**UroGenRA™-Kidney Array-CGH Assay**
for the diagnosis and subtyping of renal cortical neoplasms

**INFORM**
UroGenRA™-Kidney aCGH assesses **multiple genomic biomarker sets** providing more information than other common methods.

**PREDICT**
KidneyPath™ assists in determining **proper renal tumor subtype**.

**DECIDE**
Together with other clinical and laboratory findings, UroGenRA™-Kidney can assist in devising the **best treatment plan for an individual patient**.

CLIA and New York State Approved

For more information, please visit [www.cancergenetics.com](http://www.cancergenetics.com)
Kidney Cancer

Approximately 65,000 new cases of kidney cancer and about 13,500 deaths from the disease occur in the U.S. each year [1]. Renal cell carcinoma (RCC) is the most abundant and lethal form of kidney cancer. Incidence has been on the rise since the late 1990’s with the greatest increase observed among patients ages 70 to 90 years [2].

RCC arises in the renal cortex and is the predominant malignant type of renal cortical neoplasm. There are three main subtypes of RCC: clear cell (ccRCC), papillary (pRCC), and chromophobe (chrRCC). The next most frequent renal cortical neoplasm is oncocytoma (OC), which is benign and can be followed by active surveillance. Choice of therapy depends upon the kidney cancer subtype as well as the patient’s age and comorbidities.

Despite advancements in the diagnosis of renal tumors in recent years, the mortality rate of localized RCC (Stage I and II) is steadily increasing. As much as 20% of stage I renal masses are benign while an estimated 20% to 25% are potentially aggressive masses [2]. Nephron-sparing surgery, such as laparoscopic partial nephrectomy, or radical nephrectomy is the standard treatment. However, active surveillance may be recommended to patients who are unfit for surgical intervention or have a limited life expectancy [3]. In addition, selected patients with small renal masses (SRMs) may consider active surveillance with delayed treatment for progression [3]. Often patients with benign neoplasms are subjected to nephrectomy likely because current imaging techniques are limited in distinguishing whether an SRM is benign or malignant. Nephrectomy may predispose patients to chronic kidney disease, increased cardiovascular risk and shortened overall survival [2]. Difficulties can also arise in the differential diagnosis of chrRCC (malignant) versus OC (benign) when selecting whether or not to perform surgery. Thus accurate diagnosis and subtyping can better differentiate those patients with benign renal neoplasms and SRMs who are eligible for active surveillance and can avoid overtreatment.

Image-guided biopsies have become a common diagnostic option for better understanding of tumor nature/subtype to aid in patient management. Needle biopsies carry a minimal risk and current NCCN guidelines include needle biopsy as an option to confirm the malignancies of SRMs. However, a major challenge with needle biopsy is to obtain enough material for accurate diagnostication with about 15% of biopsies being inconclusive by histology [3]. Thus, there is a compelling need to develop ancillary assays that could assist histology to accurately classify SRMs.

Over the years, specific genetic alterations have been associated with the four main renal cortical neoplasm subtypes. For instance, alteration of the Von Hippel-Lindau (VHL) gene has been suggested to be a pathogenetic event in ccRCC. Trisomy of chromosomes 7 and 17 are frequently observed in pRCC, and widespread monosomies in chrRCC. OC display a nearly diploid genome with loss of chromosome 1, 14 and Y. Therefore, genomic imbalance may be used to classify renal neoplasm subtypes.

The UroGenRA™-Kidney Array-CGH provides genomic diagnostic information to assist routine histology in the subtyping of ccRCC, pRCC, chrRCC and OC from either core needle biopsies or resected specimens. This genomic assessment can give information to properly select the best treatment strategy and can prevent unnecessary surgical intervention.

The Process of Array-CGH

1. Patient and control DNA labeled with fluorescent dyes are applied to the microarray.
2. Patient and control DNA are hybridized to the microarray.
3. The fluorescent signals are measured by the microarray scanner.
4. Next, the data is analyzed by computer software which then generates a plot.

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In a Single Test, UroGenRA™-Kidney Provides Genomic Data for the Histologic Classification of Renal Masses

**UroGenRA™**
- UroGenRA™ has 101 regions of the human genome represented at an average resolution of 41.5kbp.
- Regions covered by UroGenRA™ can be used for gain/loss evaluation in urogenital neoplasms including kidney, prostate and bladder cancers.

**UroGenRA™-Kidney**
- UroGenRA™-Kidney assesses 16 genomic aberrations that have diagnostic significance in renal cortical neoplasms.
- UroGenRA™-Kidney can use DNA from either core needle biopsies or resected specimens, both provided as fresh frozen tissue.

**KidneyPath™**
Cancer Genetics has developed a proprietary aCGH-based algorithm for subtyping RCC and OC, KidneyPath™. The results from the UroGenRA™-Kidney test are analyzed for specific genomic aberrations. Specimens classified “normal” by the decision tree are reflexed to FISH (CCND1 break apart) in order to rule in/out OC subtype. The RCC or OC subtypes are determined based on the presence of gains and losses detected by UroGenRA™-Kidney.

Validated using:
- Over 100 fresh frozen RCC specimens (surgically-resected) and needle biopsy specimens (MSKCC).
- Publicly available data & published literature.
- The Cancer Genome Atlas (TCGA) database, >500 specimens.

References:
1. The American Cancer Society. www.cancer.org
Sample Report

Assay Specifications
Sensitivity
Limit of detection is 40% (assay sensitivity).

Specimen Requirements
For both biopsies and resected specimens, a minimum of 70% tumor population is preferred.
Biopsy: Min. 3-4 needle/core biopsies (18-gauge needle) placed in a cryovial containing saline, transport frozen.
Resected specimen: A minimum of 0.2x0.2x0.2cm tissue, snap-frozen in a cryovial and transported in frozen condition.

CPT Code: 81479

Turnaround Time: 10-14 days

**UroGenRA™ - Kidney Array-CGH Report**

<table>
<thead>
<tr>
<th>Genomic Aberration</th>
<th>Result for Aberration</th>
<th>Genomic Aberration</th>
<th>Result for Aberration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of VHL (chr3: 10.1-10.2 Mb)</td>
<td>POSITIVE</td>
<td>Gain of chr3</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>Loss of chr2</td>
<td>NEGATIVE</td>
<td>Loss of 6p25-q25</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>Gain of 17q12-q25</td>
<td>NEGATIVE</td>
<td>Loss of 10p15-q25</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>Gain of chr7</td>
<td>NEGATIVE</td>
<td>Loss of chr17</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>Gain of chr12</td>
<td>NEGATIVE</td>
<td>Loss of 8p (1-5, 19-27 Mb)</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>Gain of 16p13-p12</td>
<td>NEGATIVE</td>
<td>Loss of 1p36-q42</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>Gain of 20q13</td>
<td>NEGATIVE</td>
<td>Loss of 3p21.2-21.31</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>Gain of 5q (171-181 Mb)</td>
<td>POSITIVE</td>
<td>Loss of 21q22</td>
<td>NEGATIVE</td>
</tr>
</tbody>
</table>

**Interpretation:** Genomic alterations detected are consistent with the diagnosis of Clear Cell Renal Cell Carcinoma.

**Description:**
The gain and loss of specific genomic regions associated with RCC subtypes are considered to have diagnostic value and aid in their classification. Loss of VHL gene at the 3p25 locus is a hallmark for clear cell RCC subtype.\(^2\) Gains of chromosomes 7 and 17 are frequently observed in papillary RCC and widespread monosomies (especially loss of chromosomes 2, 6, 10 and 17) are found in chromophobe RCC.\(^1\)\(^2\) Oncocytoma display a nearly diploid genome with loss of chromosome 1 or loss of 3p21.

This assay utilizes microarray-based comparative genomic hybridization (array CGH) to simultaneously detect the gain and loss of multiple loci in specimen DNA using the human genome build GRCh37/hg19. The sensitivity of the assay is 40%. Samples in which the tumor cells are present at less than 40%, aberrations may not be detected. The results of this study are to be interpreted in context with other clinical and/or histopathological findings.

**References:**

Licensure
CAP (Laboratory #: 7191582, AU-ID: 1434060), CLIA (Certificate #: 31D1038733), New Jersey (CLIS ID #: 0002299), New York State (PFI: 8192), Pennsylvania (031978), Florida (800018142), Maryland (1395).