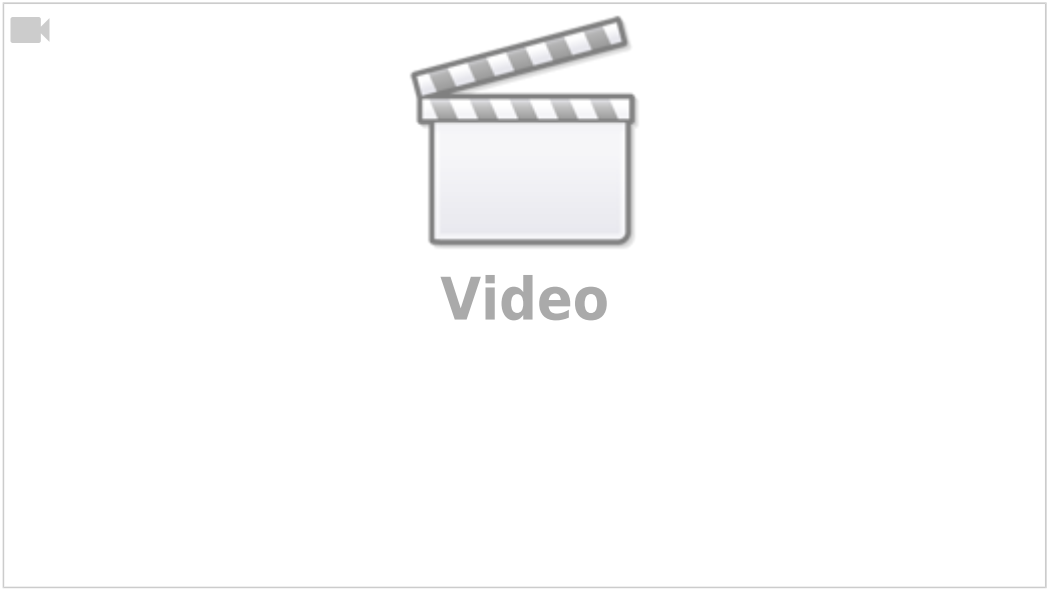
XRCC1



DNA repair protein XRCC1 also known as X-ray repair cross-complementing protein 1 is a protein that in humans is encoded by the XRCC1 gene. XRCC1 is involved in DNA repair where it complexes with DNA ligase III.

XRCC1 polymorphisms were reported to be associated with glioma in Chinese population. However, only a few studies reported on the XRCC1 expression, and cancer progression. In a study Mei et al. investigated whether XRCC1 plays a role in glioma pathogenesis. Using the tissue microarray technology, they found that XRCC1 expression is significantly decreased in glioma compared with tumor adjacent normal brain tissue ($P < 0.01$, $\chi 2$ test) and reduced XRCC1 staining was associated with WHO stages ($P < 0.05$, $\chi 2$ test). The mRNA and protein levels of XRCC1 were significantly downregulated in human primary glioma tissues ($P < 0.001$, $\chi 2$ test).

They also found that XRCC1 was significantly decreased in glioma cell lines compared to normal human astrocytes ($P < 0.01$, $\chi 2$ test). Overexpression of XRCC1 dramatically reduced the proliferation and caused cessation of cell cycle. The reduced cell proliferation is due to G1 phase arrest as cyclin D1 is diminished whereas p16 is upregulated. They further demonstrated that XRCC1 overexpression suppressed the glioma cell migration and invasion abilities by targeting MMP-2. In addition, we also found that overexpression of XRCC1 sharply inhibited angiogenesis, which correlated with down-regulation of VEGF. The data indicate that XRCC1 may be a tumor suppressor involved in the progression of glioma [1)].

In 2013 nine studies tested the associations between XRCC1 SNPs and gliomas were retrieved. Overall odds ratios (ORs) and corresponding 95 % confidence intervals were estimated using genetic models. Heterogeneity and publication bias were evaluated. The pooled OR for Arg194Trp TT versus CC were significant, which was 2.208 (95 % CI: 1.099, 4.435; P = 0.026), but it was non-significant after removal of the studies which deviated from the Hardy-Weinberg equilibrium (HWE). The pooled OR for Arg399Gln AA+GA versus GG of genotype methods subgroup and the low study appraisal score subgroup were significant in the stratification analysis, but the meta-regression results were non-

significance. No significant associations were found between the Arg280His SNPs and gliomas' risk. There was no evidence of publication bias. We conclude that SNPs in XRCC1 are not associated with the risk of gliomas. We should do more work on the relevant variants like those in TERT, RTEL1, EGFR, CDKN2A, CCDC26, and PHLDB1 and their products rather than the XRCC1. More GWAS will also need to involve sufficiently larger study populations along with analysis of tumor or gender subtypes in order to assess these risks [2].

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Mei PJ, Bai J, Miao FA, Li ZL, Chen C, Zheng JN, Fan YC. Relationship between expression of XRCC1 and tumor proliferation, migration, invasion, and angiogenesis in glioma. Invest New Drugs. 2018 Oct 17. doi: 10.1007/s10637-018-0667-9. [Epub ahead of print] PubMed PMID: 30328556.
2)
Li M, Zhou Q, Tu C, Jiang Y. A meta-analysis of an association between the XRCC1 polymorphisms and gliomas risk. J Neurooncol. 2013 Feb;111(3):221-8. doi: 10.1007/s11060-012-1022-1. Epub 2012 Dec 13. Review. PubMed PMID: 23238971.