Survivin

Survivin is an inhibitor of apoptosis protein that regulates cell cycle progression and resistance to apoptosis, is frequently expressed in human medulloblastoma MB and when expressed at high levels predicts poor clinical outcome.

Results showed the overexpression of YAP1 and Survivin as well as a decreased activity of large tumor suppressor 1 (LATS1) in high-grade glioblastoma versus anaplastic astrocytoma and low-grade glioma. Furthermore, Aguennouz et al. also demonstrated that miR-221 and miR-10b are specifically involved in Hippo signaling pathway via LATS1 regulation and that their knockdown significantly decreased glioma cell proliferation. This preliminary data confirmed the crucial role of the Hippo signaling pathway in cancer and suggested that miR 221 and miR 10b could be potential therapeutic targets for glioma treatment [1].

Survivin may have a critical role in growth and survival of MB cells and that targeting it may enhance MB therapy. Here we show that Survivin is overexpressed in tumors from patched (Ptch) mutant mice, a model of Sonic hedgehog (SHH)-driven MB. Genetic deletion of survivin in Ptch mutant tumor cells significantly inhibits proliferation and causes cell cycle arrest. Treatment with small-molecule antagonists of Survivin impairs proliferation and survival of both murine and human MB cells. Finally, Survivin antagonists impede growth of MB cells in vivo. These studies highlight the importance of Survivin in SHH-driven MB, and suggest that it may represent a novel therapeutic target in patients with this disease [2].

Up to now, survivin has been recommended as a prognostic and diagnostic indicator in glioma patients. However, there are still many controversies.

A meta-analysis was conducted to draw a more definitive conclusion on the correlation of survivin with overall survival (OS), age, gender, and WHO grade. Eligible studies were available through careful assessment, and then pooled hazard ratios (HRs) or odds ratios (ORs) with 95 % confidence intervals (95 % CIs) were estimated. Funnel plots were introduced to evaluate the publication bias. Additionally, heterogeneity and sensitivity were also evaluated. In the present meta-analysis, 15 eligible studies with a total of 1,089 patients were incorporated. Survivin expression in gliomas correlated with 2-year OS (n = 8; HR 0.17, 95 % CI 0.11-0.26) and 5-year OS (n = 7; HR 0.12, 95 % CI 0.07-0.22) in patients. In addition, a fixed-effect model revealed a significant association between survivin and age (male/+; OR 2.10, 95 % CI 1.44-3.05) and survivin and WHO grade (I+II/+; OR 0.27, 95 % CI 0.19-0.38). No heterogeneity was observed across all studies. According to Begg's and Egger's test and funnel plot, no publication bias was reported. Taken together, our meta-analysis suggests that survivin expression is associated with poor survival, older age, and higher WHO grade and could be suggested as a useful prognostic and diagnostic biomarker, or an effective therapy target [3].

1)
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