As a key regulator of DNA translesion synthesis (TLS) pathway, RAD18 is reported to be abnormally expressed in many kinds of cancers. In glioma, RAD18 was overexpressed in the primary and recurrent glioblastoma multiforme specimens, and its overexpression weakened ionizing radiation-induced apoptosis in glioma A172 cells. Moreover, A172 cells with mutational P53 also showed enhanced radiation resistance. And RAD18 activation induced by cyclin-dependent kinase 2 (CDK2) was repressed by P53. However, whether P53 involves in RAD18-induced radiation resistance remains unknown. Therefore, this study was conducted to explore the effects and mechanism of RAD18 in the radiation resistance of glioma and study P53 role in this process. Results showed that, RAD18 expression was obviously elevated in glioma tissues and cell lines such as U251, SHG-44, A172, U-87 MG and U-118 MG as compared with the normal brain tissues and neuroglia cells. Up-regulation of RAD18 in U-118 MG and A172 cells with lentivirus infection significantly increased cell growth and inhibited cell apoptosis, determined by CCK-8 and flow cytometry technologies. Besides, RAD18 overexpression enhanced cell growth and inhibited cell apoptosis after U-118 MG or A172 cells were irradiated at a dose of 4 Gy. On the contrary, silencing of endogenous RAD18 sensitized U-118 MG and A172 cells to radiation. Moreover, RAD18 and P53 proteins were co-located in the nucleus, and up-regulation of RAD18 decreased the expression of P53 protein and facilitated its nuclear export. Furthermore, cell growth promotion and cell apoptosis inhibition induced by RAD18 up-regulation were impaired when P53 expression was up-regulated under radiation condition. In a word, this study clarifies that RAD18 functions as a promoter in glioma progression and reduces glioma cells' sensibility to radiation through down-regulating P53, which provides new strategies to overcome the radiation resistance in glioma [1)].

Xie C, Wang H, Cheng H, Li J, Wang Z, Yue W. RAD18 mediates resistance to ionizing radiation in human glioma cells. Biochem Biophys Res Commun. 2014 Feb 28;445(1):263-8. doi: 10.1016/j.bbrc.2014.02.003. Epub 2014 Feb 8. PubMed PMID: 24518219.

1)
Wu B, Wang H, Zhang L, Sun C, Li H, Jiang C, Liu X. High expression of RAD18 in glioma induces radiotherapy resistance via down-regulating P53 expression. Biomed Pharmacother. 2019 Feb 21;112:108555. doi: 10.1016/j.biopha.2019.01.016. [Epub ahead of print] PubMed PMID: 30798132.