RSPO2 gene

R-spondin 2

Normal Function

The *RSPO2* gene provides instructions for making a protein called R-spondin-2. R-spondin-2 plays a role in the Wnt signaling pathway, a series of steps that affect the way cells and tissues develop. Wnt signaling is important for cell division, attachment of cells to one another (adhesion), cell movement (migration), and many other cellular activities.

During early development, Wnt signaling plays a critical role in growth and development of the skeleton and other tissues. The role of R-spondin-2 is to increase Wnt signaling. Specifically, R-spondin-2 attaches (binds) to certain proteins on the surface of cells to turn off (inactivate) proteins that block the Wnt pathway.

Health Conditions Related to Genetic Changes

Tetra-amelia syndrome

Variants (also called mutations) in the *RSPO2* gene have been found to cause tetra-amelia syndrome. This condition is very rare and characterized by the absence of all four limbs. *RSPO2* gene variants cause a form of this condition known as tetra-amelia syndrome type 2 in which affected individuals typically have a complete absence of both lungs. Because children with this condition have such serious medical problems, most are stillborn or die shortly after birth.

In individuals with tetra-amelia syndrome, *RSPO2* gene variants typically result in a complete lack of functional R-spondin-2 protein. As a result, the R-spondin-2 protein is not available on the cell surface to inactivate proteins that block the Wnt pathway, so this critical pathway is dysregulated. During early development, irregular Wnt signaling leads to poor development of the limbs, organs, and other tissues, resulting in the severe signs and symptoms of tetra-amelia syndrome type 2.

Cancers

Chromosomal rearrangements (translocations) involving the *RSPO2* gene on chromosome 8 have been associated with certain types of cancer. These genetic changes are somatic, which means they are acquired during a person's lifetime and are

present only in certain cells. In cancer cells, translocations can disrupt the region of chromosome 8 that contains the *RSPO2* gene. Researchers have found a translocation between chromosome 8 and other chromosomes in several people with a cancer of the colon, stomach, lungs, liver, or prostate.

Increased activity (overexpression) of the *RSPO2* gene has also been identified in different types of cancers, including cancer of the colon, stomach, breast, liver, and pancreas. The genetic changes involved in this overexpression are somatic. Research suggests that overexpression of the *RSPO2* gene leads to increased Wnt signaling. As a result, cell growth and division are increased, which can lead to cancer.

Other Names for This Gene

- cristin2
- R-spondin family, member 2
- R-spondin-2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of RSPO2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=340419[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(RSPO2%5BTIAB%5D)+AND+(R-SPONDIN-2%5BTIAB%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- R-SPONDIN 2; RSPO2 (https://omim.org/entry/610575)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/340419)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=RSPO2[gene])

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Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/30284717)

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Last updated February 17, 2023