

RED FLAGS TO IDENTIFY INDIVIDUALS WITH RENAL TUMOURS MOST LIKELY TO BENEFIT FROM REFERRAL TO GENETICS

Reproduced and adapted with permission from the Canadian Urological Association. Reaume, et al., 2013. Canadian guideline on genetic screening for hereditary renal cell cancers. Can Urol Assoc J. 7(9-10):319-23

Reviewed Jan 2023

INDIVIDUALS WITH ANY RENAL TUMOUR (BENIGN OR MALIGNANT) AND ANY ONE OF THE FOLLOWING:

1. Bilaterality or multifocality
2. Early age of onset (≤ 45 years of age)
3. 1st or 2nd degree relative with any renal tumour
4. A history of pneumothorax*
5. One of the following dermatologic findings:
 - a. Skin leiomyomas*
 - b. Skin fibrofolliculomas/trichodiscomas*
6. One of the following associated tumours:
 - a. Pheochromocytoma/paraganglioma*
 - b. Hemangioblastoma of the retina, brainstem, cerebellum or spinal cord*
 - c. Early onset of multiple uterine fibroids (< 30 years of age)*
7. Lymphangiomyomatosis*
8. Childhood seizure disorder*

*or 1st degree relative with same

INDIVIDUALS WITH NON-CLEAR CELL CARCINOMA WITH UNUSUAL ASSOCIATED FEATURES (E.G., CHROMOPHOBE, ONCOCYTIC OR HYBRID TUMOURS)

INDIVIDUALS, UNAFFECTED OR AFFECTED, WHO REPORT ANY FAMILY MEMBER WITH A KNOWN CLINICAL OR LABORATORY DIAGNOSIS OF ANY ONE OF THE FOLLOWING GENETIC CONDITIONS:

1. Von Hippel-Lindau syndrome
2. Birt-Hogg-Dubé syndrome
3. Hereditary leiomyomatosis and renal cell cancer
4. Hereditary papillary renal cell cancer
5. Hereditary paraganglioma/ pheochromocytoma
6. Tuberous sclerosis

BRIEF SUMMARY OF SOME RENAL CELL CARCINOMA HEREDITARY SYNDROMES (1/2)

Genetic testing is available for all six of the conditions listed.

All conditions have variable expressivity [variation in clinical presentation (onset, features and severity) even within the same family].

Renal Cell Carcinoma abbreviated to RCC

Reviewed Jan 2023

VON HIPPEL-LINDAU SYNDROME

- Autosomal dominant
- # of individuals with no family history / new (de novo) pathogenic/likely pathogenic gene variants = 20%
- Histology: Clear cell RCC
- Features:
 - Renal tumours
 - Central nervous system hemangioblastomas
 - Retinal hemangiomas
 - Adrenal pheochromocytoma/ paraganglioma
 - Pancreatic neuroendocrine tumours
 - Endolymphatic sac tumours
 - Epididymal cystadenomas
 - Broad-ligament tumours

BIRT-HOGG-DUBÉ SYNDROME

- Autosomal dominant
- # of individuals with no family history / new (de novo) pathogenic/likely pathogenic gene variants = Unknown
- Histology: Chromophobe RCC/oncocytic RCC
- Features:
 - Skin fibrofolliculomas
 - Pulmonary cysts
 - Renal tumours

HEREDITARY LEIOMYOMATOSIS AND RENAL CELL CANCER

- Autosomal dominant
- # of individuals with no family history / new (de novo) pathogenic/likely pathogenic gene variants = Unknown
- Histology: Papillary type 2 RCC
- Features:
 - Skin leiomyomas
 - Renal tumours
 - Uterine leiomyomas

BRIEF SUMMARY OF SOME RENAL CELL CARCINOMA HEREDITARY SYNDROMES (2/2)

Genetic testing is available for all six of the conditions listed.

All conditions have variable expressivity [variation in clinical presentation (onset, features and severity) even within the same family].

Renal Cell Carcinoma abbreviated to RCC

Reviewed Jan 2023

HEREDITARY PAPILLARY RENAL CELL CANCER

- Autosomal dominant
- # of individuals with no family history/new (de novo) pathogenic/likely pathogenic gene variants = Unknown
- Histology: Papillary type I RCC
- Features: Renal only

HEREDITARY PARAGANGLIOMA/PHEOCHROMOCYTOMA

- Autosomal dominant
- # of individuals with no family history/new (de novo) pathogenic/likely pathogenic gene variants = Unknown because a sufficient number of patients have not been evaluated for subtle manifestation
- Histology: Clear cell RCC
- Features: Adrenal pheochromocytoma/paraganglioma

TUBEROUS SCLEROSIS COMPLEX

- Autosomal dominant
- # of individuals with no family history/new (de novo) pathogenic/likely pathogenic gene variants = 66%
- Histology: Epithelial (various) or mesenchymal (angiomyolipoma)
- Features:
 - Skin (adenoma sebaceum, shagreen spots)
 - Retinal hamartomas
 - Central nervous system lesions (including tubers)
 - Cardiac lesions
 - Renal tumours
 - Teeth/gum lesions
 - Bone cysts