THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

IER3IP1 Analysis for MEDS

Clinical Features

MEDS (Microcephaly, Epilepsy, and Diabetes Syndrome) [OMIM#614231] is a rare disorder characterized by primary microcephaly, simplified gyral pattern, severe infantile epileptic encephalopathy and early-onset permanent diabetes (1).

Molecular Genetics

IER3IP1 [OMIM#609382] is highly expressed in the fetal brain cortex and fetal pancreas, and is thought to be involved in endoplasmic reticulum stress response (1). *IER3IP1* has been implicated in the regulation of cell survival (1). Poulton *et al* (2011) identified homozygous missense mutations in *IER3IP1* in affected children from two consanguineous families.

Inheritance

MEDS 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 *IER3IP1* gene is performed. Targets of interests are enriched and prepared for sequencing using the Agilent SureSelect system. Sequencing is performed 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 20 bp. Deletion/duplication analysis of the *IER3IP1* 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.

IER3IP1 sequencing

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81404
Turn-around time:	4 weeks

IER3IP1 deletion/duplication analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81403
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. Poulton CJ, Schot R, Kia SK et al. Microcephaly with simplified gyration, epilepsy, and infantile diabetes linked to inappropriate apoptosis of neural progenitors. Am J Hum Genet 2011: 89: 265-276.

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