

ABL1 Gene

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1. Normal Function

The *ABL1* gene provides instructions for making a protein involved in many processes in cells throughout the body. The ABL1 protein functions as a kinase, which is an enzyme that changes the activity of other proteins by adding a cluster of oxygen and phosphorus atoms (a phosphate group) at specific positions. The ABL1 kinase is normally turned off (inactive) and must be turned on (activated) to perform its functions.

The ABL1 kinase can be turned on by a number of different triggers and can add a phosphate group to many different proteins (also called substrates). This diversity allows ABL1 to be involved in a wide variety of cellular processes, including cell growth and division (proliferation), maturation (differentiation), and movement (migration). It can either aid in cell survival or trigger controlled cell death (apoptosis), depending on cellular conditions. The ABL1 kinase interacts with several proteins involved in the network of fibers called the actin cytoskeleton, which makes up the structural framework inside cells. These interactions help control cell migration and the attachment of cells to one another (adhesion), among many other processes. ABL1 can also help regulate the activity of other genes.

The *ABL1* gene belongs to a class of genes known as oncogenes. When mutated, oncogenes have the potential to cause normal cells to become cancerous.

2. Health Conditions Related to Genetic Changes

2.1 Chronic myeloid leukemia

A genetic rearrangement (translocation) involving the *ABL1* gene causes a type of cancer of blood-forming cells called chronic myeloid leukemia. This slow-growing cancer leads to an overproduction of abnormal white blood cells. Common features of the condition include excessive tiredness (fatigue), fever, weight loss, and an enlarged spleen.

The translocation involved in this condition, written as t(9;22), fuses part of the *ABL1* gene from chromosome 9 with part of the *BCR* gene from chromosome 22, creating an abnormal fusion gene called *BCR-ABL1*. The abnormal chromosome 22, containing a piece of chromosome 9 and the *BCR-ABL1* fusion gene, is commonly called the Philadelphia chromosome. The translocation is acquired during a person's lifetime and is present only in the abnormal blood cells. This type of genetic change, called a somatic mutation, is not inherited.

The protein produced from the abnormal fusion gene, called BCR-ABL1, functions as a kinase. However, unlike the ABL1 kinase, it does not require signals in the cell to turn it on. The constantly active BCR-ABL1 protein signals cells to continue dividing abnormally and prevents them from self-destructing, which leads to overproduction of the abnormal cells.

The presence of the Philadelphia chromosome provides a target for molecular therapies.

2.2 Other cancers

The *BCR-ABL1* fusion gene (described above) is also involved in fast-growing blood cell cancers called acute leukemias. It has been found in 5 percent of children and up to 30 percent of adults with B-cell acute lymphoblastic leukemia and very rarely in acute myeloid leukemia. As in chronic myeloid leukemia, the BCR-ABL1 protein stimulates overproduction of abnormal white blood cells, leading to cancer. It is likely that the form of blood cancer that develops is influenced by the type of blood cell that acquires the mutation and other genetic changes that occur.

Rarely, translocations that lead to fusion of the *ABL1* gene with genes other than *BCR* are associated with acute leukemias. For example, the *ETV6-ABL1* fusion gene has been found in a small number of cases of B-cell acute lymphoid leukemia, and a chronic leukemia that can resemble chronic myeloid leukemia. The exact mechanisms by which these rare fusion genes lead to blood cancer are not completely understood, although it is likely that the proteins produced from them promote uncontrolled growth of cells.

3. Other Names for This Gene

- Abelson tyrosine-protein kinase 1
- ABL
- bcr/abl
- bcr/c-abl oncogene protein
- c-ABL
- c-abl oncogene 1, receptor tyrosine kinase
- c-ABL1
- JTK7
- p150
- proto-oncogene c-Abl
- proto-oncogene tyrosine-protein kinase ABL1
- tyrosine-protein kinase ABL1 isoform a
- tyrosine-protein kinase ABL1 isoform b
- v-abl
- v-abl Abelson murine leukemia viral oncogene homolog 1

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