

Molecular Genetics Service Profile Pseudoachondroplasia (PSACH)

Introduction

- ◇ PSACH (MIM 177170) is an autosomal dominant osteochondrodysplasia affecting at least 1 in 20,000 individuals and is characterised by disproportionate short stature, deformity of the legs, short fingers, loose joints and ligamentous laxity. Radiographic features include small and irregular epiphyses and metaphyses.
- ◇ PSACH is caused almost exclusively by mutations in the cartilage oligomatrix protein gene (*COMP*) located on chromosome 19p13.1. (Briggs & Chapman, 2002). However, *COMP* mutations are not detected in a small proportion of PSACH cases (Kennedy *et al* 2005).

Contact details for the laboratory carrying out the genetic test for PSACH
c/o Regional Molecular Genetics Service, Department of Medical Genetics, DNA Lab, First Floor,
St. Mary's Hospital, Hathersage Road, Manchester, M13 0JH UK
Dr. Gail Jackson. Tel: +44 (0)161 276 6122. Fax: +44 (0) 161 276 6606. Email: Gail.Jackson@cmft.nhs.uk

Reasons for referral

- ◇ Mutation screening in patients with clinically confirmed, or a differential diagnosis of PSACH.
- ◇ Presymptomatic testing of relatives of an index case with a previously identified mutation.
- ◇ Prenatal diagnosis may be relevant, and can be offered by our laboratory on prior arrangement. However, we strongly recommend that this should only be offered within the context of genetic counselling. In addition, the mutation in the parent must be known.
- ◇ Screening for unknown mutations is labour intensive; therefore we cannot accept urgent referrals of this type.

Samples

- ◇ Minimum 20µg of DNA from peripheral lymphocytes from your local laboratory. Blood samples (minimum of 5mls in EDTA) can also be sent to our laboratory by express mail (FedEx / UPS). Prenatal samples must be sent with a maternal sample. Please contact our laboratory (as above) for further details.

Technical

- ◇ Mutation scanning is by fluorescent bi-directional sequencing of exons 8-19 of *COMP* and this approach will detect the majority of *COMP* mutations in PSACH. However, it has not been fully determined as to whether mutations in exons 1-7 of *COMP* can also cause PSACH (Kennedy *et al* 2005) and mutation scanning of these additional exons may be undertaken following further clinical/radiographic evaluation of the patient.

Target turn-round time

- ◇ Mutation scanning of *COMP* exons 8-19 by sequencing – 8 weeks. Routine, single mutation test - 2 weeks. Pre-natal diagnosis – 3 days, however, this should be discussed with our laboratory (see above for contact details) prior to submission of samples.
- ◇ 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

- ◇ PSACH mutation screen (*COMP* exons 8–19) cost €544. **This service is currently covered by ESDN only when referrals are made through the ESDN Case Manager.**

References

- ◇ Briggs & Chapman (2002). *Hum. Mut.* **19**: 465-478; Kennedy *et al* (2005). *Eur J Hum Genet.* **13**(5): 547-555.

ESDN Administrator contact details

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

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