EPCAM Gene

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1. Normal Function

The *EPCAM* gene provides instructions for making a protein known as epithelial cellular adhesion molecule (EpCAM). This protein is found in epithelial cells, which are the cells that line the surfaces and cavities of the body. The EpCAM protein is found spanning the membrane that surrounds epithelial cells, where it helps cells stick to one another (cell adhesion). In addition, the protein in the cell membrane can be cut at a specific location, releasing a piece called the intracellular domain (EpICD), which helps relay signals from outside the cell to the nucleus of the cell. EpICD travels to the nucleus and joins with other proteins, forming a group (complex) that regulates the activity of several genes that are involved in many cell processes, including growth and division (proliferation), maturation (differentiation), and movement (migration), all of which are important processes for the proper development of cells and tissues.

2. Health Conditions Related to Genetic Changes

2.1. Lynch syndrome

Certain mutations in the *EPCAM* gene are associated with Lynch syndrome, a condition that increases the risk of developing many types of cancer, particularly cancers of the large intestine (colon) and the rectum (collectively called colorectal cancer). These mutations account for up to 3 percent of Lynch syndrome cases. On chromosome 2, the *EPCAM* gene lies next to another gene called *MSH2*. Each gene provides instructions for making an individual messenger RNA (mRNA), which serves as the genetic blueprint for making the protein. The *EPCAM* gene mutations involved in Lynch syndrome remove a region that signals the end of the gene, which leads to formation of a long mRNA that includes both *EPCAM* and *MSH2*.

For unknown reasons, these *EPCAM* gene mutations cause the *MSH2* gene to be turned off (inactivated) by a mechanism known as promoter hypermethylation. The promoter is a region of DNA near the beginning of the gene that controls gene activity (expression). Hypermethylation occurs when too many small molecules called methyl groups are attached to the promoter region. The extra methyl groups attached to the *MSH2* promoter reduce the expression of the *MSH2* gene, which means that less protein is produced in epithelial cells.

The MSH2 protein plays an essential role in repairing errors in DNA; loss of this protein prevents proper DNA repair, and errors accumulate as the cells continue to divide. These errors can lead to uncontrolled cell growth and increase the risk of cancer.

2.2. Other disorders

Mutations in the *EPCAM* gene can also cause congenital tufting enteropathy. This condition is characterized by abnormal development of epithelial cells in the intestines. In this condition, the villi, which are small finger-like projections that line the small intestine, are abnormal. In particular, they have "tufts" of extra epithelial cells on their tips. Normally, these projections provide a greatly increased surface area to absorb nutrients. The altered villi are less able to absorb nutrients and fluids than normal tissue, which causes life-threatening diarrhea and poor growth. Congenital tufting enteropathy develops in newborns within days of birth and lasts throughout life.

People with congenital tufting enteropathy have two copies of the altered *EPCAM* gene in each cell. These mutations lead to an absence of functional EpCAM protein. The resulting loss of EpICD signaling leads to abnormal development of intestinal epithelial cells, causing congenital tufting enteropathy.

3. Other Names for This Gene

- EGP-2
- EGP34
- EGP40
- Ep-CAM
- epithelial cell adhesion molecule precursor
- epithelial glycoprotein 314
- human epithelial glycoprotein-2
- TACST-1
- TACSTD1
- TROP1
- tumor-associated calcium signal transducer 1

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