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# Inherited Syndromes Link Cancers

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In addition to treatment-related risks, some survivors discover they have a genetic syndrome that may lead to a second cancer. Scientists are finding that it may not be where cancer strikes that's important, but what's causing it in the first place.

The most well-known genetic mutations, BRCA1 and BRCA2, can signify an increased risk of developing not only breast cancer in men and women, but also ovarian cancer. Coupled with a 55 to 85 percent lifetime risk for breast cancer, individuals with the BRCA1 mutation have a 40 to 60 percent lifetime risk for developing a second breast cancer.

Li-Fraumeni syndrome, a rare genetic disorder often caused by a mutated p53 gene, can increase the risk for breast cancer, sarcoma, leukemia, brain tumors and other cancers. Studies have shown that people with the inherited mutation have at least an 85 percent chance of developing cancer during their lifetime. A study of 200 people with inherited Li-Fraumeni syndrome found that 15 percent developed a second cancer, 4 percent had a third cancer and 2 percent had four cancers. Childhood cancer survivors with the syndrome were found to be at highest risk for second cancers.

The inactivation of a tumor-suppressor gene called von Hippel-Lindau (VHL) may cause up to 85 percent of all kidney cancers. A person is born with two copies of every gene, so both VHL genes must be inactive or mutated before tumors form. Patients with one inherited VHL mutation have a much greater likelihood of developing kidney cancer since it only takes a mutation of the second VHL gene for tumors to occur. In addition to kidney cancer, VHL is associated with tumors of the eye, brain, spine and pancreas.

Genetic syndromes only account for 5 percent of all colorectal cancer cases, but hereditary nonpolyposis colorectal cancer (HNPCC), also known as Lynch syndrome, and familial adenomatous polyposis (FAP) dramatically increase the risk. HNPCC is caused by a defect in DNA repair genes, four of which have been identified. Because these genes oversee DNA cell replication, defects can cause other types of cancers, including uterine and ovarian cancer. FAP results from only one mutated gene, but it can increase the risk of developing colorectal cancer to 90 percent by age 45. Thyroid, small bowel and brain cancers have also been noted with this mutation.

For a complete list of cancer screening recommendations, visit [www.cancer.org](http://www.cancer.org) or [www.genetichealth.com](http://www.genetichealth.com). To find a genetic counselor in your area, visit the website of the National Society of Genetic Counselors at [www.nsgc.org](http://www.nsgc.org).

