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## The clinical significance of ADD3 in Glioblastoma

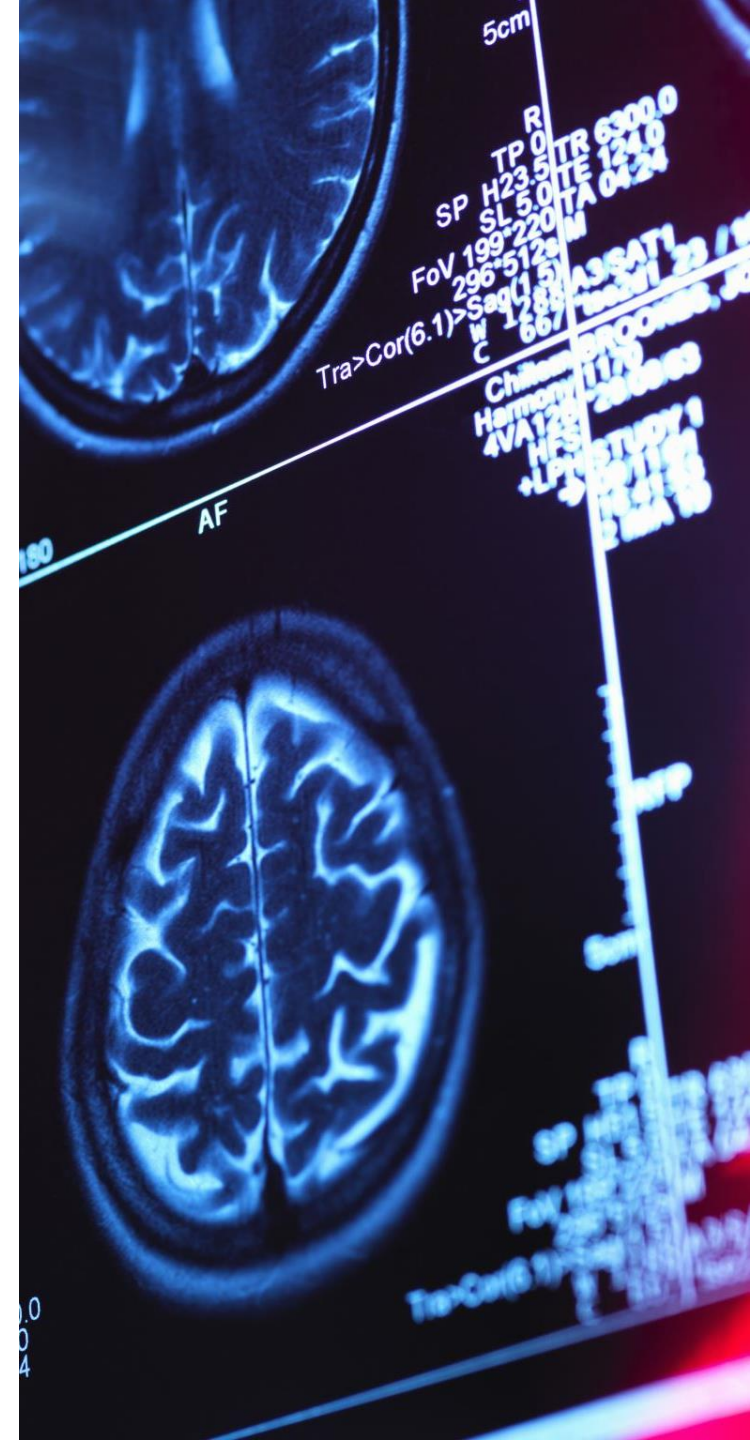
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# Background

Adducin 3 (ADD3) is a major cytoskeleton protein in cells. Our previous work showed significant downregulation of ADD3 in glioblastoma (GBM), as well its tumor suppressive role. In GBM, there are frequent loss of heterozygosity (LOH) on chromosome 10q. ADD3 is located in chromosome 10q25.1-25.2, where it is known to be a tumor-suppressor region.

It is not known whether ADD3 downregulation in GBM is associated with allelic loss in 10q. Here, we aim to investigate the diagnostic and prognostic implication of ADD3 loss in GBM.



Contents lists available at [ScienceDirect](#)

## Cancer Letters

journal homepage: [www.elsevier.com/locate/canlet](http://www.elsevier.com/locate/canlet)

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Original Articles

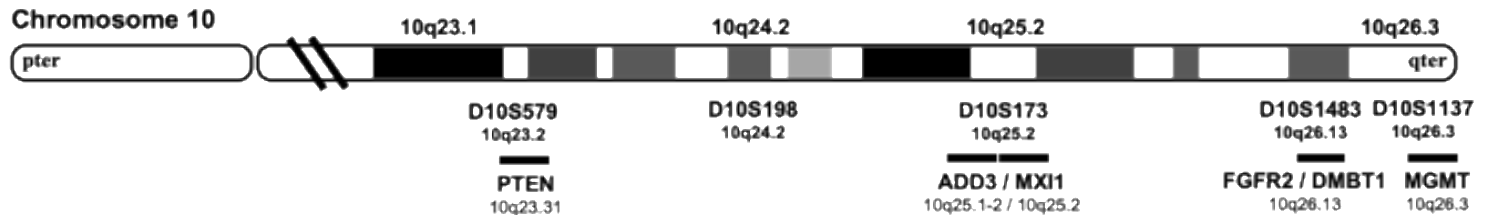
### Loss of cytoskeleton protein ADD3 promotes tumor growth and angiogenesis in glioblastoma multiforme

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# Methodology

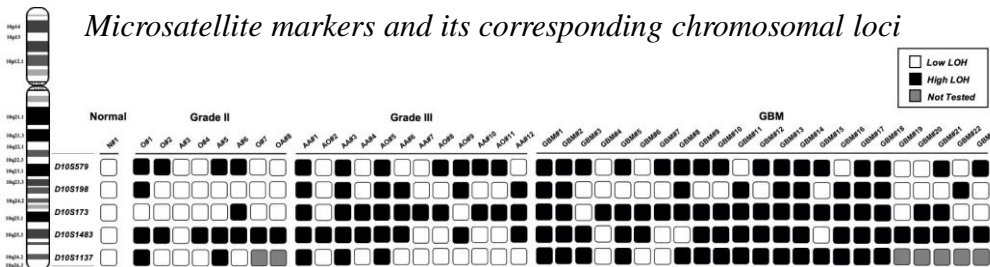
To determine 10q LOH on five different polymorphic DNA loci on glioma tissues, specimens of non-neoplastic, WHO grade II, III and IV (GBM) were included. DNA fragments were evaluated by using a PCR-based microsatellite capillary electrophoresis and analyzed by a fragment analyzer. LOH status were correlated with patient survival for potential prognostic and diagnostic implications. ADD3 protein expressions were analyzed by western blot and compared between primary and recurrent gliomas.



# Results

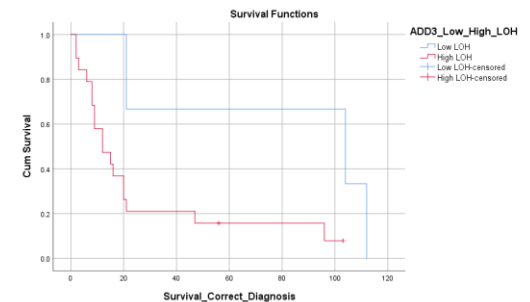
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LOH on ADD3 locus was detected in high grade gliomas (83.3% in Grade III, and 82.6% in GBM). It is revealed that downregulation of ADD3 expression in GBM is possibly associated with genetic instability of LOH in 10q and associated with poor survival (\* $p = 0.047$ ).



Microsatellite marker	Location	Size range (bp)	Forward Primer 5' - 3'	Reverse Primer 5' - 3'	LOH (%)		
					Grade II	Grade III	GBM
D10S579	10q23.2	260-276	COGATCAATGAGGAGTGCC	ATACACCCAGCCAATGCTGC	37.5	58.3	69.6
D10S198	10q24.2	184-203	TGAGGGACTCATCTTCTGTT	GTCTGTGATCCCCATGTTAG	12.5	50.0	43.5
D10S173	10q25.2	155	GCTGATTTTCTGCTGGTGC	TGTTTCTGAAGCATTTTCCTTG	12.5	83.3	82.6
D10S1483	10q26.13	130-158	CAATGCTATCCCGCTATG	TCAAGACTGCAAGCGTGT	87.5	66.7	82.6
D10S1137	10q26.3	600	GGAGACAGAGCAAGACCTG	GATGACTCTCCAGCAGCTTC	23	25	65.2

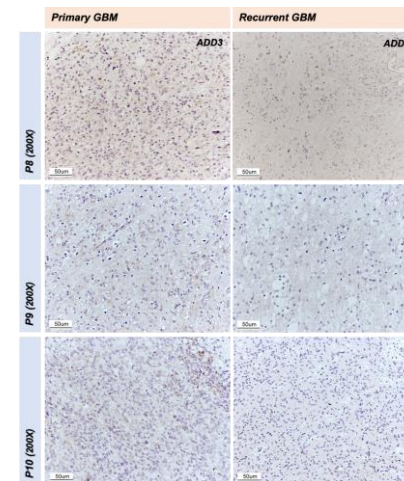
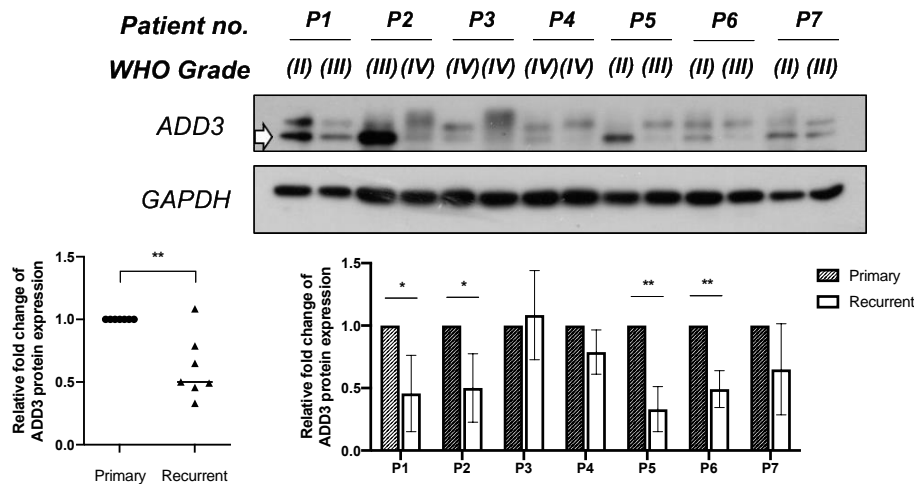
*Kaplan Meier Survival on ADD3 LOH status*  
Log rank = 0.047



# Results

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ADD3 protein expression was determined in primary and recurrent gliomas in seven patients (P1-P7). We found that ADD3 was downregulated in recurrent tumors compared to the primary lesion.



# Discussion and Conclusion

- LOH on chromosome 10 has been found exclusively in malignant gliomas and of such tumors, primarily among the most malignant form, glioblastoma. Here, we have applied LOH analysis to a large panel of gliomas in order to identify specific regions of chromosome 10 deletions, and to establish correlations between their accumulation, tumor malignancy and clinical outcome.
- Our results show the microsatellite marker D10S173 (ADD3) is among the most frequent LOH found in high grade gliomas. Furthermore, ADD3 expression was further downregulated in recurrent tumors. Suggesting that this event may be associated with the development of high grade malignancy.
- 10q LOH on ADD3 locus may account for the downregulation of ADD3 seen in high grade gliomas.
- This study will provide significant implications, particularly for understanding pathogenesis of GBM and add valuable credits on the diagnostic as well as prognostic implications.