"MAURO BASCHIROTTO"
INSTITUTE FOR RARE DISEASES

International Prader-Willi Syndrome Diagnostic Testing Initiative

IPWSO
International
Prader-Willi Syndrome
Organisation

International Prader-Willi Syndrome Organisation (IPWSO) in collaboration with the non-profit organization "Mauro Baschirotto" Institute for Rare Diseases (BIRD) are offering diagnostic testing for **Prader-Willi syndrome (PWS)** without charge for people without affordable and readily available testing in their country. The test method currently used is methylation-specific PCR amplification of the CpG islands of the SNRPN gene located inside the 15q11-q13 region. This test will detect about 99% of the cases of PWS.

MS-MLPA testing: An experimental use of the MS-MLPA method is underway and samples meeting the required quality criteria will be analyzed with this method instead. The advantage of this method is that it allows the distinction between uniparental disomy and the classical deletions in the 15q11-q13 region. This testing is conducted in collaboration with MRC Holland, producer of the MS-MLPA kit for PWS.

The tests are conducted **free of charge** on DNA isolated from dried blood spots. The turnaround time is usually 3-12 weeks, depending on the workload of the lab.
The results are written in English and sent by e-mail to the medical doctor requesting the test. Genetic counseling regarding the results of the tests is available upon request.

Please feel free to contact us for any further information.

When should Prader-Willi syndrome be considered?

Criteria sufficient to suggest a diagnosis of PWS have been published (Gunay-Aygun M. et. al.; PEDIATRICS Vol. 108 No. 5, E92 November 1, 2001) and are the basis for the eligibility for PWS testing, as shown in the following table.

Age at Assessment	Features Sufficient to Prompt DNA Testing
Birth to 2 years	Hypotonia with poor suck
2 – 6 years	Hypotonia with history of poor suck
	Global developmental delay
6 – 12 years	Hypotonia with history of poor suck
	Global developmental delay
	Excessive eating (hyperphagia; obsession with food) with central obesity if uncontrolled
>13 years	Hypotonia with history of poor suck
	Cognitive impairment; usually mild intellectual disability
	Excessive drive to eat (hyperphagia; obsession with food) with central obesity if uncontrolled
	Hypothalamic hypogonadism
	Behavior problems (including temper tantrums and obsessive-compulsive features)

Please notice that the features described in the table above are not the only ones present in this syndrome, but in their absence the diagnosis of PWS is highly unlikely. In order to promote very early diagnosis for infants, the sole presence of hypotonia is a sufficient criterion for PWS testing eligibility.

A detailed list of the major, minor and supportive features of PWS and a detailed description of the pathology can be found in Holm VA et al., PEDIATRICS, vol. 91 number 2, pages 398-402, 1993 and freely available on the internet at the Gene Reviews page http://www.ncbi.nlm.nih.gov/books/NBK1330/.

Instructions for access to the free of charge Prader-Willi tests:

1. Acceptance of the sample:

In order to be eligible for molecular testing through this program, the subject must have a clinical diagnosis or a strong clinical suspicion of Prader-Willi syndrome made by a medical doctor.
Before sending a sample please send the following information to consulenze@birdfoundation.org:

- The International PWS Sample Sending - Clinical data form
- Photos of the feet, hands, full body front and side
- Additional clinical data (if available)

The information will be reviewed and you will be informed if the sample can be accepted for testing.

PLEASE NOTICE: ONLY TESTS ORDERED BY MEDICAL DOCTORS CAN BE ACCEPTED.

2. Informed consent:

A medical professional must explain to the family the PWS methylation test, the possible results and the implications for the tested person and their family; permitting the family to ask questions and answering them. After obtaining their consent the Declaration of consent form should be filled in and signed by the parents or the legal guardian and counter signed by the medical professional obtaining the consent. If possible, also the tested person should sign the document.

3. Sample collection and preparation:

A medical professional should collect 8-12 blood spots (6-8 drops of blood each) on thick laboratory filter paper (Whatman 903 or Guthrie cards; do not use other types of paper as they can interfere with the lab procedures; for further questions please contact our lab). The spotted blood should be either without anticoagulant or with EDTA as anticoagulant (other types of anticoagulant may interfere with the test). It is fundamental that the spotted paper is kept in a clean, dry and dark environment for a few days until it is completely dry. A clean carton box or a drawer are suitable solutions. If no such place is available the samples can be loosely covered with tissue paper, to avoid dust and contaminants, and left on an even surface to dry. Once completely dry, put the filter paper inside a sterile plastic bag for laboratory use to protect it. If the sample isn't properly dried before packing in the sterile bag, the DNA will degrade over time and there is a high risk of yeast infections. On the margin of the filter paper clearly write the full name of the tested person, together with his/her date of birth.

4. Sending the sample:

Please send the sample together with the clinical data collection form and the signed informed consent as a normal letter **by regular mail** and not by express courier to the following address:

Medical Genetics Unit
"Mauro Baschirotto" Institute for Rare Diseases - B.I.R.D. Foundation n.p.o.
Via B. Bizio, 1 - 36023 Costozza di Longare (VI) - Italy

For assistance:

E-mail: consulenze@birdfoundation.org

Telephone: +39 0444 555557

To learn more about PWS and other free services offered by the International Prader-Willi Syndrome Organisation (IPWSO):

Sign up to IPWSO's mailing list at: www.ipwso.org
Email: office@ipwso.org

All samples and all the documentation will be handled with maximum respect for privacy and the tests performed follow the best practice guidelines regarding genetic testing.