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, Genetic Medicine, 6th Floor,
St. Mary's Hospital, Oxford Road, Manchester, M13 9WL UK
Dr. Gail Jackson. Tel: +44 (0)161 276 6645. 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 by 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 50μg of DNA from peripheral lymphocytes from your local laboratory, or blood samples in EDTA (minimum of 10mls in adults and 5mls in children) can be sent to our laboratory by first class post within the UK, or express mail out with the UK (FedEx/UPS). Prenatal samples must be sent with a maternal sample, and advance notice is mandatory.

Technical

◊ Mutation analysis by PCR and bi-directional fluorescent sequencing of exons 8-19 of *COMP* (including the splice donor and acceptor sites). This approach will detect the majority of 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 screening of these additional exons may be undertaken following further clinical/radiographic evaluation.

Target turn-round time

◊ Full mutation scanning: 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 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 (**also see**: http://www.mangen.org.uk/professionals/service-results/service-details/Pseudoachondroplasia.aspx)

◊ Full mutation screen: £483.

◊ Single mutation test: £138.

◊ Prenatal diagnosis: £276. **ADVANCE NOTICE IS MANDATORY**

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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