Multiple Endocrine Neoplasia Type 1: MEN1 Gene Deletion/Duplication

Test Code: VS  
Turnaround time: 2 weeks  
CPT Codes: 81404 x1

Condition Description

Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant condition that includes a varying combination of more than 20 endocrine and non-endocrine tumors. Endocrine tumors associated with MEN1 include parathyroid tumors, pituitary tumors, well-differentiated endocrine tumors of the gastro-entero-pancreatic (GEP) tract, carcinoid tumors, and adrenocortical tumors. These tumors can become evident by overproduction of hormones by the tumor or by growth of the tumor itself. Non-endocrine tumors associated with MEN1 syndrome include facial angiofibromas, collagenomas, lipomas, meningiomas, ependymomas, and leiomyomas.

Parathyroid tumors are the main MEN1-associated endocrinopathy with onset in 90% of individuals at 20-25 years of age and manifest as hypercalcemia by age 50 years. Prolactinoma is the most common pituitary tumor. GEP tract endocrine tumors include gastrinoma, insulinoma, glucagonoma, and VIPoma. Carcinoid tumors are non-hormone-secreting and manifest as a large mass after age 50 years. Adrenocortical tumors are associated with primary hypercortisolism or hyperaldosteronism.

Approximately 88% of affected individuals will have facial angiofibromas, which are benign tumors comprising blood vessels and connective tissue. These consist of acneiform papules that do not regress and that may extend across the vermillion border of the lips. Collagenomas are seen in about in 72% of affected individuals and are multiple, skin-colored, sometimes hypopigmented, cutaneous nodules symmetrically arranged on the trunk, neck, and upper limbs. They are typically asymptomatic, roundish, and firm-elastic, from a few millimeters to several centimeters in size.

Clinical diagnostic criteria for MEN1 include the presence of two endocrine tumors that are parathyroid, pituitary, or GEP tract tumors. Familial MEN1 is defined as MEN1 in an individual who has either at least one first-degree relative with at least one of these endocrine tumors or only one organ involvement and an MEN1 disease-causing germline mutation. Molecular genetic testing of MEN1(11q13), the only gene known to be associated with MEN1, detects MEN1 mutations in about 80-90% of probands with familial MEN1 and in about 65% of individuals with a single occurrence of MEN1 in the family. Approximately 10% of cases are caused by de novo mutations.

Genes

MEN1

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of MEN1 in individuals who have tested negative for sequence analysis
- Individuals at-risk for MEN1 due to family history who have tested negative for sequence analysis

Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region. Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient’s clinical and/or biochemical phenotype.

Specimen Requirements
Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequencing analysis of the MEN1 gene is available (VQ) and is required before deletion/duplication analysis.
- Prenatal testing is available to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.