



Molecular Diagnostic Laboratory
Phone: (314) 454-8685; 454-7601
FAX: (314) 454-7616
<http://www.surgery.wustl.edu/bjcmdl/>



Barbara Zehnbauer, PhD FACMG
Laboratory Director

Prader-Willi and Angelman Syndromes (PWS/AS)

Absence of portions of chromosome 15q11-13, Prader-Willi *PWCR1* and Angelman *UBE3A*

Indications for Molecular Testing

- Suspected diagnosis of a child with PWS or AS
- Suspected diagnosis of PWS with any or all of the following symptoms present:
 - severe infantile hypotonia
 - hyperphagia/obesity
 - small hands and feet
 - mild mental retardation
 - hypogonadism
 - behavior disorder
- Suspected diagnosis of AS with any or all of the following symptoms present:
 - mental retardation
 - speech impairment
 - microcephaly
 - seizures
 - ataxia
 - behavior disorder

Testing Methodology

Direct mutation testing involves determination of restriction fragment sizes and methylation status following Xba1+ Sac II restriction endonuclease digestion and genomic Southern hybridization with a *SNRPN* gene probe. Unmethylated, expressed regions are sensitive to digestion with SacII. In this assay the paternally derived, unmethylated allele is 1.0 kb and the maternally derived, methylated allele is 4.3 kb. Loss of the paternal allele produces absence of the 1.0 kb band consistent with a diagnosis of PWS (*PWCR1*). Loss of the 4.3 kb maternal allele is consistent with a diagnosis of AS (*UBE3A*). This assay detects both deletion mutations and methylation abnormalities at the 15q 11-13 region that are associated with PWS and AS.

Interpretation of DNA analysis

Prader-Willi Syndrome is caused by the absence of **paternally** derived portion of the 15q11-13 chromosomal region (*PWCR1*). Angelman Syndrome is caused by the absence of the **maternally** derived portion of this same chromosomal region (*UBE3A*). The DNA-based methylation testing distinguishes the different parental allelic regions and detects the loss of either maternal or paternal copies. DNA methylation testing detects 99% of cases of PWS and ~78% of cases of AS caused by deletions, uniparental disomy (UPD), and imprinting defects. About 11% of patients with AS have mutations in the *UBE3A* gene that are not detected in this assay. Another 11% of patients with AS have no detectable molecular changes. Normal individuals retain both alleles.

Specimen Requirements

Peripheral Blood--1 lavender-top (EDTA) tube. Invert several times to mix blood. Do not freeze, forward promptly at ambient temperature to the following address:

Molecular Diagnostic Laboratory
Barnes-Jewish Hospital North, Room 2445
Mail Stop 90-28-372
216 South Kingshighway
St. Louis, MO 63110

Clinical information must be provided with specimen referral in order to correctly interpret test results.

Current Pricing

Contact Lab Customer Service for current pricing 314 362-1470.
CPT codes: 83907, 83890, 83892, 83894, 83897, 83896, 83912.

Glenn CC, Saitoh S, Jong MTC, Filbrandt MM, Surti U, Driscoll DJ, et al. Am. J. Hum. Genet. 1996; 58:335-346.

Holm VA, Dassidy SB, Butler MG, Hancherr JM, Greenswag LR, Whitman BY, Greenberg F. Prader-Willi syndrome: consensus diagnostic criteria. Pediatrics 1993; 91:398-402.