The Genetics of Kidney Cancer

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What are genes?

Genes carry information in the form of DNA within each cell of the human body. Researchers estimate that there are 30,000 different genes in each cell. Genes are packaged onto chromosomes. There are 23 pairs of chromosomes in each cell. One chromosome of each pair is inherited from the person's father and one from the person's mother.

Genes control how a cell functions, including how quickly it grows, how often it divides, and how long it lives. To control these functions, genes produce proteins that perform specific tasks and act as messengers for the cell. Therefore, it is essential that each gene have the correct instructions or "code" for making its protein so that the protein can perform the proper function for the cell.

What role do genes play in kidney cancer?

Many cancers begin when one or more genes in a cell are mutated (changed), creating an abnormal protein or no protein at all. The information provided by an abnormal protein is different from that of a normal protein, which can cause cells to multiply uncontrollably and become cancerous.

A person may either be born with a genetic mutation in all of their cells (germline mutation) or acquire a genetic mutation in a single cell during his or her lifetime. An acquired mutation is passed on to all cells that develop from that single cell (called a somatic mutation). Somatic mutations can sometimes be caused by environmental factors, such as cigarette smoke. Most kidney cancers (about 95%) are considered sporadic, meaning that the damage to the genes occurs by chance after a person is born and there is no risk of passing on the gene to a person's children. Inherited kidney cancers are less common (about 5%) and occur when gene mutations are passed within a family from one generation to the next. Kidney cancer may also be called renal cell carcinoma.

What are the chances a mutated gene is inherited?

Every cell usually has two copies of each gene: one inherited from a person's mother and one inherited from a person's father. Hereditary kidney cancer usually follows an autosomal dominant inheritance pattern, in which a mutation needs to happen in only one copy of the gene for the person to have an increased risk of getting the disease. This means that a parent with a gene mutation may pass on a copy of the normal gene or a copy of the gene with a mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A brother, sister, or parent of a person who has a gene mutation also has a 50% chance of having the same mutation.

What is a person's average risk for kidney cancer?

A person at average risk for kidney cancer has less than a 1% chance of developing kidney cancer during his or her lifetime.

How can a person know if he or she has inherited a genetic mutation that increases his or her risk of kidney cancer?

Only genetic testing [2] can determine whether a person has a genetic mutation. Most experts strongly recommend that people considering genetic testing first consult a genetic counselor [3]. Genetic counselors are trained to explain the risks and benefits of genetic testing.

How does a person know if kidney cancer runs in the family?

If a person's first-degree relatives (parents, brothers, sisters, children) have had kidney cancer, or if there are many family members who have had the disease (including grandparents, aunts, uncles, nieces, nephews, grandchildren, cousins), there may be a chance that kidney cancer runs in the family. This is especially true when family members have been diagnosed with kidney cancer before the age of 50, had cancer in both kidneys, and/or had more than one tumor in the same kidney.

What is a person's risk if kidney cancer runs in the family?

A person has an increased risk of kidney cancer if their first-degree relatives developed kidney cancer before age 50. Finding a specific genetic condition in the family can help determine the risk that other family members will develop kidney cancer.

Which inherited genetic mutations raise the risk of kidney cancer?

There are several genetic conditions associated with an increased risk of kidney cancer. Most of these conditions are associated with a specific type of kidney cancer. Finding a specific genetic syndrome in a family can help a person and his or her doctor develop an appropriate cancer screening

plan and, in some cases, help to determine the best treatment plan. Some genetic conditions also increase a person's risk for noncancer-related health problems for which screening and early detection may be beneficial. The genetic conditions that increase a person's risk of kidney cancer are described below.

Von Hippel-Lindau syndrome (VHL) [4]. People with VHL have an increased risk of developing several types of tumors. Most of these tumors are benign (noncancerous). However, people with VHL have a risk of developing a specific type of kidney cancer called clear cell kidney cancer. People with VHL also have an increased risk of tumors in the eye (retinal angioma) [5], brain and spinal cord (hemangioblastoma) [6], adrenal glands (pheochromocytoma) [7], and ear (endolymphatic sac tumor), as well as an increased risk of developing a cyst on their kidneys and pancreas, or on a man's testicles (epididymal cystadenomas).

Hereditary non-VHL clear cell renal cell carcinoma [8]. Hereditary non-VHL clear cell renal cell carcinoma is a genetic condition that increases a person's risk of developing clear cell renal cell carcinoma (CCRCC). A family may have hereditary non-VHL CCRCC if more than one family member has been diagnosed with CCRCC.

Hereditary papillary renal cell carcinoma (HPRCC) [9]. HPRCC is a genetic condition that increases the risk of type 1 papillary renal cell carcinoma. People who have HPRCC have an increased risk of developing more than one kidney tumor and tumors on both kidneys. HPRCC is suspected when two or more close relatives have been diagnosed with type 1 papillary renal cell carcinoma.

Birt-Hogg-Dubé syndrome (BHD) [10]. BHD is a rare genetic condition associated with multiple noncancerous skin tumors, lung cysts, and an increased risk of noncancerous and cancerous kidney tumors, specifically a rare type called chromophobe or a slow-growing type called oncocytoma (a slow growing type of kidney cancer that rarely spreads). People with BHD may also develop clear cell and papillary kidney cancers.

Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) [11]. HLRCC is associated with an increased risk of developing type 2 papillary renal cell carcinoma and skin nodules called leiomyomata that are found mainly on the arms, legs, chest, and back. Women with HLRCC often develop uterine fibroids known as leiomyomas, or, less commonly, leiomyosarcoma.

Are there other genetic conditions associated with an increased risk of kidney cancer?

Other genetic conditions may be associated with an increased risk of kidney cancer, and research to find other genetic causes of kidney cancer is ongoing. The other genetic conditions that may be associated with an increased risk of kidney cancer are described below.

Beckwith-Wiedemann syndrome (BWS) [12]. Children with BWS have an increased risk of developing Wilms tumor [13] (a type of kidney cancer). BWS is a growth disorder associated with large body size, large tongue, abdominal wall defects, an increased risk of childhood tumors [14], kidney abnormalities, low blood sugar when a baby is a newborn, and unusual ear creases or pits. Children with BWS may also have body parts that are larger on one side of the body than on the other.

Li-Fraumeni syndrome (LFS) [15]. LFS is a rare condition associated with a specific genetic mutation. People with LFS have a higher risk of developing osteosarcoma [16] (a type of bone cancer), soft tissue sarcoma [17], leukemia [18], breast cancer [19], brain cancer [6], adrenal cortical tumors [7], and possibly Wilms tumor [13].

Tuberous sclerosis complex (TSC) [20]. TSC is a genetic condition associated with changes in the skin, brain, kidney, and heart. People with TSC also have an increased risk of developing kidney cancer.

Cowden syndrome (CS) [21]. CS is a rare genetic condition caused by a specific genetic mutation. People with CS have an increased risk of developing breast cancer [19] and noncancerous breast changes and noncancerous and cancerous tumors of the thyroid [22] and endometrium [23] (lining of the uterus). People with CS have also developed kidney cancer. Although, it is not known whether having CS increases a person's risk of developing kidney cancer.

What is your risk level?

In addition to family history, other environmental and lifestyle factors may increase your risk of kidney cancer. Discussing your family history and personal risk factors with a doctor helps you better understand your risk. People with a higher than average risk may benefit from genetic counseling and early detection strategies.

A risk factor [24] is anything that increases a person's risk of developing cancer. Having a particular genetic mutation linked to kidney cancer cannot predict that a person will develop cancer. Controllable risk factors, such as eating a balanced diet, maintaining a healthy weight, exercising, avoiding chemicals and asbestos, limiting alcoholic beverages, and avoiding tobacco products also play a role. Some people who develop kidney cancer have few known risk factors. Research to better understand the link between genetic mutations and kidney cancer is ongoing. Talk with a doctor for more information about risk factors, prevention, and screening for kidney cancer.

More Information

Genetics [25]

Guide to Kidney Cancer [26]

Sharing Genetic Test Results With Your Family [27]

Direct-to-Consumer Genetic Testing [28]

Links:
[1] http://www.cancer.net/about-us
[2] http://www.cancer.net/node/24895
[3] http://www.cancer.net/node/24907
[4] http://www.cancer.net/node/19322
[5] http://www.cancer.net/node/18811
[6] http://www.cancer.net/node/18562
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