Endocrine Cancer Panel: Sequencing and CNV Analysis

Test Code: MM202
Turnaround time: 4 weeks
CPT Codes: 81404 x1, 81405 x1, 81406 x1, 81321 x1

Condition Description

Thyroid cancer is divided into several subcategories: (1) differentiated (follicular, papillary and Hurthle); (2) medullary; and (3) anaplastic (aggressive undifferentiated tumor). Medullary thyroid cancer (MTC) develops from the “C” or parafollicular cells of the thyroid gland which produce calcitonin. Approximately 80% of the cases of MTC are sporadic. The remaining inherited syndromes include multiple endocrine neoplasia ( MEN ) type 2A (also known as MEN 2A), MEN 2B, and familial MTC (FMTC). All three of these subtypes, MEN 2A, MEN 2B and FMTC, are inherited in an autosomal dominant pattern and involve an elevated risk for the development of medullary carcinoma of the thyroid. MEN 2A and MEN 2B have an increased risk for the development of pheochromocytoma. MEN 2A has an elevated risk for parathyroid adenoma or hyperplasia. Additional features in MEN 2B include distinctive facies with enlarged lips, mucosal neuromas of the lips and tongue, and ganglioneuromatosis of the gastrointestinal tract. MTC generally occurs in early childhood in MEN 2B, early adulthood in MEN 2A, and middle age in FMTC.

References:

Genes
- AIP, CDC73, CDKN1B, MAX, MEN1, PRKAR1A, PTEN, RET, SDHAF2, SDHB, SDHC, SDHD, TMEM127, TP53, VHL

Indications

The test is indicated for:
- Individuals with a clinical or suspected diagnosis of endocrine cancer.

Methodology

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Copy Number Analysis: Comparative analysis of the NGS read depth (coverage) of the targeted regions of genes on this panel was performed to detect copy number variants (CNV). The accuracy of the detected variants is highly dependent on the size of the event, the sequence context and the coverage obtained for the targeted region. Due to these variables and limitations a minimum validated CNV size cannot be determined; however, single exon deletions and duplications are expected to be below the detection limit of this analysis.

Detection

Next Generation Sequencing: Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical sensitivity for sequence variant detection is ~99%.

Copy Number Analysis: The sensitivity and specificity of this method for CNV detection is highly dependent on the size of the event, sequence context and depth of coverage for the region involved. The assay is highly sensitive for CNVs of 500 base pairs or larger and those containing at least 3 exons. Smaller (< 500 base pairs) CNVs and those that involving only 1 or 2 exons may or may not be detected depending on the sequence context, size of exon(s) involved and depth of coverage.
## Specimen Requirements

Submit only 1 of the following specimen types

### Type: DNA, Isolated

**Specimen Requirements:**
- Microtainer
- 8µg

Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

### Type: Saliva

**Specimen Requirements:**
- Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

### Type: Whole Blood (EDTA)

**Specimen Requirements:**
- EDTA (Purple Top)
  - Infants and Young Children (2 years of age to 10 years old): 3-5 ml
  - Older Children & Adults: 5-10 ml
  - Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

## Special Instructions

This test is for germline mutation analysis. DNA isolated from FFPE tumor samples is not suitable for this test.

## Related Tests

- Hereditary Cancer Syndrome: Sequencing Panel.
- Endocrine Cancer: Deletion/Duplication Panel.