Hereditary Cancer Panel

Pathogenic variants in the genes analyzed by this panel cause variable phenotypes and cancer risks, and have been implicated in hereditary cancer. Hereditary predisposition is often characterized by early age of cancer onset (typically before age 50), and the development of two or more cancers, multifocal cancers, or similar cancers in an individual or in a closely related family member(s). See Genes Tested table below for more details regarding the genes and syndromes included on the Hereditary Cancer Panel.

Disease Overview

Etiology
Approximately 5-10% of cancer is associated with a hereditary cause.

Inheritance
- All genes tested on this panel are autosomal dominant with the exception of:
  - SDHD gene – autosomal dominant with paternal parent-of-origin effect
  - MAX and SDHAF2 genes – autosomal dominant with possible paternal parent-of-origin effect
  - MUTYH gene – autosomal recessive but may also have autosomal dominant risks that are not well-defined
  - MSH3 and NTHL1 – autosomal recessive
- Some genes are associated with autosomal recessive childhood cancer predisposition or other syndromes.
- See table below for additional details.

Test Description
See Genes Tested table for genes included in the panel.

Clinical Sensitivity
Variable, dependent on phenotype/condition

Testing Strategy
- Indications for ordering
  - To diagnose a hereditary cancer syndrome in an individual with a personal and/or family history consistent with more than one cancer syndrome
- Contraindications for ordering
  - Should not be ordered to detect somatic variants associated with malignancy because sensitivity for mosaic variants is low with methodology used for germline assays
  - Individuals with hematological malignancy and/or a previous allogenic bone marrow transplant should not undergo molecular genetic testing on peripheral blood specimen.
    - Testing of cultured fibroblasts is required for accurate interpretation of test results.
  - When a relative has a previously identified pathogenic variant, see Familial Mutation, Targeted Sequencing (2001961).

Limitations
- A negative result does not exclude a heritable form of cancer.
- Diagnostic errors can occur due to rare sequence variations.
- Interpretation of this test result may be impacted if this individual has had an allogeneic stem cell transplantation.

- The following will not be evaluated:
  - Variants outside the coding regions and intron-exon boundaries of the targeted genes
  - Regulatory region variants and deep intronic variants
  - Breakpoints of large deletions/duplications
  - Deletions/duplications in AXIN2, MSH3, NF1, RECQL, SMARCA4, WT1
  - Sequence variants in EPCAM
  - Noncoding transcripts
  - The following exons are not sequenced due to technical limitations of the assay:
    - CHEK2 (NM_001349956) 4; (NM_001005735) 3; (NM_007194) 10, 12, 14, 15
    - RECQL (NM_002907) 14, 15
    - SDHC (NM_001035511) 5
    - SDHD (NM_001276506) 4

- The following may not be detected:
  - Deletions/duplications/insertions of any size by massively parallel sequencing
  - Deletions/duplications less than 1kb in the targeted genes
  - Some variants due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions
  - Low-level somatic variants
  - Single exon deletions/duplications in the following exons:

<table>
<thead>
<tr>
<th>Gene</th>
<th>Exon(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APC</td>
<td>(NM_001127511) 1</td>
</tr>
<tr>
<td>BAP1</td>
<td>(NM_004656) 1</td>
</tr>
<tr>
<td>BARD1</td>
<td>(NM_000465) 1</td>
</tr>
<tr>
<td>BMPR1A</td>
<td>(NM_004329) 9</td>
</tr>
<tr>
<td>BRCA1</td>
<td>(NM_007300) 13</td>
</tr>
<tr>
<td>CDH1</td>
<td>(NM_004360) 1</td>
</tr>
<tr>
<td>CDKN2A</td>
<td>(NM_000077) 2</td>
</tr>
<tr>
<td>CDKN2A</td>
<td>(NM_058195) 2</td>
</tr>
<tr>
<td>CHEK2</td>
<td>(NM_001005735) 3</td>
</tr>
<tr>
<td>CHEK2</td>
<td>(NM_007194) 11, 12, 14, 15</td>
</tr>
<tr>
<td>FH</td>
<td>(NM_000143) 1</td>
</tr>
<tr>
<td>FLCN</td>
<td>(NM_144997) 8</td>
</tr>
<tr>
<td>MAX</td>
<td>(NM_001320415) 5</td>
</tr>
<tr>
<td>MAX</td>
<td>(NM_145113) 5</td>
</tr>
<tr>
<td>MRE11</td>
<td>(NM_005591) 2</td>
</tr>
<tr>
<td>MSH2</td>
<td>(NM_000251) 1</td>
</tr>
<tr>
<td>MSH2</td>
<td>(NM_001258281) 2</td>
</tr>
<tr>
<td>Gene</td>
<td>Exon(s)</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>MSH6</td>
<td>(NM_000179) 10</td>
</tr>
<tr>
<td>MUTYH</td>
<td>(NM_001128425) 1</td>
</tr>
<tr>
<td>NF2</td>
<td>(NM_000268) 7, 13, 16</td>
</tr>
<tr>
<td>NTHL1</td>
<td>(NM_002528) 3, 4, 5, 6</td>
</tr>
<tr>
<td>PALB2</td>
<td>(NM_024675) 1</td>
</tr>
<tr>
<td>POLD1</td>
<td>(NM_002691) 6, 18, 25</td>
</tr>
<tr>
<td>PTEN</td>
<td>(NM_000314) 8, 9</td>
</tr>
<tr>
<td>PTEN</td>
<td>(NM_001304717) 1</td>
</tr>
<tr>
<td>RAD51D</td>
<td>(NM_002878) 1</td>
</tr>
<tr>
<td>RB1</td>
<td>(NM_000321) 1</td>
</tr>
<tr>
<td>RET</td>
<td>(NM_020975) 1</td>
</tr>
<tr>
<td>SDHD</td>
<td>(NM_001276506) 4</td>
</tr>
<tr>
<td>SMARCB1</td>
<td>(NM_003073) 5</td>
</tr>
<tr>
<td>SUFU</td>
<td>(NM_001178133) 11</td>
</tr>
<tr>
<td>SUFU</td>
<td>(NM_016169) 1</td>
</tr>
<tr>
<td>TP53</td>
<td>(NM_001126113) 10</td>
</tr>
<tr>
<td>TP53</td>
<td>(NM_001126114) 10</td>
</tr>
<tr>
<td>TSC2</td>
<td>(NM_000548) 17, 29, 41</td>
</tr>
<tr>
<td>VHL</td>
<td>(NM_000551) 1</td>
</tr>
</tbody>
</table>

Analytical Sensitivity

- For Sanger sequencing and multiplex ligation-dependent probe amplification (MLPA) of PMS2: 99%
- For massively parallel sequencing:

<table>
<thead>
<tr>
<th>Variant Class</th>
<th>Analytical Sensitivity (PPA) Estimate (%)</th>
<th>Analytical Sensitivity (PPA) 95% Credibility Region (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNVs</td>
<td>99.2</td>
<td>96.9-99.4</td>
</tr>
<tr>
<td>Deletions 1-10 bp</td>
<td>93.8</td>
<td>84.3-98.2</td>
</tr>
<tr>
<td>Deletions 11-44 bp</td>
<td>100</td>
<td>87.8-100</td>
</tr>
</tbody>
</table>

*Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.
bp, base pairs; PPA, positive percent agreement; SNVs, single nucleotide variants
### Analytical Sensitivity (PPA) Estimate

<table>
<thead>
<tr>
<th>Variant Class</th>
<th>Analytical Sensitivity (PPA) Estimate (%)</th>
<th>Analytical Sensitivity (PPA) 95% Credibility Region (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insertions 1-10 bp</td>
<td>94.8</td>
<td>86.8-98.5</td>
</tr>
<tr>
<td>Insertions 11-23 bp</td>
<td>100</td>
<td>62.1-100</td>
</tr>
</tbody>
</table>

*Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

bp, base pairs; PPA, positive percent agreement; SNVs, single nucleotide variants

### Genes Tested

<table>
<thead>
<tr>
<th>Gene</th>
<th>MIM Number</th>
<th>Disorder/Associated Cancer(s)/Tumor(s)</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALK</strong></td>
<td>105590</td>
<td>Associated cancer(s)/tumor(s): neuroblastoma, ganglioneuroblastoma, ganglioneuroma</td>
<td>AD</td>
</tr>
<tr>
<td><strong>APC</strong></td>
<td>611731</td>
<td>Familial adenomatous polyposis (FAP)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Attenuated FAP (AFAP)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): colon, duodenal, thyroid, pancreas, stomach, medulloblastoma, hepatoblastoma</td>
<td></td>
</tr>
<tr>
<td><strong>ATM</strong></td>
<td>607585</td>
<td>Associated cancer(s)/tumor(s): breast, ovarian, colorectal</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ataxia-telangiectasia (AT)</td>
<td></td>
</tr>
<tr>
<td><strong>ATR</strong></td>
<td>601215</td>
<td>Familial cutaneous telangiectasia and cancer syndrome (FCTCS)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): oropharyngeal</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Seckel syndrome 1</td>
<td>AR</td>
</tr>
<tr>
<td><strong>AXIN2</strong></td>
<td>604025</td>
<td>Oligodontia-colorectal cancer syndrome (OSCRCS)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s): colon</td>
<td></td>
</tr>
<tr>
<td><strong>BAP1</strong></td>
<td>603089</td>
<td>BAP1 tumor predisposition syndrome (BAP1-TPDS)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): uveal melanoma, malignant mesothelioma, cutaneous melanoma, renal cell carcinoma, basal cell carcinoma</td>
<td></td>
</tr>
<tr>
<td><strong>BARD1</strong></td>
<td>601593</td>
<td>Associated cancer(s)/tumor(s): breast</td>
<td>AD</td>
</tr>
<tr>
<td><strong>BMPR1A</strong></td>
<td>601299</td>
<td>Juvenile polyposis syndrome (JPS)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): colon, stomach, small intestine, pancreas</td>
<td></td>
</tr>
<tr>
<td><strong>BRCA1</strong></td>
<td>113705</td>
<td>Hereditary breast and ovarian cancer (HBOC) syndrome</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): breast, ovarian, prostate, pancreas, melanoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fanconi anemia, complementation group S</td>
<td>AR</td>
</tr>
<tr>
<td><strong>BRCA2</strong></td>
<td>600185</td>
<td>Hereditary breast and ovarian cancer (HBOC) syndrome</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): breast, ovarian, prostate, pancreas, melanoma</td>
<td></td>
</tr>
</tbody>
</table>

*Association is suggested but not well-established at this time

b|Possible paternal parent-of-origin effect

Paternal parent-of-origin effect

AD, autosomal dominant; AR, autosomal recessive
<table>
<thead>
<tr>
<th>Gene</th>
<th>MIM Number</th>
<th>Disorder/Associated Cancer(s)/Tumor(s)</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRIP1</td>
<td>605882</td>
<td>Fanconi anemia, complementation group D1</td>
<td>AR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): ovarian, breast</td>
<td>AD</td>
</tr>
<tr>
<td>CDH1</td>
<td>192090</td>
<td>Hereditary diffuse gastric cancer (HDGC)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): diffuse gastric, lobular breast</td>
<td>AD</td>
</tr>
<tr>
<td>CDK4</td>
<td>123829</td>
<td>Associated cancer(s)/tumor(s): cutaneous melanoma</td>
<td>AD</td>
</tr>
<tr>
<td>CDKN1B</td>
<td>600778</td>
<td>Multiple endocrine neoplasia (MEN) Type 4</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): parathyroid, pituitary, gastrinoma, insulinoma, gastro-entero-pancreatic (GEP), carcinoid, adrenocortical, nonendocrine</td>
<td>AD</td>
</tr>
<tr>
<td>CDKN2A</td>
<td>600160</td>
<td>Familial atypical multiple mole melanoma-pancreatic carcinoma (FAMMM-PC) syndrome (also known as melanoma-pancreatic cancer syndrome)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): cutaneous melanoa, pancreas</td>
<td>AD</td>
</tr>
<tr>
<td>CHEK2</td>
<td>604373</td>
<td>Associated cancer(s)/tumor(s): breast, colorectal, prostate, thyroid</td>
<td>AD</td>
</tr>
<tr>
<td>DICER1</td>
<td>606241</td>
<td>Dicer1-related disorders</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): pleuropulmonary blastoma, ovarian sex cord-stromal tumors, cystic nephroma, thyroid</td>
<td>AD</td>
</tr>
<tr>
<td>EPCAM</td>
<td>185535</td>
<td>Lynch syndrome/hereditary nonpolyposis colorectal cancer (HNPCC)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): colorectal, endometrial, stomach, ovarian, and others</td>
<td>AD</td>
</tr>
<tr>
<td>FH</td>
<td>136850</td>
<td>Hereditary leiomyomatosis and renal cell cancer (HLRCC)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): papillary type 2 renal cancer, cutaneous and uterine leiomyomatoma</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fumarase deficiency</td>
<td>AR</td>
</tr>
<tr>
<td>FLCN</td>
<td>607273</td>
<td>Birt-Hogg-Dube syndrome (BHDS)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): renal</td>
<td>AD</td>
</tr>
<tr>
<td>MAX</td>
<td>154950</td>
<td>Associated cancer(s)/tumor(s): pheochromocytoma, parangangioma</td>
<td>AD&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>MEN1</td>
<td>613733</td>
<td>Multiple endocrine neoplasia (MEN) type 1</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): parathyroid, pituitary, gastrinoma, insulinoma, carcinoid, adrenocortical</td>
<td>AD</td>
</tr>
<tr>
<td>MET</td>
<td>164860</td>
<td>Hereditary papillary renal cell carcinoma (HPRCC)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): papillary type 1 renal cancer</td>
<td>AD</td>
</tr>
<tr>
<td>MLH1</td>
<td>120436</td>
<td>Lynch syndrome/hereditary nonpolyposis colorectal cancer (HNPCC)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): colorectal, endometrial, stomach, ovarian, and others</td>
<td>AD</td>
</tr>
</tbody>
</table>

<sup>a</sup>Association is suggested but not well-established at this time
<sup>b</sup>Possible paternal parent-of-origin effect
<sup>c</sup>Paternal parent-of-origin effect
AD, autosomal dominant; AR, autosomal recessive
<table>
<thead>
<tr>
<th>Gene</th>
<th>MIM Number</th>
<th>Disorder/Associated Cancer(s)/Tumor(s)</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRE11/MRE11A</td>
<td>600814</td>
<td>Associated cancer(s)/tumor(s): breast&lt;br&gt;Ataxia-telangiectasia-like disorder</td>
<td>AR</td>
</tr>
<tr>
<td>MSH2</td>
<td>609309</td>
<td>Lynch syndrome/hereditary nonpolyposis colorectal cancer (HNPCC)&lt;br&gt;Associated cancer(s)/tumor(s): colorectal, endometrial, stomach, ovarian, and others</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Constitutional mismatch repair deficiency (CMMRD)</td>
<td>AR</td>
</tr>
<tr>
<td>MSH3</td>
<td>600887</td>
<td>Associated cancer(s)/tumor(s): polyposis, colorectal</td>
<td>AR</td>
</tr>
<tr>
<td>MSH6</td>
<td>600678</td>
<td>Lynch syndrome/hereditary nonpolyposis colorectal cancer (HNPCC)&lt;br&gt;Associated cancer(s)/tumor(s): colorectal, endometrial, stomach, ovarian, and others</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Constitutional mismatch repair deficiency (CMMRD)</td>
<td>AR</td>
</tr>
<tr>
<td>MUTYH</td>
<td>604933</td>
<td>Associated cancer(s)/tumor(s): breast&lt;br&gt;MUTYH-Associated Polyposis (MAP)&lt;br&gt;Associated cancer(s)/tumor(s): colon, duodenal</td>
<td>AR</td>
</tr>
<tr>
<td>NBN</td>
<td>602667</td>
<td>Associated cancer(s)/tumor(s): breast</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nijmegen Breakage syndrome (NBS)</td>
<td>AR</td>
</tr>
<tr>
<td>NF1</td>
<td>613113</td>
<td>Neurofibromatosis type 1 (NF1)&lt;br&gt;Associated cancer(s)/tumor(s): breast, neurofibromas, gliomas, malignant peripheral nerve sheath tumors, gastrointestinal stromal tumor (GIST), leukemia</td>
<td>AD</td>
</tr>
<tr>
<td>NF2</td>
<td>607379</td>
<td>Neurofibromatosis type 2 (NF2)&lt;br&gt;Associated cancer(s)/tumor(s): schwannoma, meningioma</td>
<td>AD</td>
</tr>
<tr>
<td>NTHL1</td>
<td>602656</td>
<td>Associated cancer(s)/tumor(s): polyposis, colorectal</td>
<td>AR</td>
</tr>
<tr>
<td>PALB2</td>
<td>610355</td>
<td>Associated cancer(s)/tumor(s): breast, pancreatic</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fanconi Anemia, complementation group N</td>
<td>AR</td>
</tr>
<tr>
<td>PHOX2B</td>
<td>603851</td>
<td>Congenital central hypoventilation syndrome (CCHS)&lt;br&gt;Associated cancer(s)/tumor(s): neuroblastoma, ganglioneuroblastoma, ganglioneuroma</td>
<td>AD</td>
</tr>
<tr>
<td>PMS2</td>
<td>600259</td>
<td>Lynch syndrome/hereditary nonpolyposis colorectal cancer (HNPCC)&lt;br&gt;Associated cancer(s)/tumor(s): colorectal, endometrial, stomach, ovarian, and others</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Constitutional mismatch repair deficiency (CMMRD)</td>
<td>AR</td>
</tr>
</tbody>
</table>

*aAssociation is suggested but not well-established at this time
bPossible paternal parent-of-origin effect
cPaternal parent-of-origin effect
AD, autosomal dominant; AR, autosomal recessive
<table>
<thead>
<tr>
<th>Gene</th>
<th>MIM Number</th>
<th>Disorder/Associated Cancer(s)/Tumor(s)</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>POLD1</td>
<td>174761</td>
<td>Associated cancer(s)/tumor(s): polyposis, colorectal</td>
<td>AD</td>
</tr>
<tr>
<td>POLE</td>
<td>174762</td>
<td>Associated cancer(s)/tumor(s): polyposis, colorectal</td>
<td>AD</td>
</tr>
<tr>
<td>PTEN</td>
<td>601728</td>
<td>Cowden syndrome/PTEN hamartoma tumor syndrome</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): breast, endometrial, thyroid, colon, renal cell carcinoma</td>
<td></td>
</tr>
<tr>
<td>RAD51C</td>
<td>602774</td>
<td>Associated cancer(s)/tumor(s): ovarian</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fanconi anemia, complementation group O</td>
<td>AR</td>
</tr>
<tr>
<td>RAD51D</td>
<td>602994</td>
<td>Associated cancer(s)/tumor(s): ovarian</td>
<td>AD</td>
</tr>
<tr>
<td>RB1</td>
<td>614041</td>
<td>Retinoblastoma</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): retinoblastoma, retinoma, pinealoblastoma, osteosarcoma, soft tissue sarcoma, melanoma</td>
<td></td>
</tr>
<tr>
<td>RECQL</td>
<td>600537</td>
<td>Associated cancer(s)/tumor(s): breast</td>
<td>AD</td>
</tr>
<tr>
<td>RET</td>
<td>164761</td>
<td>Multiple endocrine neoplasia type 2 (MEN2)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): medullary thyroid carcinoma, pheochromocytoma, parathyroid adenoma</td>
<td></td>
</tr>
<tr>
<td>SDHAF2</td>
<td>613019</td>
<td>Associated cancer(s)/tumor(s): paragangioma</td>
<td>AD&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>SDHB</td>
<td>185470</td>
<td>Associated cancer(s)/tumor(s): paragangioma, pheochromocytoma, GIST, pulmonary chondroma, renal clear cell carcinoma</td>
<td>AD</td>
</tr>
<tr>
<td>SDHC</td>
<td>602413</td>
<td>Associated cancer(s)/tumor(s): paragangioma, pheochromocytoma, GIST, pulmonary chondroma, renal clear cell carcinoma</td>
<td>AD</td>
</tr>
<tr>
<td>SDHD</td>
<td>602690</td>
<td>Associated cancer(s)/tumor(s): paragangioma, pheochromocytoma, GIST, pulmonary chondroma, renal clear cell carcinoma</td>
<td>AD&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>SMAD4</td>
<td>600993</td>
<td>Juvenile polyposis syndrome (JPS); hereditary hemorrhagic telangiectasia (HHT) syndrome</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): colon, stomach, small intestine, pancreas</td>
<td></td>
</tr>
<tr>
<td>SMARCA4</td>
<td>603254</td>
<td>Rhabdoid tumor predisposition syndrome</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): rhabdoid tumor</td>
<td></td>
</tr>
<tr>
<td>SMARCB1</td>
<td>601607</td>
<td>Rhabdoid tumor predisposition syndrome</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): rhabdoid tumor</td>
<td></td>
</tr>
<tr>
<td>STK11</td>
<td>602216</td>
<td>Peutz-Jeghers syndrome (PJS)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): breast, colon, stomach, small intestine, pancreas, ovary, testes, lung</td>
<td></td>
</tr>
<tr>
<td>SUFU</td>
<td>607035</td>
<td>Neviod basal cell carcinoma syndrome (NBCCS)</td>
<td>AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated cancer(s)/tumor(s): basal cell carcinoma, medulloblastoma, fibroma, rhabdomyoma</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Association is suggested but not well-established at this time
<sup>b</sup>Possible paternal parent-of-origin effect
<sup>c</sup>Paternal parent-of-origin effect
AD, autosomal dominant; AR, autosomal recessive
<table>
<thead>
<tr>
<th>Gene</th>
<th>MIM Number</th>
<th>Disorder/Associated Cancer(s)/Tumor(s)</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMEM127</td>
<td>613403</td>
<td>Associated cancer(s)/tumor(s): pheochromocytoma, paranglioma, GIST, pulmonary chondroma, renal clear cell carcinoma</td>
<td>AD</td>
</tr>
<tr>
<td>TPS3</td>
<td>191170</td>
<td>Li-Fraumeni syndrome (LFS) &lt;br&gt;Associated cancer(s)/tumor(s): soft tissue sarcoma, osteosarcoma, central nervous system (CNS) tumor, breast, adrenocortical carcinoma, choroid plexus carcinoma, rhabdomyosarcoma</td>
<td>AD</td>
</tr>
<tr>
<td>TSC1</td>
<td>605284</td>
<td>Tuberous sclerosis complex (TSC) &lt;br&gt;Associated cancer(s)/tumor(s): cardiac rhabdomyoma, retinal and other hamartomas, renal angiomyolipoma, subependymal giant cell astrocytoma (SEGA), fibromas</td>
<td>AD</td>
</tr>
<tr>
<td>TSC2</td>
<td>191092</td>
<td>Tuberous sclerosis complex (TSC) &lt;br&gt;Associated cancer(s)/tumor(s): cardiac rhabdomyoma, retinal and other hamartomas, renal angiomyolipoma, subependymal giant cell astrocytoma (SEGA), fibromas</td>
<td>AD</td>
</tr>
<tr>
<td>VHL</td>
<td>608537</td>
<td>Von Hippel-Lindau (VHL) syndrome &lt;br&gt;Associated cancer(s)/tumor(s): hemangioblasma, renal angioma, renal cell carcinoma, pheochromocytoma, neuroendocrine tumors, endolymphatic sac tumors, epididymal and broad ligament cystadenomas</td>
<td>AD</td>
</tr>
<tr>
<td>WT1</td>
<td>607102</td>
<td>WT1-related Wilms tumor &lt;br&gt;WAGR syndrome &lt;br&gt;Denys-Drash syndrome (DDS) &lt;br&gt;Frasier syndrome &lt;br&gt;Associated cancer(s)/tumor(s): Wilms tumor</td>
<td>AD</td>
</tr>
</tbody>
</table>

*Association is suggested but not well-established at this time<br>
*Possible paternal parent-of-origin effect<br>
*Paternal parent-of-origin effect<br>
AD, autosomal dominant; AR, autosomal recessive

### Additional Resources


Related Information

Breast Cancer Biomarkers
Colorectal Cancer
Neuroblastoma
Ovarian Cancer

Related Tests

BRCA1 and BRCA2-Associated HBOC Syndrome Panel, Sequencing and Deletion/Duplication 3001855
Method: Massively Parallel Sequencing/Multiplex Ligation-dependent Probe Amplification

Familial Adenomatous Polyposis Panel: (APC) Sequencing and Deletion/Duplication, (MUTYH) 2 Mutations 2004915
Method: Polymerase Chain Reaction/Sequencing/Multiplex Ligation-dependent Probe Amplification

Hereditary Breast and Ovarian Cancer Panel, Sequencing and Deletion/Duplication 2012026
Method: Massively Parallel Sequencing/Exonic Oligonucleotide-based CGH Microarray

Hereditary Cancer Panel, Sequencing and Deletion/Duplication 2012032
Method: Massively Parallel Sequencing/Exonic Oligonucleotide-based CGH Microarray

Hereditary Gastrointestinal Cancer Panel, Sequencing and Deletion/Duplication 2013449
Method: Massively Parallel Sequencing/Exonic Oligonucleotide-based CGH Microarray/Sequencing/Multiplex Ligation-dependent Probe Amplification

Hereditary Paraganglioma-Pheochromocytoma (SDHB, SDHC, and SDHD) Sequencing and Deletion/Duplication Panel 2007167
Method: Polymerase Chain Reaction/Sequencing/Multiplex Ligation-dependent Probe Amplification

Hereditary Renal Cancer Panel, Sequencing and Deletion/Duplication 2010214
Method: Massively Parallel Sequencing/Exonic Oligonucleotide-based CGH Microarray

HNPCC/Lynch Syndrome (MLH1) Sequencing and Deletion/Duplication 0051650
Method: Polymerase Chain Reaction/Sequencing/Multiplex Ligation-dependent Probe Amplification

HNPCC/Lynch Syndrome (MSH2) Sequencing and Deletion/Duplication 0051654
Method: Polymerase Chain Reaction/Sequencing/Multiplex Ligation-dependent Probe Amplification

HNPCC/Lynch Syndrome (MSH6) Sequencing and Deletion/Duplication 0051656

HNPCC/Lynch Syndrome (PMS2) Sequencing and Deletion/Duplication 0051737

Juvenile Polyposis (SMA4) Sequencing and Deletion/Duplication 2001971

Juvenile Polyposis Syndrome (BMPR1A) Sequencing and Deletion/Duplication 2004992

Li-Fraumeni (TP53) Sequencing and Deletion/Duplication 2009313

Multiple Endocrine Neoplasia Type 1 (MEN1) Sequencing and Deletion/Duplication 2005360

Multiple Endocrine Neoplasia Type 2 (MEN2), RET Gene Mutations by Sequencing 0051390

Neurofibromatosis Type 1 (NF1) Sequencing and Deletion/Duplication 2007154

Peutz-Jeghers Syndrome (STK11) Sequencing and Deletion/Duplication 2008398

PTEN-Related Disorders (PTEN) Sequencing and Deletion/Duplication 2002470

von Hippel-Lindau (VHL) Sequencing and Deletion/Duplication 2002965