Uniparental Disomy of Chromosome 6 (UPD6): Methylation Analysis

Test Code: TU
Turnaround time: 3 weeks
CPT Codes: 81402 x1

### Condition Description

6q24-related transient neonatal diabetes mellitus (TNDM) is one of the most common causes of neonatal diabetes, with an estimated incidence of 1 in 400,000 live births [1]. TNDM begins in the first six weeks of life and resolves by 18 months of age. Neonates present with severe growth retardation and persistent hyperglycemia. According to one study [2], the average birth weight is 1930 g at 39 weeks gestation, and the average age at presentation is 7 days. Insulin levels are low or undetectable at presentation, and ketonuria is generally absent. Macroglossia occurs in about 1/3 of cases. Umbilical and inguinal hernias have also been reported. The average length of time on insulin is 111 days. There is no association with HLA antigens common in type 1 diabetes. While affected infants recover by three months of age, around 50% will develop type 2 diabetes later in life.

TNDM is caused by overexpression of two imprinted genes at 6q24, *PLAGL1 (ZAC)* and *HYMAI*. Both *PLAGL1 (ZAC)* and *HYMAI* are expressed from the paternally inherited chromosome 6. Approximately 35% of TNDM cases are caused by paternal uniparental disomy of chromosome 6.

Methylation-specific PCR is used to assess a differentially methylated region that controls expression of *PLAGL1 (ZAC)* and *HYMAI*. Both paternal UPD6 and some isolated methylation defects of this imprinted region will be detected by this analysis.

References:

### Genes

HYMAI, PLAGL1 (ZAC)

### Indications

This test is indicated for:
- Confirmation of a clinical/biochemical diagnosis of patUPD6

### Methodology

DNA methylation specific PCR assay targeting the differentially methylated region (DMR) upstream of the *PLAGL1 (ZAC)* and *HYMAI* genes on chromosome 6q24 is used to test for paternal uniparental disomy of chromosome 6 (patUPD14). Parental samples are NOT required for patUPD6 analysis, but may be requested to confirm a diagnosis.

### Specimen Requirements

Submit only 1 of the following specimen types

**Type: DNA, Isolated**

**Specimen Requirements:**
- Microtainer
- 3 µg

Isolation using the Perkin Elmer™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
- Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**
- EDTA (Purple Top)
- Infants and Young Children (2 years of age to 10 years old): 3-5 ml
- Older Children & Adults: 5-10 ml
- Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
- Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

### Special Instructions

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

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