive extrapyramidal defects (1). Additional findings may include sensorineural deafness, decreased signal intensity in the basal ganglia, T-wave abnormalities and depressed insulin-like growth factor 1 (IGF-1) levels (2).

Molecular Genetics

Mutations in the *DCAF17* gene [OMIM#612515] are associated with Woodhouse-Sakati syndrome (1, 2). *DCAF17* (also known as *C2orf37)* encodes a nucleolar protein, and the nucleoli of affected patients have enhanced sensitivity to transcriptional blockade (2). To date, nonsense, splice site and frameshift mutations have been described in the *DCAF17* gene (1).

Inheritance

Woodhouse-Sakati syndrome is inherited in an autosomal recessive inheritance pattern. Therefore, 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 *DCAF17* 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 novel and/or potentially 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. Our CNV detection algorithm was developed and its performance determined for the sole purpose of identifying deletions and duplications within the coding region of the gene(s) tested. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by this methodology. Regions of high homology and repetitive regions may not be analyzed. This methodology will not detect low level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of our deletion/duplication assay may be reduced when DNA extracted by an outside laboratory is provided.

DCAF17 sequencing and deletion/duplication analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81405
	81406
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. Alazami AM, Schneider SA, Bonneau D et al. C2orf37 mutational spectrum in Woodhouse-Sakati syndrome patients. Clin Genet 2010: 78: 585-590.
2. Alazami AM, Al-Saif A, Al-Semari A et al. Mutations in C2orf37, encoding a nucleolar protein, cause hypogonadism, alopecia, diabetes mellitus, mental retardation, and extrapyramidal syndrome. Am J Hum Genet 2008: 83: 684-691.

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