

Cancer Genetics Summary

Von Hippel Lindau Syndrome (VHL)

Von Hippel Lindau Syndrome is a type of cancer-predisposing syndrome that affects 1 in 32,000 individuals. This inherited disorder is characterized by the formation of noncancerous or cancerous tumors and fluid-filled sacs (cysts) in different parts of the body. Tumors usually appear during young adulthood; however, the signs and symptoms of Von Hippel Lindau syndrome can occur throughout life. Virtually all affected individuals exhibit symptoms by age 65. The tumors can appear in the brain, spine, retina, pancreas and kidneys. About 80 percent of VHL mutations are inherited; the remainder result from new mutations.

There are two major types of Von Hippel Lindau syndrome: Type 1 has a low risk of developing pheochromocytoma (a neuroendocrine tumor associated with high blood pressure and other symptoms.) Type 2 is characterized by a much higher risk and can be further divided into types 2A, 2B, and 2C, depending on the probability of developing renal cell carcinoma and hemangioblastomas.

VHL Tumor Risks

Tumors called angiomas or hemangioblastomas are growths made of newly formed blood vessels and are typically noncancerous. Hemangioblastomas that develop in the brain and spinal cord can cause headaches, vomiting, weakness and a loss of muscle coordination. These lesions occur in 21 to 72 percent of individuals who have VHL, depending on the type of mutation. The average age of onset is 29 years, but lesions have occurred in people ages 9 to 78.

Hemangioblastomas can also occur in the light-sensitive tissue that lines the back of the eye (the retina). These retinal angiomas may cause vision loss, retinal detachment, glaucoma and cataracts. Retinal lesions occur in 43 to 60 percent of individuals with VHL. They usually located at the sides of the retina and can be bilateral and recurring.

People with Von Hippel Lindau syndrome commonly develop cysts in the kidneys, pancreas or male genital tract. Kidney cysts appear in from 24 to 45 percent of individuals with VHL. Onset ranges from age 25 to 50, with 37 as the average. VHL patients are also at an increased risk of developing a kidney cancer called clear cell renal carcinoma and a noncancerous tumor called a pheochromocytoma. Pheochromocytomas affect the adrenal glands (small hormone-producing glands located on top of each kidney). These tumors often cause no symptoms, but can lead to dangerously high blood pressure and become cancerous about 1 percent of the time.

About 10 percent of people with Von Hippel Lindau syndrome develop noncancerous tumors (called endolymphatic sac tumors) in the inner ear. These growths can cause hearing loss in one or both ears, as well as ringing in the ears (tinnitus) and problems with balance.

VHL Gene

Mutations in the VHL gene cause Von Hippel Lindau syndrome. The VHL gene, a tumor suppressor, keeps cells from growing and dividing too rapidly or in an uncontrolled way. Mutations in this gene prevent production of the VHL protein or lead to the production of an abnormal version of the protein. An altered or missing VHL protein cannot effectively regulate cell survival and division, allowing cells to grow and divide uncontrollably to form the tumors and cysts characteristic of Von Hippel Lindau syndrome. The VHL gene is located on the short arm of chromosome 3.

Every person has two copies of each gene; if a mutation occurs in one of their VHL genes they have a backup copy to protect them. People with FAP start life with one copy mutated; if the other copy becomes mutated, it may no longer be able to regulate cell growth and this can lead to tumor formation.

Genetic Testing for VHL

Gene testing is available to identify a mutation in the VHL gene. Identifying a mutation confirms a diagnosis of Von Hippel Lindau syndrome and the risks associated with VHL. Predisposition gene testing is best performed on someone who has had cancer. If that individual is found to have a change in the suspect gene, then other relatives can be reliably tested.

If a mutation in the VHL gene is found in your family but your test results show you did not inherit the gene mutation, your chance of developing cancer would be the same as for the general population. If you do not have the gene mutation, your children will not inherit the mutation from you.

For more information or questions, call 503-413-6534.

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