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Parkin interferes with hypoxia-inducible factors expression in glioblastoma cells

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Parkin, also known as PARK2, is one of the largest genes in the human genome encoding for an E3 ubiquitin ligase. Its mutation cause a form of autosomal recessive juvenile-onset of Parkinson's disease, but recently it has been linked in a wide variety of malignancies, including glioblastoma multiforme (GBM) (1). This is the most common and aggressive primary brain tumor in adults, characterized by hypoxic areas. The insufficient oxygen supply causes expression of hypoxia-inducible factors (HIF) which induce tumor growth and vascularization. In particular, in this condition increases expression of HIF-1α which has been correlated with angiogenesis, glucose metabolism and poor prognosis in glioblastoma. Instead HIF-3α is a negative regulator of HIF-1 α. In the present study we investigated if parkin interferes with such HIFs expression during hypoxic event. Parkin knockdown in glioblastoma cells induces a significant increase of HIF-1α expression in normoxia, whereas during hypoxia the absence of parkin abolishes its expression. HIF-3α expression significantly decreases both in normoxic or hypoxic condition following parkin silencing. These data have also been confirmed by immunofluorescence analysis.

These results suggest that parkin is implicated in HIF regulation, therefore its modulation might be considered in GBM progression.

References

[1] Yeo et al. (2012) Parkin pathway activation mitigates glioma cell proliferation and predicts patient survival. Cancer Res 72: 2543-2553.

Keywords

Parkin; glioblastoma cells; HIF-1α; HIF-3α.