Renal19
Hereditary Cancer Gene Panel

including: sequencing and high resolution deletion/duplication analysis

PANEL DESCRIPTION:
Using sequencing and high resolution deletion/duplication analysis, the Hereditary Renal19 Cancer Panel analyzes 19 genes for genetic variants that predispose a person to renal cancer and, in some cases, other cancers and noncancerous conditions. Identifying a causative genetic variant provides valuable information for the patient’s diagnosis, medical management, surveillance (early screening for other associated cancers), and familial screening. Affected individuals often warrant increased surveillance due to earlier onset of disease and have an increased potential for complex medical issues such as bilateral kidney involvement.

TEST DETAILS:
- This panel includes both sequencing and high resolution deletion/duplication analysis of the genes specified when performed on a blood specimen.
  - Sequencing is performed using a customized next generation sequencing library. Analysis includes the coding exons of all genes in the panel plus ten bases into the introns and untranslated regions (5' and 3'). Sanger sequencing is performed to confirm variants classified as pathogenic or suspected pathogenic.
    - Of note, deletions of EPCAM are the only known pathogenic variants in this gene; therefore, sequencing analysis of EPCAM is not performed.
  - Deletion/duplication analysis is performed using a high resolution, custom microarray platform designed to target the genes of interest at the exon level.
    - In addition, deletion/duplication analysis of PMS2 is performed using Multiplex Ligation-dependent Probe Amplification (MLPA) because of the presence of highly homologous pseudogenes. A rare rearrangement of exons 1-7 in the MSH2 gene, the Boland inversion, is also detected using MLPA. However, MLPA cannot be performed on a buccal specimen.
- Detection rates are limited to the genes specified; this test does not provide whole genome analysis.
- Gene panels are a more cost-effective approach than single gene testing to confirm or establish a diagnosis. However, if single gene testing is desired for the patient or family members of an individual with a known mutation, that must be ordered separately.

INDICATIONS FOR TESTING:
- Family history of renal cancer in multiple individuals
- Renal cancer diagnosed < age 45
- Multifocal or bilateral renal cancer
- Multiple primary cancers in the same person which may include the skin, brain, heart, lungs, pancreas, colon, paraganglioma, pheochromocytoma, or other neuroendocrine tumors
- Renal cancer and other findings, such as cysts in the lung, kidneys, pancreas, adnexa or epididymis; pneumothorax, uterine fibroids; or skin findings such as cutaneous leiomyoma, fibrofolliculoma, or angiofibroma
- Personal and/or family history raising concern for the syndromes included in this panel
  - Hereditary papillary renal carcinoma
  - PTEN hamartoma (Cowden) syndrome GeneReviews® http://www.ncbi.nlm.nih.gov/books/NBK1226/
- Known familial variant in any of the genes included in this panel (targeted analysis)
SPECIMEN COLLECTION & TRANSPORT:
Complimentary test kits are available upon request, but are not required.

SAMPLE TYPE and REQUIREMENTS:
- **blood**: 3-5 ml whole blood in an EDTA tube (purple top)
- **buccal mucosa swab**: 5 swabs
- **extracted DNA (from blood or buccal)**: 5 µg in a DNA microcentrifuge tube

^ Deletion/duplication and rearrangement analyses cannot be performed for indicated genes on a buccal specimen.

SHIPPING:
- Maintain and ship samples at room temperature.
- Coordinate transport for sample to be received in our laboratory within 24-48 hours of collection.
  - **LOCAL**: Call 402-559-5070 (option 1)
  - **OUT OF AREA**: Prior to shipment, please fax the completed test request form to 402-559-7248, including the FedEx® airbill tracking number.
    - Saturday delivery MUST be checked when sending FedEx® on Friday.
    - Please include Internal Billing Reference # 3155070600 on the FedEx® airbill.
  - **Ship To**: Human Genetics Laboratory – Zip 5440
  - UNMC Shipping & Receiving Dock
  - 601 S. Saddle Creek Road
  - Omaha, NE 68106

FORMS FOR TESTING: The following forms can be downloaded via our website.
- **Required**: Hereditary Cancer Test Request Form
- **Optional**: Informed Consent for Hereditary Cancer Genetic Testing

POTENTIAL TEST RESULTS:
- **Positive for a Pathogenic Variant** – This designation is reported when a pathogenic change is identified in a gene and the change is known to increase the risk for certain cancers.
- **Negative** – This designation is reported when no harmful or uncertain changes are found in any of the genes tested.
- **A Variant of Uncertain Clinical Significance (UCS)** – This designation is reported when an inconclusive change in a gene is found; the change may increase the risk for cancer or be harmless. Variants of uncertain clinical significance may also be classified as “Likely Pathogenic” or “Likely Benign” based on the ACMG recommendations for variant classification.

TURNAROUND TIME: For all sample types, results are typically available in 14 days.

BILLING: Our laboratory offers patient/self-pay, insurance (including Medicare/Medicaid), and client/institution billing options. Verifying coverage requirements or obtaining preauthorization PRIOR TO OR AT THE TIME OF SPECIMEN COLLECTION is often necessary. We provide preauthorization services upon request by calling 402-559-5070 (option 3); the following form is helpful for obtaining the information required by insurance providers and can be downloaded via our website.
- **Insurance Preauthorization Request**

In some circumstances, a test may be warranted even though insurance coverage is denied or not guaranteed. For these situations, we request the following form be signed by the patient and submitted with the sample. This helps inform patients of their potential financial responsibility, should the costs of genetic testing not be paid by their insurance provider.
- **Advanced Beneficiary Notice of Noncoverage (ABN)** – required when billing Medicare
CPT CODES: 81405

PRICING: For current costs contact the laboratory billing staff at 402-559-5070 (option 3).

GENE LIST:

<table>
<thead>
<tr>
<th>CDC73</th>
<th>MET</th>
<th>MSH6</th>
<th>SDHB</th>
<th>TSC1</th>
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<tbody>
<tr>
<td>EPCAM</td>
<td>MITF</td>
<td>PMS2 ^</td>
<td>SDHC</td>
<td>TSC2</td>
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<tr>
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<tr>
<td>FLCN</td>
<td>MSH2 ^</td>
<td>SDHA</td>
<td>TP53</td>
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</tr>
</tbody>
</table>

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RESOURCES: The following resource can be downloaded via our website, or you may request brochures for your clinic by contacting our marketing specialist at 402-559-6935 | humangenetics@unmc.edu.

- PATIENT BROCHURE: Renal19

REFERENCES:


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