

EWSR1 gene

EWS RNA binding protein 1

Normal Function

The *EWSR1* gene provides instructions for making the EWS protein, whose function is not completely understood. The EWS protein has two regions that contribute to its function. One region, the transcriptional activation domain, allows the EWS protein to turn on (activate) the first step in the production of proteins from genes (transcription). The other region, the RNA-binding domain, allows the EWS protein to attach (bind) to the genetic blueprint for proteins called RNA. The EWS protein may be involved in piecing together this blueprint. Some studies suggest that the RNA-binding domain is able to block (inhibit) the activity of the transcriptional activation domain, and thus regulate the function of the EWS protein.

Health Conditions Related to Genetic Changes

Ewing sarcoma

Mutations involving the *EWSR1* gene can cause a type of cancerous tumor known as Ewing sarcoma. These tumors develop in bones or soft tissues, such as nerves and cartilage. There are several types of Ewing sarcoma, including Ewing sarcoma of bone, extrasosseous Ewing sarcoma, peripheral primitive neuroectodermal tumor, and Askin tumor. The mutations that cause these tumors are acquired during a person's lifetime and are present only in the tumor cells. This type of genetic change, called a somatic mutation, is not inherited. The most common mutation that causes Ewing sarcoma is a rearrangement (translocation) of genetic material between chromosome 22 and chromosome 11. This translocation, written as t(11;22), fuses part of the *EWSR1* gene on chromosome 22 with part of another gene on chromosome 11 called *FLI1*, creating an *EWSR1/FLI1* fusion gene.

The protein produced from the *EWSR1/FLI1* fusion gene, called EWS/FLI, has functions of the protein products of both genes. The FLI protein, produced from the *FLI1* gene, attaches to DNA and regulates transcription. This protein controls the growth and development of some cell types. The EWS/FLI protein has the DNA-binding function of the FLI protein as well as the transcription regulation function of the EWS protein. It is thought that the EWS/FLI protein turns the transcription of a variety of genes on and off abnormally. This dysregulation of transcription leads to uncontrolled growth and division (proliferation) and abnormal maturation and survival of cells, causing tumor

development.

The *EWSR1/FLI1* fusion gene occurs in approximately 85 percent of Ewing sarcomas. Translocations that fuse the *EWSR1* gene with other genes that are related to the *FLI1* gene can also cause these types of tumors, although these alternative translocations are relatively uncommon. The fusion proteins produced from the less common translocations have the same function as the EWS/FLI protein.

Other cancers

Translocations involving the *EWSR1* gene are involved in many types of soft tissue sarcoma, which are cancers that cause tumors in soft tissues such as fat, muscles, and nerves. These translocations fuse the *EWSR1* gene with one of several other genes. These other genes, sometimes referred to as fusion partners, seem to determine the type of tumor that develops.

The *EWSR1/WT1* fusion gene causes desmoplastic small round cell tumor, a type of soft tissue sarcoma that often occurs in the abdomen. The *EWSR1/ATF1* fusion gene is involved in a rare type of cancer called soft tissue clear cell sarcoma (or malignant melanoma of soft parts). In this type of cancer, tumors usually develop in the tendons, especially in the knees, feet, and ankles. A translocation that creates the *EWSR1/NR4A3* fusion gene causes extraskeletal myxoid chondrosarcoma, which is a rare type of soft tissue tumor that usually occurs in the lower body, such as the thighs or buttocks. The *EWSR1/DDIT3* fusion gene is sometimes found in myxoid liposarcomas, although it is an uncommon cause of this type of cancer. Myxoid liposarcomas occur in fatty tissue in many parts of the body.

Other Names for This Gene

- Ewing sarcoma breakpoint region 1
- Ewings sarcoma EWS-Flil (type 1) oncogene
- EWS
- EWS RNA-binding protein 1
- EWS_HUMAN
- RNA-binding protein EWS

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of EWSR1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2130\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2130[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28EWSR1%5BTIAB%5D%29+OR+%28Ewing+sarcoma+breakpoint+region+1%5BTIAB%5D%29%29+AND+%28EWS+RNA-binding+protein+1%5BHUMAN%5D%29%29>)

28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- EWS RNA-BINDING PROTEIN 1; EWSR1 (<https://omim.org/entry/133450>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/2130>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=EWSR1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=EWSR1[gene]))

References

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Genomic Location

The *EWSR1* gene is found on chromosome 22 (<https://medlineplus.gov/genetics/chromosome/22/>).

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