Oxford Molecular Genetics Laboratory
Genetics Laboratories, Churchill Hospital, Old Road, Headington, Oxford, OX3 7LE
www.ouh.nhs.uk/geneticslab

HYPERPARATHYROIDISM-JAW TUMOUR SYNDROME (HPT-JT) – OMIM #145001

INTRODUCTION

Hyperparathyroidism-jaw tumour syndrome (HPT-JT) is an aggressive autosomal dominant condition characterised by primary HPT which may develop in late childhood. Patients are also at risk of developing fibro-osseous jaw tumours (~30%), renal lesions (~15%) and approximately 15% of patients also develop parathyroid carcinoma. Up to 75% of female HPT-JT patients develop uterine tumours/polyposis. The penetrance of each symptom is variable, but overall is ~70-80%.

The condition may be caused by a pathogenic mutation in the *CDC73* gene (previously known as *HRPT2* and *C1orf28*) (1q25-q32) which encodes the protein parafibromin.

TESTING

Diagnostic:	Clinically affected patients.
Presymptomatic:	Individuals at risk of developing HPT-JT. Relatives of individuals in whom a *CDC73* pathogenic mutation has been identified.
Prenatal:	Prenatal testing is not usually requested.

REFERRALS

All samples MUST be accompanied by a completed pre-referral form (click here)**.**

- Clinical guidance and advice to direct appropriate gene screening is available from Professor Raj Thakker, Professor of Medicine, OCDEM, Churchill Hospital (rajesh.thakker@ndm.ox.ac.uk).
- UK diagnostic referrals are accepted from Clinical Genetics, Endocrinology and consultants from other relevant specialties.
- Presymptomatic referrals should ideally be referred through/in collaboration with Clinical Genetics departments.
- Requests for presymptomatic testing should either be discussed with the laboratory in advance or be accompanied by details regarding the known pathogenic mutation in the family.
- Prenatal requests are only accepted from Clinical Genetics and must be discussed with the laboratory and arranged in advance.

STRATEGY & TECHNICAL INFORMATION

- Mutation screening in diagnostic referrals is undertaken by fluorescent sequencing of the entire coding region and exon/intron boundaries of the *CDC73* gene (exons 1-17) and MLPA analysis for detection of deletions and duplications of one or more exon.
- When a pathogenic mutation has been identified in an individual, subsequent testing of family members (presymptomatic or diagnostic confirmation) involves testing for the familial mutation only.
- Clinical Sensitivity: Germline Pathogenic *CDC73* variants may be found in:
  - >50% of patients with a clinical diagnosis of HPT-JT syndrome.
  - ~20-29% of young patients with apparently sporadic parathyroid carcinoma. (Rich *et al*, Gene Reviews http://www.ncbi.nlm.nih.gov/books/NBK3789/)
  - 0-33% (combined frequency 14%) of individuals with familial isolated hyperparathyroidism (FIHP) (Newey *et al*, 2010, *Human Mutation*, **31**:295–307).
- Analytical Sensitivity: this analysis detects approx. 99% of sequence variants within the coding region and exon-intron boundaries of *CDC73*, and also deletions/duplications of one or more exon. Partial exon deletions/duplications may not be detected.

TARGET REPORTING TIMES

Diagnostic test:	40 days
Presymptomatic/Familial Mutation test:	10 days

N.B. Details are correct for the date of printing only – last updated 15/07/2015