Clinical Features

Wiedemann-Steiner syndrome [OMIM#605130] is a rare disorder characterized by excessive growth of terminal hair around the elbows (hypertrichosis cubiti), short stature, intellectual disability and characteristic facial features (1). Facial features include long eyelashes, think or arched eyebrows, downslanting and vertically narrow palpebral fissures, broad nasal bridge and wide nasal tip (1).

Molecular Genetics

Jones et al. (2012) identified mutations in KMT2A (MLL) [OMIM#159555] in five out of six patients with clinical features consistent with Wiedemann-Steiner syndrome (1). All mutations were predicted to result in protein truncation. KMT2A encodes for a histone methyltransferase that regulates chromatin-mediated transcription.

Inheritance

Wiedemann-Steiner syndrome is an autosomal dominant condition. All mutations identified in KMT2A to date have been de novo. Recurrence risk for parents in cases with a confirmed de novo mutation is <1%.

Test methods

We offer mutation analysis of all coding exons and intron/exon boundaries of KMT2A by direct sequencing of amplification products in both the forward and reverse directions. Deletion/duplication analysis is performed by oligonucleotide array-CGH. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. 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.

KMT2A (MLL) sequencing

Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $2,900
CPT codes: 81407
Turn-around time: 4 - 6 weeks

KMT2A (MLL) deletion/duplication analysis

Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1000
CPT codes: 81406
Turn-around time: 4 weeks

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

Testing for a known mutation in additional family members by sequence analysis

Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $390
CPT codes: 81403
Turn-around time: 3-4 weeks

Prenatal testing for a known mutation by sequence analysis

Sample specifications: 2 T25 flasks of cultured cells from amniocentesis or CVS or 10 mL of amniotic fluid
Cost: $540
CPT codes: 81403
Turn-around time: 1-2 weeks

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.

References: