Neuroblastoma - Childhood - Risk Factors

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Risk Factors

For most types of cancer, a risk factor [2] describes anything that increases a person?s chance of developing cancer. Although risk factors often influence the development of cancer, most do not directly cause cancer. Some people with several risk factors never develop cancer, while others with no known risk factors do. For neuroblastoma, the term ?risk factor? is more commonly used to describe the factors that are used to predict how the tumor will grow and how well treatment will work (see Staging and Risk Grouping [3]).

Neuroblastoma occurs more often in boys than in girls. So far, no environmental factors have been shown to increase the risk of developing neuroblastoma. Rarely, more than one member of a family is diagnosed with neuroblastoma. Researchers have found inherited gene mutations (changes) that play a role in the development of neuroblastoma for children with a family history of the disease. Other genetic changes, called single-nucleotide polymorphisms or SNPs, may contribute to the development of neuroblastoma in children who do not have a family history. These two sets of risk factors involving genetics are explained in more detail below.

Family history and genetic predisposition

Approximately 1% to 2% of children with neuroblastoma have a family history of the disease. Children with an inherited likelihood of neuroblastoma tend to develop the disease, on average, nine to thirteen months earlier than other children with neuroblastoma. In children who have a family history of neuroblastoma, the disease may occur in two or more organs.

Neuroblastoma can be linked with Hirschsprung disease (a disease of the large intestine), congenital central hypoventilation syndrome (CCHS; a condition that affects a person?s nighttime breathing), pheochromocytoma [4], and neurofibromatosis type 1 [5]. The genes that cause these disorders have been studied, and loss of function from germline mutations (a mutation passed directly from parent to child) in *PHOX2B* (a gene that is mutated in CCHS that controls nerve cell development) have been found in a small number of patients with neuroblastoma.

Most of the time, when multiple members of a family have neuroblastoma, they have germline mutations in the *anaplastic lymphoma kinase* (*ALK*) gene. These mutations can be found in a blood sample. However, *ALK* mutations have also been found in DNA from tumors in some patients without a family history.

Neuroblastoma has also been diagnosed in several patients who are missing portions of chromosomes 1p and 11q that are thought to prevent tumor growth.

Genetic factors without a family history

The genetic factors that have a role in the development of neuroblastoma in patients who do not have a family history are not well understood. Genetic changes or SNPs on chromosome 6p and chromosome 2p within the *BARD1* gene have been linked with an increased risk of developing neuroblastoma in genetic studies [6], particularly aggressive (fast-growing) neuroblastoma. More recently, researchers have found an increased risk of aggressive neuroblastoma is linked with *LMO1* on the 11p15.4 chromosome, as well as the *HACE1* and *LIN28B* genes on chromosome 6q16. Changes in chromosome 1 (1q21.1) have also been shown to be linked with neuroblastoma, as have genetic changes within the *DUSP12* gene on chromosome 1q23.3 and the *DDX4* and *IL31RA* genes on chromosome 5q11.2. Changes in *HSD17B12* on chromosome 11p11.2 are associated with the less aggressive form of the disease.

Links:
[1] http://www.cancer.net/about-us
[2] http://www.cancer.net/node/24868
[3] http://www.cancer.net/node/19429
[4] http://www.cancer.net/node/19437
[5] http://www.cancer.net/node/19450
[6] http://www.genome.gov