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Renal Cancer Panel: Information for Ordering Providers

Approximately 1-2% of individuals will develop renal cancer in their lifetime.[1] An estimated 3-5% of renal cancers are associated with a pathogenic variant in a single cancer predisposition gene.[2] Features suggestive of a hereditary cancer predisposition include:

- Younger age at diagnosis
- Multiple primary cancers in a single individual
- Several relatives affected with related cancers spanning multiple generations

Individuals who carry a pathogenic variant in a hereditary cancer gene have an increased risk of certain cancers compared to the general population. Cancer risks depend on the gene(s) in which the variant(s) is identified. These individuals are eligible for increased cancer screening and/or risk reducing surgeries and therapeutic interventions. In addition, results may influence treatment plans for individuals with cancer.

Indications for testing:
Patients with a personal and/or family history suggestive of a predisposition to renal cancer are eligible for testing.

Ordering privileges
Please refer to the APL Test Directory (http://ahsweb.ca/lab/apl-td-lab-test-directory) for specific ordering restrictions.

Renal Cancer NGS panel

Gene(s)	Associated cancers and/or clinical features[3]	Associated Hereditary Syndrome[4]
VHL	Renal tumors, adrenal pheochromocytoma, neuroendocrine tumors, and hemangioblastomas of the brain, spinal cord, and retina. The lifetime risk of renal cell carcinoma is approximately 25%-70%.	Von Hippel Lindau syndrome
MET	Bilateral papillary renal cancer	Hereditary papillary renal cancer
FLCN	Cutaneous fibrofolliculomas, pulmonary cysts, and renal tumors. Bilateral renal tumors occur in up to 34% of affected people. Secondary clinical findings can include spontaneous pneumothoraces	Birt-Hogg-Dube syndrome
FH	Renal cancer (20% lifetime risk), cutaneous and uterine leiomyomas/fibroids (~98% lifetime risk)	Hereditary leiomyomatosis and renal cell carcinoma
MLH1, *MSH2*, *MSH6*, *PMS2* or *EPCAM*	Colorectal cancer (up to 82% lifetime risk), uterine cancer, ovarian cancer and stomach cancer	Lynch syndrome
PTEN	Multiple hamartoma syndrome with an increased risk of breast, thyroid, endometrial, and renal cancers	*PTEN* Hamartoma syndrome (includes Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome)
TP53	Lifetime risk of 68%-93% to develop cancer. The most common tumor types include soft tissue, osteosarcomas, breast cancer, and brain cancer	Li-Fraumeni syndrome

SDHA, SDHB, SDHC, SDHD	Head and neck paragangliomas, extra-adrenal paragangliomas and/or pheochromocytomas, GISTs, and renal clear cell carcinoma (rare)	Hereditary paraganglioma/ pheochromocytoma syndrome
BAP1	A newly described gene that has been identified in families with renal cancer, uveal melanoma, and cutaneous melanoma. While lifetime cancer risks are increased, they are not yet well defined.	*BAP1* tumour predisposition syndrome

Associated Disorders[3]
Hereditary cancer predispositions are typically inherited in an autosomal dominant fashion. Some of the genes on this panel are associated with other rare disorders including:

Constitutional mismatch repair deficiency syndrome is a rare autosomal recessive condition that occurs in individuals who have two pathogenic variants in one of the following genes: *EPCAM, MLH1, MSH2, MSH6 or PMS2.* Affected individuals often have onset of colon/intestinal cancer before the age of 20 years and may have a cutaneous phenotype similar to that seen in neurofibromatosis type I.

Fumarate Hydratase Deficiency is an autosomal recessive disorder caused by pathogenic variants in *FH*. Individuals with fumarate hydratase deficiency (two pathogenic *FH* variants) have brain anomalies, epilepsy, dysmorphic features, and global developmental delay. Most affected individuals die in early childhood.

Mitochondrial complex deficiencies are rare autosomal recessive conditions with highly variable phenotypes. Pathogenic variants have been reported in *SDHA SDHB* and *SDHD.*

PTEN hamartoma tumor syndrome (PHTS) is an autosomal dominant condition characterized by hamartomatous tumors and germline PTEN pathogenic variant. PHTS includes Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, PTEN- related Proteus syndrome and Proteus-like syndrome.

When can I expect results?
Results may take up to 4 months.

How are results reported?
Results are sent to the ordering provider and available in Netcare and Connect Care.

Contact Information
Genetic Counsellors, Genetics & Genomics
Calgary: 403-955-3097

Requisition forms, contact information and other resources can be found at:
http://ahsweb.ca/lab/if-lab-genetics-and-genomics

References

1. Canadian Cancer Statistics Advisory Committee in collaboration with the Canadian Cancer Society, Statistics Canada and the Public Health Agency of Canada. Canadian Cancer Statistics 2021. Toronto, ON: Canadian Cancer Society; 2021. Available at: cancer.ca/Canadian-Cancer-Statistics-2021-EN (accessed [2022 July]).

2. Haas NB, Nathanson KL. Hereditary kidney cancer syndromes. Adv Chronic Kidney Dis. 2014 Jan;21(1):81-90. doi: 10.1053/j.ackd.2013.10.001. PMID: 24359990; PMCID: PMC3872053.

3. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018 [cited 2017 Dec]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/

4. Online Mendelian Inheritance in Man, OMIM® . McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD), Available from: https://omim.org/ (accessed [2022 August])