

# The Genetics of Wilms Tumor

by Vicki Huff, PhD, Molecular Biologist

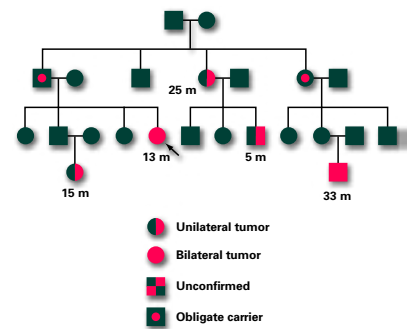
The development of Wilms tumor is thought to involve changes in a number of genes that normally function to control normal kidney development and growth. Cells that sustain alterations in these genes may multiply, develop abnormally, and accumulate additional genetic changes, ultimately resulting in a Wilms tumor. Understanding what genes have been altered in Wilms tumors will greatly aid in understanding how cancer develops, how kidneys normally develop, and how best to treat patients with Wilms tumor.

There are many approaches for identifying changed genes found in Wilms tumor. One way is to study the tumors themselves. However by the time a tumor is detectable it has sustained many genetic changes, and it is sometimes difficult to identify which changes were critical to the development of the tumor. Another approach for identifying Wilms tumor genes is to study people who have an inherited predisposition to Wilms tumor.

The vast majority of Wilms tumors are not due to an inherited genetic alteration, but rather develop as a result of genetic alterations that occur in just a few cells in the body (i.e., somatic alterations). However, roughly 2% of children diagnosed with Wilms tumor have a relative who was also diagnosed with Wilms tumor. Families with two or more Wilms tumor patients are considered Wilms tumor families. The occurrence of these rare Wilms tumor families suggests that the Wilms tumor patients in these families have inherited an altered gene that is important in the development of Wilms tumor. This altered gene alone will not result in a Wilms tumor; other genetic changes also have to occur. Some individuals may inherit a predisposition gene, but never develop Wilms tumor. However, the identification of that inherited altered gene will identify one critically important step in the path to tumor development.

To date, only one Wilms tumor gene called WT1, has been identified. WT1 is mutated in roughly a fifth of all Wilms tumors. Inherited WT1 alterations have also been observed in a few small Wilms tumor families, but studies of large Wilms tumor families have demonstrated that their inherited predisposition is not due to an altered WT1 gene. More recent studies have localized two familial predisposition genes, one to chromosome 19 and one to chromosome 17, but the actual identification of these two predisposition genes is still being determined. It is also known that predisposition in some families is not due to WT1 nor to the chromosome 19 or 17 genes, implying that other WT predisposition genes exist.

## Hypothetical Wilms Tumor Family



The goal of the Familial Wilms Tumor Study is to identify genes that predispose individuals to Wilms tumor and to understand the function of

those genes. Analysis of DNA from members of Wilms tumor families can help us localize more precisely the predisposition genes, a first step in the process of identifying the genes. The most important people to study in these families are those who have been diagnosed with Wilms tumor, their parents and any other family members who are the genetic “link” between the Wilms tumor patients. Further analysis of DNA from patients can help us determine if a particular gene within a localized region is, in fact, a predisposition gene. Since these genes likely will play a role in non-familial cases of WT also, this work will help in understanding the development of Wilms tumors in general.

### GLOSSARY:

**Gene alteration, gene mutation:** A change in a gene that changes its function and may result in disease.

**Inherited/familial predisposition genes:** Altered genes that are present in the germ cells (eggs or sperm) and therefore can be passed through the generations, from parent to child. When an individual inherits a predisposition gene, all cells in their body carry that gene alteration, and the individual is at an increased risk of developing a particular disease.

**Somatic alterations:** Gene alterations that occur in non-germ cell DNA. This type of genetic alteration cannot be passed from parent to child since it has not occurred in an individual’s egg or sperm cells. This type of alteration will be present in only some of the cells in the body.

**Localized region:** A small, unique part of the DNA in a cell that has been identified as being the location of a disease-causing gene alteration.

**Non-familial:** Wilms tumor not due to an inherited predisposition gene alteration.