SKI gene

SKI proto-oncogene

Normal Function

The *SKI* gene provides instructions for making a protein involved in a signaling pathway that transmits chemical signals from the cell surface to the nucleus. This pathway, called the transforming growth factor beta (TGF-β) pathway, allows the environment outside the cell to affect how the cell produces other proteins. It helps regulate cell growth and division (proliferation), the process by which cells mature to carry out special functions (differentiation), cell movement (motility), and the self-destruction of cells (apoptosis). Through this pathway, a group of proteins called the SMAD complex is turned on (activated). The activated SMAD protein complex moves to the cell nucleus and attaches (binds) to specific areas of DNA to control the activity of particular genes, which help regulate various cellular processes.

The SKI protein controls the activity of the TGF-β pathway by binding to certain SMAD proteins, which interrupts signaling through the pathway. SKI protein binding within the cell can keep the SMAD protein complex from entering the nucleus, so it is unable to activate genes. Binding of the SKI protein can also occur in the nucleus. Although the SMAD complex binds to DNA, the SKI protein attracts other proteins (corepressors) that block its ability to turn genes on.

The SKI protein is found in many cell types throughout the body and appears to play a role in the development of many tissues, including the skull, other bones, skin, and brain.

Health Conditions Related to Genetic Changes

Shprintzen-Goldberg syndrome

At least 10 mutations in the *SKI* gene have been found in people with Shprintzen-Goldberg syndrome, a condition characterized by distinctive facial features, skeletal abnormalities, and intellectual disability. Most of these mutations change single protein building blocks (amino acids) in the SKI protein. Many of the mutations alter the region of the SKI protein that binds to SMAD proteins. It is thought that altered SKI proteins are unable to attach to SMAD proteins, which allows TGF-β signaling to continue uncontrolled. Excess TGF-β signaling changes the regulation of gene activity and likely disrupts development of many body systems, including the bones and brain, resulting in

the wide range of signs and symptoms of Shprintzen-Goldberg syndrome.

Other Names for This Gene

- proto-oncogene c-Ski
- ski oncogene
- ski oncoprotein
- SKI_HUMAN
- v-ski avian sarcoma viral oncogene homolog
- v-ski sarcoma viral oncogene homolog (avian)

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SKI (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6497[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SKI%5BTIAB%5D%29+OR+%28v-ski+sarcoma+viral+oncogene+homolog%5BTIAB%5D%29+NOT+%28sphingosine+kinase%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SKI PROTOONCOGENE; SKI (https://omim.org/entry/164780)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6497)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SKI[gene])

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Genomic Location

The *SKI* gene is found on chromosome 1 (https://medlineplus.gov/genetics/chromosom e/1/).

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