Oxford Molecular Genetics Laboratory

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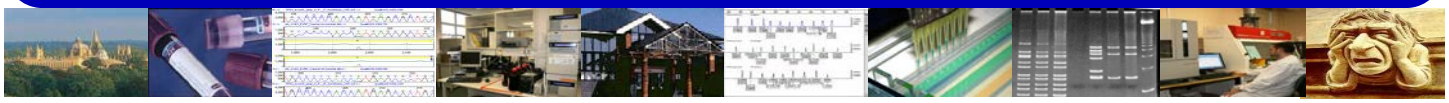

MULTIPLE ENDOCRINE NEOPLASIA (MEN1, MEN2, MEN3, MEN4, HPT-JT, FIPA) – OMIM 131100, 171400, 162300, 610755, 145001, 608266, 605555

INTRODUCTION

Multiple endocrine neoplasia (MEN) describes a dominant familial predisposition to tumours of endocrine organs.

The most common, MEN1 (*MEN1*) is characterised by hyperparathyroidism due to parathyroid gland hyperplasia or adenoma, functional or non-functional neuroendocrine tumours and anterior pituitary tumours. MEN2 (*RET*) is characterised by medullary thyroid carcinoma, pheochromocytoma and hyperparathyroidism, with MEN3 (MEN2B) also associated with ganglioneuromas of the lips, tongue and colon, and a marfanoid habitus. MEN4 (*CDKN1B*) has extensive clinical overlap with MEN1, and the most common features are parathyroid and pituitary neoplasias, possibly causing acromegaly. FIPA (also known as 'pituitary adenoma predisposition') is a condition that displays an autosomal dominant inheritance with incomplete penetrance. 15-20% of FIPA families have been identified to have mutations within the *AIP* gene. Families with *AIP* mutations are generally characterised by young onset somatotroph or lactotroph macroadenomas and frequently associated acromegaly. Hyperparathyroidism Jaw–Tumour syndrome (HPT-JT) is an aggressive autosomal dominant condition caused by mutations in the *CDC73* gene, and characterised by primary hyperparathyroidism (HPT) which may develop in late childhood. Patients with HPT-JT are at risk of developing fibro-osseous jaw tumours (~30%), renal lesions and uterine lesions, and approximately 15% of patients also develop parathyroid carcinoma (which is very rare in the general population).

TESTING

Diagnostic:	Clinically affected patients
Presymptomatic:	Individuals at risk of developing the associated syndrome. Clinically unaffected relatives of individuals in whom a pathogenic mutation has been identified.
Prenatal:	Prenatal testing is not usually requested

REFERRALS

All samples should 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 listed genes, and dosage analysis by multiplex ligation-dependent probe amplification (MLPA) for large scale rearrangements (*MEN1*, *CDC73, AIP* & *CDKN1B* only).
- Testing is undertaken simultaneously as a panel test comprising: *MEN1*, *CDC73*, *CDKN1B* (including analysis of uORF in the 5' UTR), *RET* (exons 5, 8, 10, 11, 13-16 only) and *AIP*.
- 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.

TARGET REPORTING TIMES

Diagnostic test:	42 days
Presymptomatic/Familial Mutation test:	14 days

N.B. Details are correct for the date of printing only – last updated 07/11/2019