

The University of Chicago Genetic Services Laboratories



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Prader-Willi Syndrome Testing

Clinical Features:

Prader-Willi syndrome (PWS) [OMIM #176270] is a genetic disorder which causes hypotonia and poor feeding in infancy, followed by the development of hyperphagia and subsequent obesity. Physical characteristics of PWS also include short stature, small hands and feet, and a characteristic facial appearance consisting of a thin upper-lip, down-turned mouth, dental crowding, and almond shaped eyes. Developmental milestones are delayed, and learning disabilities are always present, but may vary in severity. Behavioral problems include temper tantrums, obsessive compulsive tendencies, and skin-picking. Psychosis occurs in 5-10% of patients as young adults [1]. Individuals with PWS do not undergo spontaneous pubertal development and are infertile [1,2].

Inheritance:

PWS is an imprinting disorder caused by the lack of expression of the paternal copy of 15q11-q13. This can occur by one of several mechanisms including a de novo paternal deletion in this region, maternal uniparental disomy (UPD), an imprinting center defect, or a paternal chromosomal translocation. The recurrence risk depends on the mechanism involved and may be up to 50%. PWS affects approximately 1 in 25,000 births and displays no ethnic or gender preference [2,3].

Molecular Genetics:

- Approximately 70% of individuals with PWS have a de novo deletion of 15q11-q13 on the paternally contributed chromosome, corresponding to a less than 1% recurrence risk [2].
- Approximately 25% of PWS is due to maternal UPD15, corresponding to a less than 1% recurrence risk [2].
- Up to 3% of patients have a microdeletion of the imprinting center of 15q11-q13, corresponding to a recurrence risk of up to 50% [2].
- Less than 1% of PWS is due to a paternal chromosome 15 translocation, which may result in a recurrence risk of up to 25% [2].

Additional Resources:

Prader-Willi Syndrome Association

5700 Midnight Pass Road, Suite 6
Sarasota, FL 34242
Phone: 800-926-4797
email: national@pwsausa.org
www.pwsausa.org/index.html

Test methods:

M-PCR is a rapid, inexpensive test to identify individuals with PWS due to deletions of 15q11-q13, UPD15 or imprinting abnormalities.

We recommend chromosome analysis in conjunction with M-PCR as the first testing for a child with PWS. For a patient identified as having PWS by M-PCR, additional testing is required to determine if the individual has a deletion, maternal UPD15, or an imprinting mutation and to provide thorough genetic counseling.

Our laboratories offer chromosome analysis, FISH analysis for deletions of 15q11-q13, polymorphic microsatellite analysis for UPD15, and real-time qualitative PCR (RT-QPCR) for imprinting center deletion analysis.

Chromosome analysis

Sample specifications:	3-10 cc of blood in a green top/sodium heparin tube
Turnaround time:	12 days, STAT analysis available
Cost:	\$700
CPT Codes	88230, 88262, 88291

Methylation-specific PCR (M-PCR)

Sample specifications:	3-10 cc of blood in a purple top EDTA tube
Turnaround time:	2 – 4 weeks
Cost:	\$315
CPT Codes	83891, 83898, 83894, 83912

FISH for deletions of 15q11-q13

Sample specifications:	3-10cc of blood in a green top/sodium heparin tube
Turnaround time:	10 – 12 days
Cost:	\$325
CPT codes:	88230, 88271, 88291, 88273

Microsatellite analysis for UPD15 testing

Sample specifications:	3-10 cc blood from patient and BOTH parents in purple top EDTA tubes
Turnaround time:	2 – 4 weeks
Cost:	\$540 (total for a patient's and both parents' blood samples)
CPT codes:	83891, 83898 x 4, 83894, 83912

Real-time quantitative PCR (RT-QPCR) for imprinting center (IC) deletions

Sample specifications:	3-10 cc of blood in a purple top (EDTA) tube
Turnaround time:	2 - 4 weeks
Cost:	\$450
CPT codes:	83891, 83900, 83901, 83912

Results

You will be informed of the results of your case as soon as it has been completed. Results, along with an interpretive report, will be faxed and mailed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

Laboratory Faculty and Staff:

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ABMG Certified Molecular Geneticist

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References:

1. Chen C et al. Prader-Willi Syndrome; An update and Review for the Primary Pediatrician 2007 Clinical Pediatrics.
2. Cassidy S, Schwartz S. Prader-Willi Syndrome (2006). GeneReviews. www.genetests.com
3. Whittington JE et al. Population Prevalence and estimated birth incidence and mortality rate for people with Prader-Willi syndrome in one UK Health Region (2001) J. Med. Genet. 38: 792-798.

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