Pathol Oncol Res. 2013 Apr;19(2):329-43. doi: 10.1007/s12253-012-9588-7. Epub 2012 Dec 20.

DARPP32, STAT5 and STAT3 mRNA expression ratios in glioblastomas are associated with patient outcome.

Televantou D, Karkavelas G, Hytiroglou P, Lampaki S, Iliadis G, Selviaridis P, Polyzoidis KS, Fountzilas G, Kotoula V.

Source

Department of Pathology, School of Medicine, Aristotle University of Thessaloniki, University Campus, 54006, Thessaloniki, Greece.

Abstract

Based on recent developments in glioblastoma subtyping, we examined DARPP32 (PPP1R1B), a neuronal marker against STAT5 and STAT3 that are pro-oncogenic in glioblastoma. mRNA ratios of DARPP32, STAT1, STAT3, STAT5A and STAT5B were assessed in routinely diagnosed gliomas s including a series of glioblastomas from patients (n = 67) treated with chemoradiotherapy (temozolomide), out of which 88 % had sequencing validated IDH-negative disease. DARPP32/STAT1 (p = 0.0007), DARPP32/STAT3 (p = 0.0004) and DARPP32/STAT5B (p = 0.0039) ratios were significantly higher in grade II and III as compared to grade IV tumours. The same high ratios were also associated with absence of immunohistochemically assessed AKT/PKB phosphorylation and survivin protein expression. High DARPP32/STAT3, DARPP32/STAT5B, and STAT5B/STAT3 ratios were associated with longer patient progression free (PFS) and overall survival (OS). Upon multivariate analysis, total/subtotal removal of the tumour (HR:0.431; 95%CI:0.241-0.771, Wald p = 0.005), high DARPP32/STAT5B (HR:0.341; 95%CI:0.169-0.690; Wald p = 0.003) and STAT5B/STAT3 mRNA ratios (HR:0.480; 95%CI:0.280-0.824; Wald p = 0.008) were independent favorable parameters for prolonged PFS. Extent of surgery (HR:0.198; 95%CI:0.101-0.390; p < 0.001) and high DARPP32/STAT5A ratios (HR:0.320; 95%CI:0.160-0.638, p = 0.001) were independently predictive for longer OS. The presented approach is applicable for prospective validation and appears promising towards an effective glioblastoma patient stratification in addition to IDH mutations. These data may contribute to understanding the biology of gliomas with respect to their potential neuronal characteristics and justify STAT-inhibiting therapeutic interventions in the same tumour system.