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Loss of p53 Concurrent with RAS and TERT Activation Induces Glioma Formation

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Abstract

There is an ongoing debate regarding whether gliomas originate due to functional or genetic changes in neural stem cells (NSCs). Genetic engineering has made it possible to use NSCs to establish glioma models with the pathological features of human tumors. Here, we found that RAS, TERT, and p53

mutations or abnormal expression were associated with the occurrence of glioma in the mouse tumor transplantation model. Moreover, EZH2 palmitoylation mediated by ZDHHC5 played a significant role in this malignant transformation. EZH2 palmitoylation activates H3K27me3, which in turn decreases miR-1275, increases glial fibrillary acidic protein (GFAP) expression, and weakens the binding of DNA methyltransferase 3A (DNMT3A) to the OCT4 promoter region. Thus, these findings are significant because RAS, TERT, and p53 oncogenes in human neural stem cells are conducive to a fully malignant and rapid transformation, suggesting that gene changes and specific combinations of susceptible cell types are important factors in determining the occurrence of gliomas.

Keywords: EZH2; Gliomagenesis; RAS; TERT; p53.

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