

Epiregulin induced human neuroblastoma cells differentiation through ERK1/2 signaling pathway

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Neuroblastoma is one of the most frequent undifferentiated childhood extracranial solid tumor, arising from neural crest primitive neuroepithelial cells [1]. Epidermal growth factor (EGF) has been described as a modulator of neuroblastoma cells behavior [2]. The newest EGF family member, Epiregulin (Epi) is characterized by the broadest ErbB binding specificity and it is known to be a more potent stimulating factor than EGF alone [3]. SK-N-BE human neuroblastoma cell line was used in order to observe the effect of Epi on neuroblastoma cell proliferation and differentiation.

After 72 h treatment, Epi (50-1000 ng/ml) reduced SK-N-BE cells proliferation and induced their differentiation towards a neuronal-like phenotype. Morphological differentiation has been confirmed by the increased expression of matrix metalloproteinase 9 (MMP-9), a differentiation marker for SK-N-BE cells [4]. Moreover Epi induced ERK1/2 phosphorylation in SK-N-BE and the presence of U0126 (10 μ M, ERK1/2 inhibitor) completely abolished Epi-induced differentiation, while PD98059 (5 μ M, MAPK/ERK1 inhibitor) only reduced it. These data suggest a potential use of Epi as a therapeutic tool for neuroblastoma treatment.

References

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