Papillary Renal Carcinoma: MET Gene Sequencing

Test Code: UX
Turnaround time: 4 weeks
CPT Codes: 81479 x1

Condition Description

Papillary renal tumors, which account for 15 to 20% of renal carcinomas, occur in both sporadic and familial forms. Hereditary papillary renal carcinoma (HPRC) is an autosomal dominant hereditary cancer syndrome in which affected individuals are at risk of developing bilateral, multifocal type 1 papillary renal carcinoma, often at a late age of onset (50 to 70 years). Today, the kidney is the only organ to be affected in HPRC patients. The tumours are mostly well differentiated; however, they are malignant and can metastasize. HPRC is a highly penetrant disease in which affected individuals are highly likely to develop bilateral, multifocal type 1 papillary kidney cancer. In the early reports, this disease was described as having a late onset; however, recently an early onset form of this disease has been described.

Germline mutations in the MET gene on chromosome 7 were identified in a hereditary form of papillary renal carcinoma. MET belongs to the family of tyrosine kinases, the members of which play important roles in transmitting signals from the cellular surface to the nucleus. Missense mutations in the tyrosine kinase domain of the Met proto-oncogene at 7q31 are responsible for constitutive activation of the MET protein in HPRC.

For patients with suspected hereditary papillary renal carcinoma, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References


Click here for the OMIM summary on this condition.

Genes

MET

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of hereditary papillary renal carcinoma
- Individuals at-risk for hereditary papillary renal carcinoma due to family history

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.

Detection

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ≈99%

Specimen Requirements

Submit only 1 of the following specimen types

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 24 hours of collection. Do not refrigerate or freeze.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
8µg
Isolation using the Perkin Elmer™Chemagen™ 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.

Related Tests

- Deletion/duplication analysis of the \textit{MET} gene by CGH array is available for those individuals in whom sequence analysis is negative (UY).
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing 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.