Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

GLI1 (glioma-associated oncogene homolog 1)

Anna Dahlén, Fredrik Mertens, Nils Mandahl, Ioannis Panagopoulos

Department of Clinical Genetics, Lund University Hospital, SE-221 85 Lund, Sweden (AD, FM, NM, IP)

Published in Atlas Database: March 2005

Online updated version: http://AtlasGeneticsOncology.org/Genes/GLIID310ch12q13.html
DOI: 10.4267/2042/38184

Identity

Other names: GLI; Zinc finger protein GLI1 (glioma-associated oncogene); Oncogene GLI; Glioma-associated oncogene homolog 1

HGNC (Hugo): GLI1

Location: 12q13.2-q13.3

Location (base pair): Position 56140200-56152312 on the chromosome 12 genomic sequence.

Local order: Telomeric to the ATF1 gene; centromeric to the OS-9, SAS and CDK4 genes.

Note: GLI1 was the first human member of the Krüppel zinc finger proteins to be identified, and constitutes the archetype of this family of human genes. Other members are GLI2 (2q14) and GLI3 (7p13). GLI4/HKR4 (8q24) was misclassified as member of the human GLI gene family.

DNA/RNA

Description

12 exons, spans approximately 12 kb of genomic DNA in the centromere-to-telomere orientation. The translation initiation codon is located to exon 2, and the stop codon to exon 12.

Transcription

mRNA of 3.6 kb.

Protein

Description

The open reading frame encodes a 1106 amino acid protein, with an estimated molecular weight of approximately 118 kDa. The protein contains five DNA-binding zinc fingers between amino acids 235 and 393 (encoded by exons 7-10), and a transactivating domain constituted by amino acids 1020-1091 (encoded by exon 12).

Expression

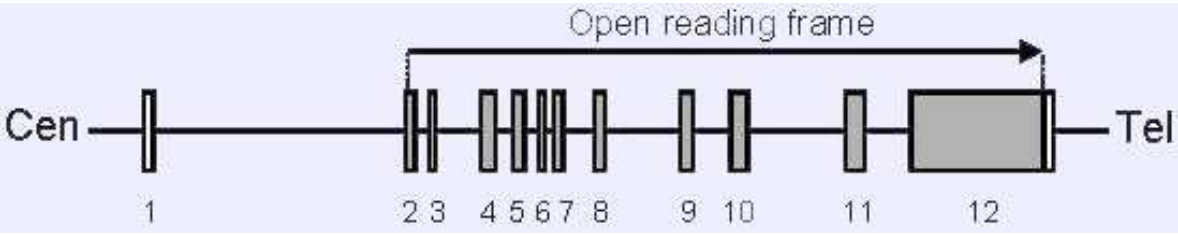
GLI proteins function as direct effectors of sonic hedgehog-signaling during embryogenesis. GLI1 (also GLI2 and GLI3) are therefore likely to be involved in the tissue-specific proliferation of the central nervous system, the zones of polarizing activity in the developing limb, and of the gut. In the adult human, GLI1 expression has been demonstrated in the testes, myometrium and Fallopian tubes.

Localisation

Nuclear. Might be fluctuating between the cytoplasm and the nucleus.

Function

DNA-binding transcription factor.



Genomic organization of the GLI1 gene.

Mutations

Germinal

An abnormal activity of GLI, caused by mutations affecting upstream components of the sonic hedgehog-signaling pathway (sonic hedgehog, patched or smoothened) are associated with developmental disorders.

Somatic

Various tumors of mesenchymal and lymphocytic origin.

Implicated in

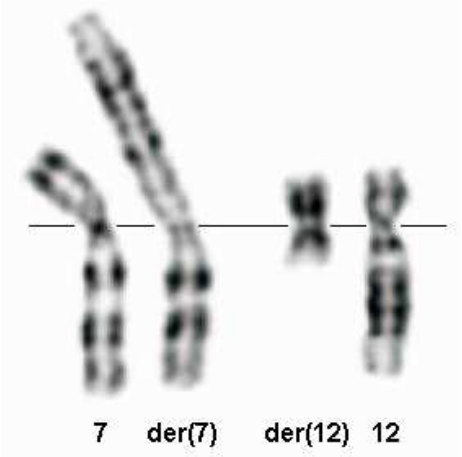
Note
Rearrangement and fusion of the GLI1 gene.

Disease
Pericytoma with t(7;12)

Prognosis
Benign or low-malignant.

Cytogenetics
t(7;12)(p22;q13)

Hybrid/Mutated gene
ACTB-GLI1 fusion gene. The breakpoints reported so far have been located to introns 1, 2 or 3 within the ACTB gene, and to introns 5 or 6 or to exon 7 within the GLI1 gene. Reciprocal GLI1-ACTB gene fusions have also been detected. The breakpoints have been located to introns 5 or 7 within the GLI1 gene, and to intron 3 of the ACTB gene.



Representative G-banded partial karyotype of the t(7;12)(p22;q13).

Abnormal protein
The ACTB-GLI1 fusion protein contains the N-terminal of ACTB and the C-terminal of GLI1, including the DNA-binding zinc finger motifs (encoded by exons 7-10) and transactivating motifs (exon 12).

Oncogenesis
It is suggested that the strong ACTB promoter causes an overexpression of GLI1 sequences important for transcriptional activation of downstream target genes, akin to the oncogenic mechanisms of the COL1A1-PDGFB fusion gene detected in dermatofibrosarcoma protuberans.

Note
Amplification of the GLI1 gene.

Disease
Glioma, B-cell lymphoma, sarcoma

Prognosis
Depends on tumor type.

Oncogenesis
Overexpression of GLI1 sequences. Might be of prognostic importance.

References

Kinzler KW, Bigner SH, Bigner DD, Trent JM, Law ML, O'Brien SJ, Wong AJ, Vogelstein B. Identification of an amplified, highly expressed gene in a human glioma. Science. 1987 Apr 3;236(4797):70-3

Kinzler KW, Ruppert JM, Bigner SH, Vogelstein B. The GLI gene is a member of the Kruppel family of zinc finger proteins. Nature. 1988 Mar 24;332(6162):371-4

Arheden K, Rønne M, Mandahl N, Heim S, Kinzler KW, Vogelstein B, Mitelman F. In situ hybridization localizes the human putative oncogene GLI to chromosome subbands 12q13.3-14.1. Hum Genet. 1989 Apr;82(1):1-2

Roberts WM, Douglass EC, Peiper SC, Houghton PJ, Look AT. Amplification of the gli gene in childhood sarcomas. Cancer Res. 1989 Oct 1;49(19):5407-13

Kinzler KW, Vogelstein B. The GLI gene encodes a nuclear protein which binds specific sequences in the human genome. Mol Cell Biol. 1990 Feb;10(2):634-42

Ruppert JM, Vogelstein B, Arheden K, Kinzler KW. GLI3 encodes a 190-kilodalton protein with multiple regions of GLI similarity. Mol Cell Biol. 1990 Oct;10(10):5408-15

Kas K, Wlodarska I, Meyen E, Van den Berghe H, Van de Ven WJ. Assignment of the gene encoding human Krüppel-related zinc finger protein 4 (GLI4) to 8q24.3 by fluorescent in situ hybridization. Cytogenet Cell Genet. 1996;72(4):297-8

Matsumoto N, Fujimoto M, Kato R, Niikawa N. Assignment of the human GLI2 gene to 2q14 by fluorescence in situ hybridization. Genomics. 1996 Aug 15;36(1):220-1

Simon MP, Pedeutour F, Sirvent N, Grosgeorge J, Minoletti F, Coindre JM, Terrier-Lacombe MJ, Mandahl N, Craver RD, Blin N, Sozzi G, Turc-Carel C, O'Brien KP, Kedra D, Fransson I, Guilbaud C, Dumanski JP. Deregulation of the platelet-derived growth factor B-chain gene via fusion with collagen gene COL1A1 in dermatofibrosarcoma protuberans and giant-cell fibroblastoma. Nat Genet. 1997 Jan;15(1):95-8

Werner CA, Döhner H, Joos S, Trümper LH, Baudis M, Barth TF, Ott G, Möller P, Lichter P, Bentz M. High-level DNA amplifications are common genetic aberrations in B-cell neoplasms. Am J Pathol. 1997 Aug;151(2):335-42

Liu CZ, Yang JT, Yoon JW, Villavicencio E, Pfendler K, Walterhouse D, Iannaccone P. Characterization of the promoter region and genomic organization of GLI, a member of the Sonic hedgehog-Patched signaling pathway. Gene. 1998 Mar 16;209(1-2):1-11

Odent S, Atti-Bitach T, Blayau M, Mathieu M, Aug J, Delezo de AL, Gall JY, Le Marec B, Munnich A, David V, Vekemans M. Expression of the Sonic hedgehog (SHH) gene during early human development and phenotypic expression of new mutations causing holoprosencephaly. Hum Mol Genet. 1999 Sep;8(9):1683-9

Villavicencio EH, Walterhouse DO, Iannaccone PM. The sonic hedgehog-patched-gli pathway in human development and disease. Am J Hum Genet. 2000 Nov;67(5):1047-54

Dahlén A, Fletcher CD, Mertens F, Fletcher JA, Perez-Atayde AR, Hicks MJ, Debiec-Rychter M, Sciot R, Wejde J, Wedin R, Mandahl N, Panagopoulos I. Activation of the GLI oncogene through fusion with the beta-actin gene (ACTB) in a group of distinctive pericytic neoplasms: pericytoma with t(7;12). Am J Pathol. 2004 May;164(5):1645-53

Dahlén A, Mertens F, Mandahl N, Panagopoulos I. Molecular genetic characterization of the genomic ACTB-GLI fusion in pericytoma with t(7;12). Biochem Biophys Res Commun. 2004 Dec 24;325(4):1318-23

This article should be referenced as such:

Dahlén A, Mertens F, Mandahl N, Panagopoulos I. GLI1 (glioma-associated oncogene homolog 1). Atlas Genet Cytogenet Oncol Haematol. 2005; 9(2):136-138.