



## Test Information Sheet

# **Genetic Testing for X-Linked Recessive Chondrodysplasia Punctata Information for Non-genetics Professionals**

### **Clinical Features**

Patients with X-Linked Recessive Chondrodysplasia Punctata (CDPX1) also known as Brachytelephalangi Chondrodysplasia Punctata have features characterized by nasal and midface hypoplasia, stippled epiphyses, and brachytelephalangy (hypoplasia of distal phalanges). Other findings include hearing loss and short stature. Intelligence is usually normal. More severe clinical pictures have been described which include respiratory impairment, cervical spine abnormalities and mental retardation. The severe clinical picture has led to early demise in some cases.

The suggested minimal diagnostic criteria for this disorder include all of the following:

- **Chondrodysplasia punctata**, especially in the hands and feet
- **Nasomaxillary hypoplasia**, with absence of the anterior nasal spine and perialar flatness
- **Brachytelephalangy**
- **Male sex**

### **Inheritance and Etiology**

CDPX1 is caused by a mutation in the Arylsulfatase E (*ARSE*) gene on Xp22.3, resulting in deficient arylsulfatase E protein. ARSE is essential for the correct composition of cartilage during bone development, and its deficiency results in the skeletal changes typical of CDPX1.

CDPX1 is inherited in a X-linked recessive manner. When a mother is a carrier, each pregnancy has a 25% chance of resulting in an affected boy, a 25% chance of resulting in a carrier girl, a 25% chance of resulting in an unaffected boy, and a 25% chance of resulting in a girl who is not a carrier. Approximately 2/3 of mothers of boys affected are carriers. Carrier mothers are typically not clinically affected. Molecular genetic testing may also be used for prenatal testing, if the *ARSE* mutation has been identified in an affected boy in the family. Biochemical testing is not available for this disorder.

### **Exclusionary Testing**

A normal routine karyotype analysis is strongly recommended prior to gene testing

### **Genetic Testing**

The first person to be tested in any family would be the individual with features of CDPX1. Testing is performed by direct sequencing of the 11 exons of this gene. Once a mutation is identified in the individual with CDPX1, targeted testing for other family members, or prenatal testing, can then be performed. Several studies have shown the sensitivity of full gene sequencing in affected males to be up to 60%.

### **Reasons for Genetic Testing for CDPX1**

- Confirm the diagnosis
- Evaluate carrier status of mother
- Provide accurate recurrence risks for future pregnancies
- Provide accurate information during a pregnancy regarding possible CDPX1 in the fetus

### **Possible Result of Genetics Testing**

- **Mutation detected**  
Finding a mutation will confirm a diagnosis of CDPX1. Once a change has been identified in an affected individual, targeted testing can then be performed for other family members if they choose.
- **No mutation detected**  
Not finding a mutation does not rule out the diagnosis of CDPX1, but does make it less likely. There are other disorders that mimic the clinical picture of CDPX1 and these can be evaluated.
- **Variant of unknown significance**  
A small number of patients will have a variation in *ARSE* in which there is not enough data to state whether or not it causes CDPX1.

### **Reporting of Results**

You will be informed of the results of your case as soon as it is completed. Results, along with an interpretive report, will be faxed to the referring physician. All abnormal results will be reported by telephone.

### **Test Ordering and Billing**

Clinical testing for CDPX1 is now available at Gene Dx laboratory. A test requisition form, billing form, consent form and clinical data sheet are required for testing. These forms can be found on the lab website ([www.genedx.com](http://www.genedx.com)) or by calling the lab. If there is any question about ordering testing please contact the lab. If there is any question please contact Ms Ferguson at (301) 519-2100 X133.

### **Specimen Requirements and Shipping/Handling**

- *Blood*: A single tube with 1-5 mL whole blood in EDTA. Ship overnight at ambient temperature, using a cool pack in hot weather. Specimens may be refrigerated for 3 days prior to shipping.
- *Buccal Brushes*: As an alternative to blood, use a GeneDx buccal kit (others not accepted). Submit by mail. Buccal brushes are not accepted on children under 6 months of age.
- *Prenatal Diagnosis*: 10 mL amniotic fluid, 5 mg CVS, or 2 T25 flasks. Ship overnight at ambient temperature, using a cool pack in hot weather. Call to discuss requirements for parental blood. Keep backup cultures.

### **Prices and Turn-Around Time - Fees are subject to change without notice:**

Test # TBD: Mutation detection in a new patient = \$ 1500; Approximately 6 weeks

Test # 9011: Testing of a relative for a specific known mutation = \$ 350; Approximately 2-4 weeks

Test # 902: Prenatal diagnosis for a specific known mutation = \$1500; Approximately 2 weeks

All insurance companies are different, but most of them should cover at least part of the cost of testing. We recommend that a parent or physician's office contact the patient's insurance company with specific CPT codes (below) to learn more about the specific coverage prior to testing. GeneDx will bill the patient's insurance company, hospital or referring laboratory. The patient may receive a bill for any amount not covered by the insurance company. If the patient does not have medical insurance and we cannot bill their institution, we will require from the patient by check or credit card before beginning testing.

**CPT codes for mutation detection in a new patient** - All codes and units apply:

83891 x 11 units = \$ 160

83898 x 11 units = \$ 400

83894 x 11 units = \$ 160

83904 x 22 units = \$ 680

83892 x 2 units = \$ 40

83912 x 2 units = \$ 60

**TOTAL                \$ 1500**

**Possible ICD9 Codes:**

756.59 chondrodysplasia punctata epiphysealis

**References Cited:**

Brunetti-Pierri, N. et al. (2003) X-Linked Recessive Chondrodysplasia Punctata: Spectrum of Arylsulfatase E Gene Mutations and Expanded Clinical Variability *Am J Med Genet* 117A:164-168; Sheffield, L.J. et al. (1998) Segregation of mutations in arylsulphatase E and correlation with the clinical presentation of chodrodysplasia punctata *J Med Genet* 35:1004-1008; Franco B. et al. (1995) A Cluster of Sulfatase Genes on Xp22.3: Mutations in Chondrodysplasia Punctata(CDPX) and Implications for Warafin Embryopathy *Cell* 81:15-25.