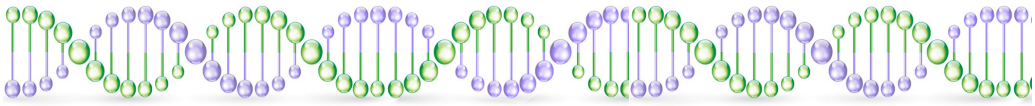
Information Sheet



Hereditary Leiomyomatosis and Renal Cell Cancer syndrome (HLRCC) and the FH gene.

Hereditary Leiomyomatosis and Renal Cell Cancer syndrome (HLRCC) is caused by mutations in the FH gene. It is rare, affecting 1 in 200,000 people.

How is Hereditary Leiomyomatosis and Renal Cell Cancer syndrome (HLRCC) diagnosed?
The clinical features of hereditary leiomyomatosis and renal cell cancer syndrome are:

- cutaneous leiomyomas on the face, shoulders and chest
- uterine fibroids occurring in the 20s and 30s
- kidney cancer, especially with type II papillary features

What are Cutaneous Leiomyomas?
Cutaneous leiomyomas are flesh-coloured lesions can be solitary or multiple, ranging in size from several millimetres to 1 cm. They are fixed to skin but moveable and may coalesce to form plaques. They are most commonly found on the face, neck, backs of the arms as well as the chest and shoulders.

Both men and women with hereditary leiomyomatosis and renal cell cancer syndrome tend to develop cutaneous leiomyomas, usually in their 20s and 30s. They only very rarely develop into a cancer (leiomyosarcoma).

Cutaneous leiomyomas are painful in around 90% of individuals, either spontaneously or secondary to cold, pressure, or emotion. Different treatments exist, including surgical removal, although recurrence is common.

What are uterine leiomyomas?
Uterine leiomyomas are growths occurring in the muscle layer of the uterine (Leio = smooth, Myo = muscle). They are known as fibroids and many women have them.

Women with hereditary leiomyomatosis and renal cell cancer syndrome have a very high lifetime likelihood of developing fibroids (uterine leiomyomas). These fibroids are likely to occur very young and be symptomatic. More than half the women with HLRCC require either a myomectomy (removal of the muscle layer) or a hysterectomy (removal of the uterus) in their mid-30s to control symptoms such as menorrhagia (heavy periods) or dysmenorrhea (painful periods).

While transformation of a fibroid (leiomyoma) to cancer (leiomyosarcoma) has been described, the likelihood is low.

If a woman in her 20s or 30s had the fibroid removed, it should be tested using FH immunohistochemical testing (FH IHC). If there is loss of staining, there is a 50% chance she carries an FH mutation and genetic testing would be strongly recommended.

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Hereditary Health and Hope

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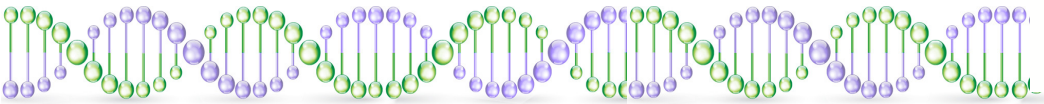

What is Type 2 Papillary Renal Cell Carcinoma?
Type 2 papillary describes how a kidney cancer looks under the microscope. 10% of kidney cancer are type 2 papillary RCCs. (Clear cell is the most common kind of kidney cancer).

Men and women who have hereditary leiomyomatosis and renal cell cancer syndrome have a 10% to 16% lifetime risk of kidney cancer. These cancers are usually Type 2 Papillary renal cell cancers, tend to be aggressive and can metastasise (spread) when very small. The average age of onset is 44 years but isolated cases have occurred in children.

All Type 2 papillary renal cell carcinomas should be tested using FH immunohistochemical testing (FH IHC). If there is loss of staining, then genetic testing would be strongly recommended. Also, if the kidney cancer has spread (metastatic) and it was not of the clear cell kind, there is a 10% chance that person carries an FH gene mutation and genetic testing would be strongly recommended.

How is Hereditary Leiomyomatosis and Renal Cell Cancer syndrome managed?
Management guidelines are aimed at detecting any changes in the kidney early before a cancer can spread as well as preventing the small but real possibility of a leiomyosarcoma from occurring. Management includes:

- Annual MRI of the kidneys, starting at age 15. Note: CT scans and ultrasounds are not sensitive enough to detect small cancers.
- Myomectomy or hysterectomy for symptomatic fibroids

Who should have genetic testing for Hereditary Leiomyomatosis and Renal Cell Cancer syndrome?
Genetic testing should be considered if there is:

- loss of FH on IHC testing of a kidney cancer or a young onset uterine fibroid
- a kidney cancer, especially with type 2 papillary features or if diagnosed before age 40. (Other hereditary renal cancer genes may be tested as well).
- metastatic non-clear cell renal cancer
- an individual with multiple cutaneous leiomyomas

Hereditary Leiomyomatosis and Renal Cell Cancer syndrome inherited?
Yes. Hereditary leiomyomatosis and renal cell cancer syndrome (HLRCC) is a hereditary cancer syndrome caused by a mutation in the FH gene.

There is a 50% chance of a person who carries a germline FH mutation, whether male or female, passing the mutation to their son or daughter. If a mutation is identified, then predictive testing is available for blood relatives.

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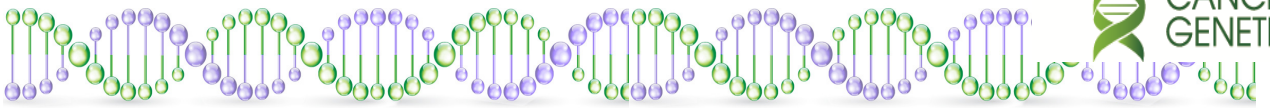

Does this sound like you or your family?
Do you have cutaneous leiomyomas or have you had symptomatic uterine fibroids at at young age? Has an FH gene mutation been detected in a blood relative? Genetic testing is available.

Make an appointment with Dr Hilda High at Sydney Cancer Genetics. It is a confidential opportunity to discuss your personal and family history of cancer and genetic testing can be organised, if needed.

More information is available on our website, including links to the following:

- Because it is a rare syndrome, there is no specific Australian based support group for Hereditary Leiomyomatosis and Renal Cell Cancer syndrome. Rare Connect is an international group helping to connect patients with rare diseases globally.
- The Cancer Genetics section of the Cancer Institute's eviQ website provides up-to-date Australian-based management guidelines
- The US National Library of Medicine website has more information about this syndrome.

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