Oxford Molecular Genetics Laboratory

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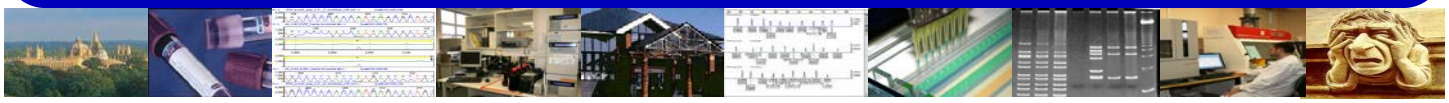

MULTIPLE ENDOCRINE NEOPLASIA TYPE 2 (MEN2A & MEN2B) – OMIM #171400 & 162300 & FAMILIAL MEDULLARY THYROID CARCINOMA (FMTC) – OMIM #155240

INTRODUCTION

Multiple endocrine neoplasia is characterised by the occurrence of tumours involving two or more endocrine glands.
MEN2 and FMTC are autosomal dominant conditions associated with pathogenic gain of function/activating variants in the *RET* proto-oncogene.
MEN2A is classically characterised by medullary carcinoma of the thyroid, plus pheochromocytoma or parathyroid adenoma/hyperplasia.
MEN2B is classically characterised by medullary carcinoma of the thyroid, pheochromocytoma, mucosal neuromas of the lips & tongue and a "Marfanoid" body habitus.
FMTC: ~75% of MTC is sporadic. Familial MTC is the autosomal dominant inheritance of MTC with no extra thyroid manifestations of MEN2.

TESTING

Diagnostic:	Clinically affected patients
Presymptomatic:	Individuals at risk of developing MEN2/FMTC. Clinically unaffected relatives of individuals in whom a *RET* 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

- Targeted mutation screening in diagnostic referrals is undertaken by fluorescent sequencing of *RET* exons 5, 8, 10, 11, 13-16.
  - MEN2A: ~95% of MEN2A individuals have a pathogenic variant occurring in *RET* exon 10 or 11 at codon 609,611,618,620 or 634
  - FMTC: ~85% of FMTC individuals have a pathogenic variant occurring in *RET* exon 10 or 11 at codon 609,611,618,620 or 634
  - MEN2B: ~94% of MEN2B cases are accounted for by a single mutation (p.Met918Thr) in *RET* exon 16.
- 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