PLK1

Serine/threonine-protein kinase PLK1, also known as polo-like kinase 1 (PLK-1) or serine/threonine-protein kinase 13 (STPK13), is an enzyme that in humans is encoded by the PLK1 (polo-like kinase 1) gene.

Plk1 is considered a proto oncogene, whose overexpression is often observed in tumor cells. Aneuploidy and tumorigenesis can also result from centrosome abnormality, particularly centrosome amplification defects. Centrosome duplication and maturation regulated by Plk1 occurs from late S phase to prophase. Abnormal centrosome amplification may lead to multipolar spindles and results in unequal segregation of chromosomes.Plk1 overexpression also increases the centrosome size and/or centrosome number, which will also lead to improper segregation of chromosomes, aneuploidy, and tumorigenesis.

Oncogenic properties of PLK1 are believed to be due to its role in driving cell cycle progression. Supporting evidence comes from the overexpression studies of PLK1 in NIH3T3 cell line. These cells become capable of forming foci and growing in soft agar and more importantly, these cells can form tumors in nude mice due to PLK1 overexpression.

PLK1 has also been linked to known pathways that are altered during the neoplastic transformation. Retinoblastoma tumor suppressor (RB) pathway activation results in the repression of PLK1 promoter in a SWI/SNF chromatin remodeling complex dependent manner. In case of RB inactivation, PLK1 expression seems to be deregulated. This new finding suggests that PLK1 may be a target of the retinoblastoma tumor suppressor (RB) pathway.

Moreover, PLK1 seems to be involved in the tumor suppressor p53 related pathways. Evidence suggests that PLK1 can inhibit transactivation and pro-apoptotic functions of p53 function by physical interaction and phosphorylation.

The objective of a study was to investigate the effects of polo-like kinase 1 (PLK1) and the phosphorylation of human cell division cycle protein 14A (Cdc14A) by PLK1 on β-cell function and cell cycle regulation. Mouse β-TC3 cells were incubated with small interfering RNA (siRNA) to knock down the expression of PLK1. Cell cycle analysis was performed using flow cytometry, and cell proliferation and apoptosis was determined. Insulin secretion was evaluated by a radioimmunoassay under both low and high glucose conditions. Mouse β-TC3 cells were transfected with a wild type or a non-phosphorylatable Cdc14A mutant (Cdc14AS351A/363A; Cdc14AAA) to investigate whether the phosphorylation of Cdc14A is involved in cellular regulation of PLK1 under high glucose conditions. It was found that PLK1 siRNA significantly promoted cellular apoptosis, inhibited cell proliferation, decreased insulin secretion and reduced Cdc14A expression under both low and high glucose conditions. Cdc14A overexpression promoted β-TC3 cell proliferation and insulin secretion, while Cdc14AAA overexpression inhibited cell proliferation and insulin secretion under high glucose conditions. PLK1 siRNA partially reversed the proliferation-promoting effects of Cdc14A and further intensified the inhibition of proliferation by Cdc14AAA under high glucose conditions. Similarly, Cdc14A overexpression partially reversed the insulin-inhibiting effects of PLK1 siRNA, while Cdc14AAA overexpression showed a synergistic inhibitory effect on insulin secretion with PLK1 siRNA under high glucose conditions. In conclusion, PLK1 promoted cell proliferation and insulin secretion while inhibiting cellular apoptosis in β-TC3 cell lines under both low and high glucose conditions. In addition, the phospho-regulation of Cdc14A by PLK1 may be involved in β-TC3 cell cycle regulation and insulin

secretion under high glucose conditions [1].

Findings suggest that targeting PLK1 with small-molecule inhibitors, in combination with radiation therapy, will hold a novel strategy in the treatment of Diffuse intrinsic pontine glioma (DIPG) that warrants further investigation [2].

Cohen et al. found that HA-LNPs can successfully bind to glioblastoma GBM cell lines and primary neurospheres of GBM patients. HA-LNPs loaded with Polo-Like Kinase 1 (PLK1) siRNAs (siPLK1) dramatically reduced the expression of PLK1 mRNA and cumulated in cell death even under shear flow that simulate the flow of the cerebrospinal fluid compared with control groups. Next, a human GBM U87MG orthotopic xenograft model was established by intracranial injection of U87MG cells into nude mice. Convection of Cy3-siRNA entrapped in HA-LNPs was performed, and specific Cy3 uptake was observed in U87MG cells. Moreover, convection of siPLK1 entrapped in HA-LNPs reduced mRNA levels by more than 80% and significantly prolonged survival of treated mice in the orthotopic model. Taken together, this results suggest that RNAi therapeutics could effectively be delivered in a localized manner with HA-coated LNPs and ultimately may become a therapeutic modality for GBM [3].

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