Endocrine|Paraganglioma-Pheochromocytoma17
Hereditary Cancer Gene Panel

including: sequencing and high resolution deletion/duplication analysis

PANEL DESCRIPTION:
Using sequencing and high resolution deletion/duplication analysis, the Hereditary Endocrine|Paraganglioma-Pheochromocytoma17 Cancer Panel analyzes 17 genes for genetic variants that predispose a person to paragangliomas (PGLs), including pheochromocytomas (PCCs), and other neuroendocrine tumors. Many neuroendocrine tumors are benign, localized, and sporadic; however, they may also be part of a hereditary cancer predisposition syndrome and may increase the patient’s risk for other medical conditions, such as hypertension and stroke. Individuals with hereditary neuroendocrine tumors are more likely to present earlier, to have multifocal or bilateral disease, and to experience recurrence and metastasis. Identifying a causative genetic variant provides valuable information for the patient’s diagnosis, medical management, malignancy potential, surveillance (early screening for other associated tumors), and familial screening.

TEST DETAILS:
• This panel includes both sequencing and high resolution deletion/duplication analysis of the genes specified.
  o 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.
  o Deletion/duplication analysis is performed using a high resolution, custom microarray platform designed to target the genes of interest at the exon level.
• 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 paraganglioma, pheochromocytoma, or other neuroendocrine tumors, which may include tumors of the thyroid, parathyroid, pituitary gland, lung, pancreas, kidney, and/or gastrointestinal tract (e.g., gastrointestinal stromal tumors [GIST])
• Neuroendocrine tumor with a second primary lesion
• Personal and/or family history of
  o Sympathetic or malignant extra-adrenal paragangliomas
  o Bilateral or multifocal paragangliomas or pheochromocytomas
  o Paraganglioma or pheochromocytoma
• Personal and/or family history raising concern for the syndromes included in this panel
  o Familial medullary thyroid carcinoma (FMTC) GeneReviews® http://www.ncbi.nlm.nih.gov/books/NBK1345/
  o Hereditary paraganglioma-pheochromocytoma syndrome (PGL/PCC) GeneReviews®
  o Li-Fraumeni syndrome GeneReviews® http://www.ncbi.nlm.nih.gov/books/NBK1311/
  o Multiple endocrine neoplasia (MEN2) type I and II GeneReviews® http://www.ncbi.nlm.nih.gov/books/NBK1257/
  o Neurofibromatosis type I (NF1) GeneReviews® http://www.ncbi.nlm.nih.gov/books/NBK1109/
• **PTEN hamartoma tumor (Cowden) syndrome** GeneReviews® http://www.ncbi.nlm.nih.gov/books/NBK1488/
• 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

**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: 81437, 81438

PRICING: Contact the laboratory billing staff for current costs.

GENE LIST:

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<tr>
<th>CDC73</th>
<th>NF1</th>
<th>RET</th>
<th>SDHB</th>
<th>TMEM127</th>
<th>TSC2</th>
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<td>PRKAR1A</td>
<td>SDHA</td>
<td>SDHC</td>
<td>TP53</td>
<td>VHL</td>
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<tr>
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<td>SDHAF2</td>
<td>SDHD</td>
<td>TSC1</td>
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</tbody>
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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: Endocrine|Paraganglioma-Pheochromocytoma17

REFERENCES:


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