**SLC19A2 Analysis for TRMA syndrome**

**Clinical Features**
TRMA syndrome [thiamine-responsive megaloblastic anaemia syndrome, OMIM#249270] is associated with the classic clinical triad of diabetes, deafness, and megaloblastic anaemia (1). Diabetes in this condition typically occurs in infancy but has been reported in association with neonatal diabetes in rare cases (1). Other additional features which may be observed in affected individuals include congenital heart malformations, tri-lineage myelodysplasia, and visual issues such as optic atrophy or retinitis pigmentosa (1).

**Molecular Genetics**
Homozygous or compounded heterozygous mutations in the SLC19A2 gene [OMIM#603941] are associated with TRMA (2). SLC19A2 encodes a high-affinity thiamine transporter, and studies on the fibroblasts of affected individuals have shown that absence of this transporter protein results in low intracellular thiamine levels (2). The mechanism by which absence of this protein leads to the divergent symptoms associated with TRMA remains unknown (2).

**Inheritance**
TRMA 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 SLC19A2 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.

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.

**SLC19A2 sequencing**
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1000
CPT codes: 81405
Turn-around time: 4 weeks

**SLC19A2 deletion/duplication analysis**
Sample specifications: 3 to 10 cc of blood in a purple top (EDTA) tube
Cost: $1000
CPT codes: 81404
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:**