eIF3e

Eukaryotic initiation factors 3 (EIF3) complex is essential for initiation of protein synthesis for both cells and virus. It consists of 13 subunits (EIF3A to M), among which EIF3B serves as a major scaffolding subunit.

Liang et al., showed that EIF3B was expressed in human glioblastoma (Grade I-IV) and human glioblastoma cell lines (U251, U87, A172 and U373). Loss of function analysis was performed on U87 cells using lentivirus-mediated siRNA against EIF3B. EIF3B-shRNA expressing lentivirus could effectively infect U87 glioma cells and downregulate EIF3B expression. Knockdown of EIF3B expression significantly inhibited proliferation of U87 cells. Further study showed that the proliferation inhibitory effect was associated with accumulation in G0/G1-phase cell number and an increased rate of apoptosis. In conclusion, EIF3B promotes the proliferation of U87 cells and may play an important role in human glioblastoma development [1)]

Recent research on translation and protein synthesis in several pathologies, including cancer, peripheral artery disease, and wound healing, demonstrates the key role played by translational factors in tumorigenic and angiogenic processes.

eIF3e/Int6 is a component of the multi-subunit eIF3 complex, which binds directly to the 40S ribosome to facilitate ribosome recruitment to mRNA and hence protein synthesis. Reduced expression of eIF3e/Int6 has been found in up to 37% of human breast cancers, and expression of a truncated mutant version of the mouse eIF3e/Int6 protein leads to malignant transformation of normal mammary cells.

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eIF3e was identified as novel regulator of HIF-2α. Eukaryotic initiation factors (eIFs) are key factors regulating total protein synthesis, which controls cell growth, size and proliferation. The functional significance of Int6 and the effect of Int6/EIF3E gene silencing on human brain GBM has not yet been described and its role on the HIFs is unknown in glioma cells. In the present study, we show that Int6/eIF3e suppression affects cell proliferation, cell cycle and apoptosis of various GBM cells. We highlight that Int6 inhibition induces a diminution of proliferation through cell cycle arrest and increased apoptosis. Surprisingly, these phenotypes are independent of global cell translation inhibition and are accompanied by decreased HIF expression when Int6 is silenced. In conclusion, we demonstrate here that Int6/eIF3e is essential for proliferation and survival of GBM cells, presumably through modulation of the HIFs [2)].

Interestingly, INT6/eIF3e is a double-edged sword that has both oncogenic and tumor suppressive abilities. In addition to its role in tumorigenesis, its silencing has recently been suggested as a potential therapeutic strategy to improve cell survival and function after ischemic injuries. Although a deeper understanding of the molecular mechanisms involved in these pathophysiological functions is essential, particularly to transform the in vitro/in vivo findings into clinical applications, INT6/eIF3e modulation could provide therapeutic benefit for a variety of human diseases such as cancer or vascular diseases [3)].

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