

Gab1

Grb2-associated binding 1 ([Gab1](#)) expression and microRNA-29a-3p ("miR-29a-3p") expression in human [glioma cells](#) and [tissues](#) were tested by [Western blotting assay](#) and qRT-PCR assay. [shRNA/siRNA](#) strategy was applied to silence Gab1 in human glioma cells. miR-29a or anti-sense miR-29a construct was transfected to human glioma cells. [Cell proliferation](#) was tested by [BrdU ELISA](#) assay and [cell counting](#) assay.

Shao et al., from the Department of Neurosurgery, the Third Affiliated Hospital of Soochow University, [Changzhou, China](#) show that expression of Gab1 was significantly elevated in human [glioma tissues](#) and [cells](#), which correlated with [downregulation](#) of its putative [microRNA](#): miR-29a-3p. In [A172](#) glioma cells and primary human glioma cells, Gab1 shRNA/siRNA inhibited [Akt-Erk](#) activation and cell proliferation. Forced-expression of miR-29a-3p downregulated Gab1, inhibiting glioma cell proliferation, whereas miR-29a-3p was in-effective on cell proliferation in Gab1-silenced A172 cells. Furthermore, introduction of a 3'-untranslated region (3'-UTR) mutant Gab1 (UTR-G160A) blocked miR-29a-3p-induced inhibition on Akt signaling and A172 cell proliferation.

miR-29a-3p downregulation leads to Gab1 upregulation to promote glioma cell proliferation ¹⁾.

Pediatric meningiomas share certain phenotypic and cytogenetic characteristics with adult counterparts, but GAB and stathmin co-expression in the majority of cases and non-significant difference in frequency of 1p/14q co-deletion between low- and high-grade meningiomas indicate an inherently aggressive nature. Characteristic AKT/SMO, KLF4/TRAFF7 and pTERT genetic alterations seen in adults are distinctly absent in pediatric meningiomas ²⁾.

Immunoprecipitation analyses with ErbB-modulated cells indicate that association between SHP-2 and Grb2-associated binder 1 (Gab1) is the critical step in the formation of the signalosome linking EGFR to NF-kappaB activation. We also show that EGFR-induced NF-kappaB activation is mediated by the PI3-kinase/Akt activation loop. Overexpression of SHP-2, Gab1, and myristoylated Akt significantly upregulated NF-kappaB transcriptional activity and DNA binding activity in glioblastoma cells. Interestingly, overexpression of either one of the two SH2 domain mutants of SHP-2, R32E or R138E, slightly reduced NF-kappaB activity relative to that of wild-type SHP-2, indicating that the SH2 domains of SHP-2 are required for EGFR-induced NF-kappaB activation. On the other hand, ectopic overexpression of either a Gab1 mutant incapable of binding to SHP-2 (Y627F) or a phosphatase-inactive SHP-2 mutant (C459S) caused a significant increase in NF-kappaB activity. Moreover, SHP-2 C459S-expressing cells displayed higher Gab1 phosphotyrosine content, suggesting that SHP-2 regulates Gab1 phosphorylation through its phosphatase domain, which confers a negative regulatory effect on NF-kappaB activity. These results indicate that SHP-2/Gab1 association is critical for linking EGFR to NF-kappaB transcriptional activity via the PI3-kinase/Akt signaling axis in glioblastoma cells and that SHP-2 acts as a dual regulator of NF-kappaB activation ³⁾.

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Shao NY, Wang DX, Wang Y, Li Y, Zhang ZQ, Jiang Q, Luo W, Cao C. MicroRNA-29a-3p Downregulation Causes Gab1 Upregulation to Promote Glioma Cell Proliferation. *Cell Physiol Biochem*. 2018 Jul 17;48(2):450-460. doi: 10.1159/000491776. [Epub ahead of print] PubMed PMID: 30016785.

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