Bosnian Journal of Basic Medical Sciences 2020 vol.20 N1, pages 63-69

Long noncoding rna malat1 may be a prognostic biomarker in idh1/2 wild-type primary glioblastomas

Argadal O.G., Mutlu M., Aksoy S.A., Kocaeli H., Tunca B., Civan M.N., Egeli U., Cecener G., Bekar A., Taskapilioglu M.O., Tekin C., Tezcan G., Tolunay S.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2019 ABMSFBIH. Primary glioblastoma (GB) is the most aggressive type of brain tumors. While mutations in isocitrate dehydrogenase (IDH) genes are frequent in secondary GBs and correlate with a better prognosis, most primary GBs are IDH wild-type. Recent studies have shown that the long noncoding RNA metastasis associated lung adenocarcinoma transcript-1 (MALAT1) is associated with aggressive tumor phenotypes in different cancers. Our aim was to clarify the prognostic significance of MALAT1 in IDH1/2 wild-type primary GB tumors. We analyzed IDH1/2 mutation status in 75 patients with primary GB by DNA sequencing. The expression of MALAT1 was detected in the 75 primary GB tissues and 5 normal brain tissues using reverse transcription quantitative PCR (RT-qPCR). The associations between MALAT1 expression, IDH1/2 mutation status, and clinicopathological variables of patients were determined. IDH1 (R132H) mutation was observed in 5/75 primary GBs. IDH2 (R172H) mutation was not detected in any of our cases. MALAT1 expression was significantly upregulated in primary GB vs. normal brain tissues ($p = 0.025$). Increased MALAT1 expression in IDH1/2 wild-type primary GBs correlated with patient age and tumor localization ($p = 0.032$ and $p = 0.025$, respectively). A multivariate analysis showed that high MALAT1 expression was an unfavorable prognostic factor for overall survival ($p = 0.034$) in IDH1/2 wild-type primary GBs. High MALAT1 expression may have a prognostic role in primary GBs independent of IDH mutations.

http://dx.doi.org/10.17305/bjbms.2019.4297

Keywords

Biomarker, IDH1/2, Isocitrate dehydrogenase, Long noncoding RNA, MALAT1, Primary glioblastoma, Prognosis

References

[1] Ostrom QT, Gittleman H, Farah P, Ondracek A, Chen Y, Wolinsky Y, et al. CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2006-2010. Neuro Oncol 2013;15(Suppl 2):ii1-56. https://doi.org/10.1093/neuonc/not151.

[2] Walker MD, Green SB, Byar DP, Alexander E Jr, Batzdorf U, Brooks WH, et al. Randomized comparisons of radiotherapy and nitrosoureas for the treatment of malignant glioma after surgery. N Engl J Med 1980;303(23):1323-9. https://doi.org/10.1056/NEJM198012043032303.

[3] Kleihues P, Ohgaki H. Primary and secondary glioblastomas: From concept to clinical diagnosis. Neuro Oncol 1999;1(1):44-51. https://doi.org/10.1093/neuonc/1.1.44.

[4] Ohgaki H, Kleihues P. Genetic pathways to primary and secondary glioblastoma. Am J Pathol 2007;170:1445-53. https://doi.org/10.2353/ajpath.2007.070011.

[5] Parsons DW, Jones S, Zhang X, Lin JC, Leary RJ, Angenendt P, et al. An integrated genomic analysis of human glioblastoma multiforme. Science 2008;321:1807-12. https://doi.org/10.1126/science.1164382.

[6] Zorzan M, Giordan E, Redaelli M, Caretta A, Mucignat-Caretta C. Molecular targets in glioblastoma. Future Oncol 2015;11:1407-20. https://doi.org/10.2217/fon.15.22.

[7] Kafka A, Karin-Kujundžić V, Šerman L, Bukovac A, Njirić N, Jakovčević A, et al. Hypermethylation of secreted frizzled related protein 1 gene promoter in different astrocytoma grades. Croat Med J 2018;59(5):213-23. https://doi.org/10.3325/cmj.2018.59.213.

[8] Chen JR, Yao Y, Xu HZ, Qin ZY. Isocitrate dehydrogenase (IDH)1/2 mutations as prognostic markers in patients with glioblastomas. Medicine (Baltimore) 2016;95(9):e2583. https://doi.org/10.1097/MD.0000000000002583.

[9] Cohen AL, Holmen SL, Colman H. IDH1 and IDH2 mutations in gliomas. Curr Neurol Neurosci Rep 2013;13:345. https://doi.org/10.1007/s11910-013-0345-4.

[10] Toedt G, Barbus S, Wolter M, Felsberg J, Tews B, Blond F, et al. Molecular signatures classify astrocytic gliomas by IDH1 mutation status. Int J Cancer 2011;128:1095-103. https://doi.org/10.1002/ijc.25448.

[11] Ponting CP, Oliver PL, Reik W. Evolution and functions of long non-coding RNAs. Cell 2009;136:629-41. https://doi.org/10.1016/j.cell.2009.02.006.

[12] Poller W, Tank J, Skurk C, Gast M. Cardiovascular RNA interference therapy: The broadening tool and target spectrum. Circ Res 2013;113(5):588-602. https://doi.org/10.1161/CIRCRESAHA.113.301056.

[13] Ji P, Diederichs S, Wang W, Boing S, Metzger R, Schneider PM, et al. MALAT-1, a novel noncoding RNA, and thymosin beta4 predict metastasis and survival in early-stage non-small cell lung cancer. Oncogene 2003;22(39):8031-41. https://doi.org/10.1038/sj.onc.1206928.

[14] Ma KX, Wang HJ, Li XR, Li T, Su G, Yang P, et al. Long noncoding RNA MALAT1 associates with the malignant status and poor prognosis in glioma. Tumour Biol 2015;36(5):3355-9. https://doi.org/10.1007/s13277-01--2969-7.

[15] Cai T, Liu Y, Xiao J. Long noncoding RNA MALAT1 knockdown reverses chemoresistance to temozolomide via promoting microRNA-101 in glioblastoma. Cancer Med 2018;7(4):1404-15. https://doi.org/10.1002/cam4.1384.

[16] Li H, Yuan X, Yan D, Li D, Guan F, Dong Y, et al. Long non-coding RNA MALAT1 decreases the sensitivity of resistant glioblastoma cell lines to temozolomide. Cell Physiol Biochem 2017;42(3):1192-1201. https://doi.org/10.1159/000478917.

[17] Tian X, Xu G. Clinical value of lncRNA MALAT1 as a prognostic marker in human cancer: Systematic review and meta-analysis. BMJ Open 2015;5(9):e008653. https://doi.org/10.1136/bmjopen-2015-008653.

[18] Kang MR, Kim MS, Oh JE, Kim YR, Song SY, Seo SI, et al. Mutational analysis of IDH1 codon 132 in glioblastomas and other common cancers. Int J Cancer 2009;125(2):353-5. https://doi.org/10.1002/ijc.24379.

[19] Barresi V, Simbolo M, Mafficini A, Piredda ML, Caffo M, Cardali SM, et al. Ultra-mutation in IDH wild-type glioblastomas of patients younger than 55 years is associated with defective mismatch repair, microsatellite ınstability, and giant cell enrichment. Cancers 2019;11(9):1279. https://doi.org/10.3390/cancers11091279.

[20] Ludwig K, Kornblum HI. Molecular markers in glioma. J Neurooncol 2017;134(3):505-12. https://doi.org/10.1007/s11060-017-2379-y.

[21] Ohgaki H, Kleihues P. Genetic pathways to primary and secondary glioblastoma. Am J Pathol 2007;170:1445-53. https://doi.org/10.2353/ajpath.2007.070011.

[22] Ohka F, Natsume A, Motomura K, Kishida Y, Kondo Y, Abe T, et al. The global DNA methylation surrogate LINE-1 methylation is correlated with MGMT promoter methylation and is a better prognostic factor for glioma. PLoS One 2011;6(8):e23332. https://doi.org/10.1371/journal.pone.0023332.

[23] Yan W, Zhang W, You G, Bao Z, Wang Y, Liu Y, et al. Correlation of IDH1 mutation with clinicopathologic factors and prognosis in primary glioblastoma: A report of 118 patients from China. PLoS One 2012;7(1):e30339. https://doi.org/10.1371/journal.pone.0030339.

[24] Kalkan R, Atli Eİ, Özdemir M, Çiftçi E, Aydin HE, Artan S, et al. IDH1 mutations is prognostic marker for primary glioblastoma multiforme but MGMT hypermethylation is not prognostic for primary glioblastoma multiforme. Gene 2015;554:81-6. https://doi.org/10.1016/j.gene.2014.10.027.

[25] Chen W, Xu XK, Li JL, Kong KK, Li H, Chen C, et al. MALAT1 is a prognostic factor in glioblastoma multiforme and induces chemoresistance to temozolomide through suppressing miR-203 and promoting thymidylate synthase expression. Oncotarget 2017;8(14):22783-99. https://doi.org/10.18632/oncotarget.15199.

[26] Fawzy MS, Toraih EA, Abdallah HY. Long noncoding RNA metas-tasis-associated lung adenocarcinoma transcript 1 (MALAT1): A molecular predictor of poor survival in glioblastoma multiforme in Egyptian patients. Egypt J Med Hum Genet 2017;18(3):231-9. https://doi.org/10.1016/j.ejmhg.2016.08.003.

[27] Han Y, Wu Z, Wu T, Huang Y, Cheng Z, Li X, et al. Tumor-suppressive function of long noncoding RNA MALAT1 in glioma cells by downregulation of MMP2 and inactivation of ERK/MAPK signaling. Cell Death Dis 2016;7:2123-52. https://doi.org/10.1038/cddis.2015.407.