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**

**Type: Whole Blood**

Specimen Requirements:
- In EDTA (purple top) tube:
  - Infants (2 years): 3-5 ml
  - Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

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**Special Instructions**

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