Papillary Renal Carcinoma: \textit{MET} Gene Sequencing

\textbf{Test Code:} UX  
\textbf{Turnaround time:} 4 weeks  
\textbf{CPT Codes:} 81479 x1

\section*{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). To date, the kidney is the only organ to be affected in HPRC patients. The tumors are most often 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 \textit{MET} gene on chromosome 7 were identified in a hereditary form of papillary renal carcinoma. \textit{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. \textit{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.

\section*{References}


Click here for the OMIM summary on this condition.

\section*{Genes}

\textbf{MET}

\section*{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

\section*{Methodology}

\textbf{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.

\section*{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%

\section*{Specimen Requirements}

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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.

**Related Tests**

- Deletion/duplication analysis of the 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.