RAF1 Gene

Subjects: Genetics
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Definition

Raf-1 proto-oncogene, serine/threonine kinase

1. Normal Function

The *RAF1* gene provides instructions for making a protein that is part of a signaling pathway called the RAS/MAPK pathway, which transmits chemical signals from outside the cell to the cell's nucleus. RAS/MAPK signaling helps control the growth and division (proliferation) of cells, the process by which cells mature to carry out specific functions (differentiation), cell movement (migration), and the self-destruction of cells (apoptosis).

The *RAF1* 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. Noonan syndrome

More than 25 mutations causing Noonan syndrome have been identified in the *RAF1* gene. Noonan syndrome is characterized by mildly unusual facial characteristics, short stature, heart defects, bleeding problems, skeletal malformations, and many other signs and symptoms. The *RAF1* gene mutations change single protein building blocks (amino acids) in the RAF1 protein. These changes increase protein activity and disrupt the regulation of the RAS/MAPK signaling pathway causing problems with cell division, apoptosis, cell differentiation, and cell migration. Researchers believe that this disruption in normal cell processes plays a role in the signs and symptoms of Noonan syndrome, specifically cardiac abnormalities. It has been noted that people with Noonan syndrome caused by a *RAF1* gene mutation have a greater incidence of heart defects than other people with Noonan syndrome, specifically a condition called hypertrophic cardiomyopathy, which is a thickening of the heart muscle that forces the heart to work harder to pump blood.

2.2. Noonan syndrome with multiple lentigines

At least two mutations in the *RAF1* gene have been found to cause Noonan syndrome with multiple lentigines (formerly called LEOPARD syndrome). This condition is characterized by multiple brown skin spots (lentigines), heart defects, short stature, a sunken or protruding chest, and distinctive facial features. The *RAF1* gene mutations change single amino acids in the RAF1 protein: One mutation replaces the amino acid serine with the amino acid leucine at position 257 (written Ser257Leu or S257L) and the other mutation replaces the amino acid leucine with the amino acid valine at position 613 (written Leu613Val or L613V).

The *RAF1* gene changes that cause Noonan syndrome with multiple lentigines are believed to abnormally activate the RAF1 protein, which disrupts the regulation of the RAS/MAPK signaling pathway that controls cell functions such as growth and division. This misregulation can result in the various features of Noonan syndrome with multiple lentigines.

2.3. Cancers

Some gene mutations are acquired during a person's lifetime and are present only in certain cells. These

changes are called somatic mutations and are not inherited. Somatic mutations in the *RAF1* gene are involved in the development of several types of cancer. These mutations lead to a RAF1 protein that is always active and can direct cells to grow and divide uncontrollably. Studies suggest that *RAF1* gene mutations may be found in ovarian, lung, and colorectal cancers. Somatic mutations in the *RAF1* gene are a rare cause of cancer.

For reasons that are unclear, inherited mutations in the *RAF1* gene do not appear to increase the risk of cancer in people with Noonan syndrome with multiple lentigines or Noonan syndrome.

3. Other Names for This Gene

- c-Raf
- CRAF
- Oncogene RAF1
- raf proto-oncogene serine/threonine protein kinase
- Raf-1
- RAF1_HUMAN

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Keywords

genes