

Molecular Genetics Service Profile

Progressive Pseudorheumatoid Chondrodysplasia (PPRD)

Introduction

- ◇ PPRD (OMIM No. 208230) is characterized by joint pain; generalized, progressive joint contractures; osseous expansion of the ends of the tubular bones, notably the phalanges; and negative laboratory signs of juvenile rheumatoid arthritis. Affected individuals are usually asymptomatic in early childhood; finger involvement is typical and begins between the ages of 3 and 6 years. Over time joints become progressively stiff and contracted, and pain spreads to other joints. There is a continued cartilage loss, which leads to destructive bone changes necessitating joint replacement by the third decade in several cases.
- ◇ Radiological features include: flattened vertebral bodies, broad lower ilia with lateral extensions, irregular acetabular roof, progressive deformity and arthrotic changes of the femoral heads, expanded articular ends of the tubular bones, narrow joint space, secondary osteopenia and arthrotic changes.
- ◇ PPRD is caused by mutations in *WISP3*, a gene coding for a mesenchymal signalling secreted protein involved in cell growth and differentiation.

Contact details for the laboratory carrying out the genetic test for PPRD

Division of Molecular Pediatrics, Centre Hospitalier Universitaire Vaudois, Clinique Infantile 02-35 Av. Pierre Decker 2, CH-1011 Lausanne, Switzerland.

Dr. Luisa Bonafé. Tel: +41 21 314 3483. Fax: +41 21 314 3546. Email: laureane.mittaz-crettol@chuv.ch

Reasons for referral

- ◇ Mutation analysis in patients with a diagnostic suspicion of PPRD on clinical and/or radiographic grounds.
- ◇ Differential diagnosis of spondylo-epiphyseal dysplasias and drug-resistant polyarthritis in childhood.
- ◇ Carrier testing of relatives of an index case with a previously identified mutation.
- ◇ Prenatal diagnosis may be an option. We recommend that this be offered only within the context of appropriate genetic counselling. Moreover, prenatal testing is possible only in families where the mutations in the index case have been confirmed in advance. Screening for unknown mutations in a prenatal sample is not feasible.

Samples

- ◇ Minimum 50µg of DNA from peripheral lymphocytes or fibroblasts from your local laboratory. Blood samples (minimum of 5ml in EDTA) can also be sent to our laboratory by express mail (FedEx / UPS) at room temperature. Prenatal samples must be sent with parental samples. Please contact our laboratory (as above) for further details, including the minimal amount of DNA required for babies and small children.

Technical

- ◇ Mutation analysis by PCR amplification and bi-directional fluorescent sequencing.

Target turn-round time

- ◇ Mutation analysis of *WISP3* gene by sequencing: 6-12 months. Prenatal diagnosis - only in families with known mutations: 1 - 2 weeks.
- ◇ Turn-round times are from the receipt of all required samples and information, including appropriate clinical information and radiographs. Relevant clinical-radiographic expertise is currently offered at no cost through the use of the secure online submission system (the **ESDN Case Manager**). Testing is only performed after clinical and radiographic evidence has been reviewed using the **ESDN Case Manager**. To obtain a username and password for the **ESDN Case Manager** please email info@esdn.org.

Cost

- ◇ Mutation analysis in an index case and parents: CHF 500 (€310) if the specimen is extracted DNA. Additional cost: CHF 50 (€30) if the specimen is a blood sample.
- ◇ Prenatal diagnosis: CHF 800 (€500). ADVANCE NOTICE IS MANDATORY.
- ◇ Carrier testing: CHF 100 (€60) if the specimen is extracted DNA. Additional cost: CHF 50 (€30) if the specimen is a blood sample.

References

- ◇ Hurvitz, J.R. *et al.* (1999) *Nature Genet.* **23**:94-98.

ESDN Administrator contact details

- ◇ Email: info@esdn.org Website: www.esdn.org

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