

## LIT1 / KCNQ1OT1 Methylation (Beckwith-Wiedemann Syndrome, BWS)

### DESCRIPTION:

- The clinical presentation of BWS includes overgrowth (large birth weight or large for gestation), macroglossia, omphalocele/umbilical hernia, hemihyperplasia, minor facial and ear anomalies, hypoglycemia, organomegaly, and tumor predisposition.
- This test examines parent-specific methylation at LIT1 / KCNQ1OT1, within the KVLQT1 / KCNQ1 gene located at 11p15.5, and is reported to detect abnormal imprinting in 60% of patients who meet clinical criteria for BWS (*PNAS*, 1999, 96:5203-5208, *PNAS*, 1999, 96:8064-8069, *Hum Mol Gen*, 1999, 8:1209-1217).
- Hypomethylation of the maternal copy of LIT1 / KCNQ1OT1 in BWS is proposed to increase transcription, which in turn suppresses other maternally expressed growth inhibitors in the region (KVLQT1 / KCNQ1, p57KIP 2 / CDKN1C, H19).

### REASONS FOR REFERRAL

- This is not a diagnostic test for BWS. Positive results are consistent with a clinical diagnosis of the syndrome, and negative results rule out one mechanism apparently involved in causing the syndrome
- A prenatal test can be considered when omphalocele is observed on ultrasound, fetal chromosomes are normal, and BWS is a possible diagnosis.

### METHOD OF ANALYSIS:

- Upon Southern hybridization to a BamHI/ NotI digest of genomic DNA, a 370 bp LIT1 / KCNQ1OT1 probe (containing EST 592241) detects two bands for a normal biparental pattern (Lee et al., *PNAS*, 1999, 96:5203-8).
- Complete or almost complete absence of the normally methylated maternal band supports a clinical diagnosis of Beckwith-Wiedemann syndrome. Greater intensity of the paternal band relative to the maternal can be seen in mosaic uniparental disomy (UPD), a mechanism involved in about 20% of BWS patients. UPD can be tested for separately, and requires parental specimens.
- Results are reported within 3 weeks or less of receipt of sample.  
PRENATAL TURNAROUND TIME IS TARGETED AT 14 DAYS OR LESS.

### SAMPLE REQUIREMENTS:

- For DNA testing, 5 to 10 milliliters of blood (minimum 1 ml) in EDTA (purple top) tubes should be sent by overnight carrier at room temperature.
- Prenatal testing: two (2) confluent T25 flasks of amniocytes or cultured CVS cells.

### TEST CPT CODES:

CPT 83891 DNA extraction highly purified  
CPT 83892 DNA enzymatic digestion X 2  
CPT 83894 DNA separation X 3  
CPT 83896 DNA probe  
CPT 83897 DNA blot  
CPT 83898 DNA amplification  
CPT 83912 DNA interpretation and report

*Discounts from list price are available for institutional billing under contractual arrangement with the laboratory. Contact Ellen Livers at 800-447-6614 ext 7523.*