UT Southwestern Harold C. Simmons Comprehensive Cancer Center | NCI Designated Comprehensive Cancer Center

FH Mutations

What You Should Know About *FH* Mutations

Individuals with one *FH* mutation have a condition called Hereditary Leiomyomatosis Renal Cell Cancer syndrome (HLRCC). HLRCC causes leiomyomas (benign tumors) of the skin and uterus (otherwise known as uterine fibroids) and an increased risk for kidney cancer.

Cancer Risks Associated with a *FH* Mutation

- Cutaneous Leiomyomas: The majority (76%) of individuals with HLRCC present with a single or multiple cutaneous leiomyoma. Cutaneous leiomyomas appear as skin-colored to light brown bumps or raised areas of skin.
- Uterine Fibroids: Almost all women with HLRCC have uterine fibroids. Typically these fibroids are larger, more numerous, and occur at a younger age than uterine fibroids in the general population (in other words, those that are not caused by HLRCC).
- Kidney Cancer: The estimated kidney cancer risk for individuals with a *FH* is 15%. Most kidney tumors in individuals with HLRCC are classified as type 2 papillary renal cancer. Kidney cancers associated with HLRCC tend to be aggressive.
- Pheochromocytoma/Paraganglioma (PCC/PGL): It has recently been suggested that *FH* mutations may rarely be associated with PCC (a tumor of the adrenal gland, which is located above each kidney) or PGL (a tumor that begins in nerve cells of the neuroendocrine system) and pediatric PCC.

Risks to Family Members

Mutations in the *FH* gene are inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with a *FH* mutation have a 1 in 2 (or 50%) chance of having the mutation as well. Individuals with a *FH* mutation may develop leiomyomas of the skin or uterus, kidney cancer, or none of the above. Both males and females can inherit a familial *FH* mutation and both males and females can pass a *FH* mutation on to their children. When an individual inherits two *FH* gene mutations (one from each parent), this causes a different syndrome called fumarase hydratase deficiency (FH deficiency).

Managing Cancer Risks

There is currently no consensus on what surveillance to offer to individuals with HLRCC. However, several groups have proposed surveillance guidelines, such as the American Association for Cancer Research and HLRCC Family Alliance.

- Cutaneous Leiomyomas: Annual full body skin examination to assess the extent of disease and to evaluate for cancerous changes
- Uterine Fibroids: Annual gynecological exam beginning at 20 years of age (or earlier if symptoms) to assess severity of uterine fibroids and to evaluate for cancerous changes. Pelvic ultrasound as needed. Consider myomectomy (removal of fibroids) or hysterectomy (removal of uterus) for symptomatic fibroids.
- Kidney Cancer: Annual abdominal MRI with renal protocol beginning at age 8. May be offered a baseline CT scan and/or ultrasound. Ultrasound examination alone is never sufficient for the common tumors seen in HLRCC.
- PCC/PGL: Consider biochemical screening (testing the blood/urine) and imaging studies (CT, MRI).

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