

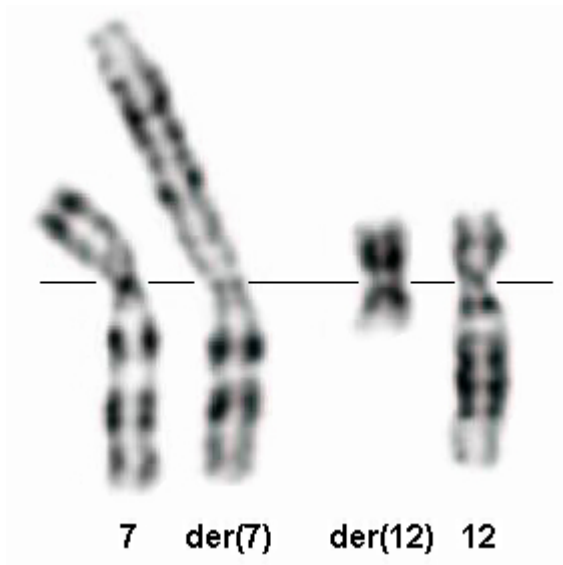
Pericytoma with t(7;12)

Clinics and Pathology

Disease	Pericytoma with t(7;12)
Phenotype / cell stem origin	Unknown
Embryonic origin	The cellular origin is unknown, but it presumably derives from the mesoderm. The tumor cells display cytoarchitectural, immunohistochemical and ultrastructural features highly suggestive of pericytic differentiation, and it seems likely that these lesions fall within the spectrum of myopericytic neoplasms.
Etiology	Unknown.
Epidemiology	Presumably rare, but differential diagnostic problems may have hampered the distinction of these tumors in the past. Tumors that fall within the differential diagnosis include cellular examples of solitary fibrous tumors (also known as hemangiopericytoma), myofibroma(tosis), monophasic synovial sarcoma , mesenchymal chondrosarcoma , and metastatic endometrial stromal sarcoma. Affects both men and woman of all ages. No familial cases are known.
Clinics	Seems to present as a solitary pain-less nodule. The locations reported so far have been the tongue (3 cases), the stomach (1 case) and the calf (1 case).
Pathology	Pericytomas with t(7;12) display a multilobulated, infiltrative growth pattern, and are composed of uniform spindle-shaped pericytic cells that are consistently arranged around small, thin-walled arborizing vessels. The spindle cells present small amounts of eosinophilic cytoplasm, and ovoid-to-tapered nuclei with vesicular chromatin and often a single nucleolus. No significant atypia or pleomorphism is present, and mitotic figures are rare.
Treatment	Preoperative chemotherapy has not proven efficient. Surgical excision seems to be the treatment of choice.
Prognosis	Based on a limited follow-up (22-120 months), pericytomas with t(7;12) are seemingly benign or low-malignant tumors. No signs of recurrence or metastasis have been reported.

Cytogenetics

Cytogenetics The recurrently observed t(7;12)(p22;q13) is a specific translocation Morphological characteristic for the tumor type.



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

Cytogenetics Molecular	Metaphase FISH mapping analysis on one case revealed that the breakpoints were located to BAC probes RP11-1275H24, and RP11-93G19 on 7p22, and to BAC probes 181L23, and 772E1 on 12q13. The probes gave split signals on the respective derivatives. On the normal chromosomes, intact signals were seen.
Probes	BAC probes RP11-1275H24 (AC092171; substantially larger than the 85 kb reported by the NCBI), and RP11-93G19 (BAC ends: AQ321651, AQ321650) spanning the ACTB locus, and BAC probes 181L23 (AC022506), and 772E1 (AC063917) spanning the GLI1 locus.

Genes involved and Proteins

Note	The t(7;12)(p22;q13), fuses the ACTB gene in 7p22, to the GLI1 gene in 12q13.
Gene Name	ACTB
Location	7p22
Dna / Rna	Six exons, spans approximately 3.4 kb of genomic DNA in the centromere-to-teleomere orientation. The translation initiation codon ATG is located to exon 2, and the stop codon to exon 6. The ACTB mRNA is approximately 1.8 kb. ACTB is abundantly expressed in all mammalian and avian non-muscle cells.
Protein	The open reading frame encodes a 374 amino acid protein, with an estimated molecular weight of approximately 41.7 kDa. The ACTB protein is located in the cytoplasm where it is a component (together with actin g) of the cytoskeleton.

Gene Name	GLI1
Location	12q13
Dna / Rna	Twelve exons, spans approximately 12 kb of genomic DNA in the centromere-to-telomere orientation. The translation initiation codon is located in exon 2, and the stop codon in exon 12. The GLI1 mRNA transcript is 3.6 kb.
Protein	<p>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.</p> <p>The open reading frame encodes an 1106 amino acid protein, with an estimated molecular weight of approximately 118 kDa. The GLI protein is a DNA binding transcription factor, also the last known step in the sonic hedgehog-signaling pathway. The GLI1 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).</p>

Result of the chromosomal anomaly

Hybrid Gene

Note	To date, five cases of pericytoma with t(7;12) have been reported. All of them expressed an ACTB-GLI1 transcript, and two of them also expressed a reciprocal GLI1-ACTB fusion transcript. The genomic breakpoints of these fusions have been characterized, revealing that the respective breakpoints shared short common oligomers.
Detection	A detailed description of a protocol for the detection of ACTB-GLI1 and GLI1-ACTB chimeras has been reported.

Fusion Protein

Note	The function of the ACTB-GLI1 chimera is unknown, but it is suggested that the strong ACTB promoter causes an over-expression of GLI1 sequences important for transcriptional activation of downstream target genes.
Description	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).

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