Oncoprotein stabilization in brain tumors.

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Abstract
Proteins involved in promoting cell proliferation and viability need to be timely expressed and carefully controlled for the proper development of the brain but also efficiently degraded in order to prevent cells from becoming brain cancer cells. A major pathway for targeted protein degradation in cells is the ubiquitin-proteasome system (UPS). Oncoproteins that drive tumor development and tumor maintenance are often deregulated and stabilized in malignant cells. This can occur when oncoproteins escape degradation by the UPS because of mutations in either the oncoprotein itself or in the UPS components responsible for recognition and ubiquitylation of the oncoprotein. As the pathogenic accumulation of an oncoprotein can lead to effectively sustained cell growth, viability and tumor progression, it is an indisputable target for cancer treatment. The most common types of malignant brain tumors in children and adults are medulloblastoma and glioma, respectively. Here, we review different ways of how deregulated proteolysis of oncoproteins involved in major signaling cancer pathways contributes to medulloblastoma and glioma development. We also describe means of targeting relevant oncoproteins in brain tumors with treatments affecting their stability or therapeutic strategies directed against the UPS itself. Oncogene advance online publication, 28 October 2013; doi:10.1038/onc.2013.445.

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