MULTIPLE ENDOCRINE NEOPLASIA: TYPE 1

London Health Sciences Centre | St. Joseph's Health Care London

Pathology and Laboratory Medicine

Orderable – E-order/Requisition

Turnaround Time: 4-6 weeks **STAT: 4 weeks**

Laboratory:
Molecular Diagnostics Lab

Requisition:
MOLECULAR DIAGNOSTICS REQUISITION

Method of Analysis:
All coding exons and 20 bp of flanking intronic sequence are enriched using an LHSC custom targeted hybridization protocol (Roche Nimblegen), followed by high throughput sequencing (Illumina). Sequence variants and copy number changes are assessed and interpreted using clinically validated algorithms and commercial software (SoftGenetics: Nextgene, Geneticist Assistant, Mutation Surveyor; and Alamut Visual). All exons have >300x mean read depth coverage, with a minimum 100x coverage at a single nucleotide resolution. This assay meets the sensitivity and specificity of combined Sanger sequencing and

Alternate Name(s):

MEN 1

Specimen:

Whole blood-2 x 4 mL Lavender EDTA top Vacutainer tube

Collection Information:

Blood samples must be maintained at room temperature.

Reference Ranges:

See report

Interpretive Comments:

Multiple endocrine neoplasia type 1 (MEN 1) is a familial cancer syndrome characterised by parathyroid hyperplasia, pituitary adenomas, and neuroendocrine tumours of the pancreas and duodenum. In 1997, the MEN1 tumour suppressor gene was identified, and since then numerous germline mutations have been reported to be distributed throughout the gene (PMID:15714081, PMID:10090472, PMID:16595707, PMID:17342152). These mutations include missense, nonsense, and frameshift mutations, as well as mutations potentially responsible for abnormal RNA splicing, and highlight the need to investigate the entire MEN1 gene when characterizing new MEN 1 families. Coding sequence mutations that may disrupt the MEN1 gene can be screened for by direct sequence analysis of PCR-amplified fragments encompassing each of the exons, including flanking 5'(20bp) and 3'(10bp) intronic sequence, comprising the coding region of the MEN1 gene. Less common deleterious mutations consisting of genomic rearrangements of the MEN1 gene may be detected by the Multiplex Ligation-dependent Probe Amplification method (MLPA)5, which may be confirmed by LR-PCR, (unless the genomic deletion occurs at the extreme 5' or 3' ends of the gene), or by gene dosage determination (e.g. using a

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quantitative PCR-based approach). The approach described above is expected to provide an efficiency of MEN1 gene mutation detection approaching 100%.

Critical Information:

Pedigree required.

Storage and Shipment:

Must be received within 5 days of collection, shipped at room temperature by courier/overnight delivery.

MLPA copy number analysis. All variants interpreted as either ACMG category 1, 2, or 3 (pathogenic, likely pathogenic, VUS; PMID: 25741868) are confirmed using Sanger sequencing, MLPA, or other assays. ACMG category 4 and 5 variants (likely benign, benign) are not reported, but are available upon request. This assay has been validated at a level of sensitivity equivalent to the Sanger sequencing and standard copy number analysis (>99%; PMID: 27376475).

Test Schedule:
As required,
Monday to Friday 0800-1600 hours