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
- 3µg 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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