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Gene Section
Review

PLK1 (polo-like kinase 1 (Drosophila))

Ayse Elif Erson, Elizabeth M. Petty

Biology Department, Room: 141, Middle East Technical University, Ankara 06531, Turkey (AEE); Departments of Human Genetics and Internal Medicine, University of Michigan Medical School, Ann Arbor, MI 48109, USA (EMP)

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Identity

Other names: PLK; STPK13 (SERINE/THREONINE PROTEIN KINASE 13)

HGNC (Hugo): PLK1

Location: 16p12.1

Local order: Genes flanking PLK1 in centromere to telomere direction on 16p12 are:
UBPH, 16p12, similar to ubiquitin binding protein
NDUFAB1, 16p12.1, NADH dehydrogenase (ubiquinone) 1, alpha/beta subcomplex, 1,8kDa
FLJ21816, 16p12.1, hypothetical protein FLJ21816
MGC3248, 16p12.1, dynactin 4
PLK1, 16p12.1, polo-like kinase 1 (Drosophila)
LOC388226, 16p12.1, similar to endoplasmic reticulum (ER) to nucleus signaling 2; inositol-requiring 1 (Yeast homologue)
LOC63928, 16p12.1, hepatocellular carcinoma antigen gene 520
PRKCB1, 16p11.2, protein kinase C, beta 1
CACNG3, 16p12-p13.1, calcium channel, voltage-dependent, gamma subunit 3

Note
Polo like kinases belong to serine/threonine kinases that are conserved from yeast to human cells. Polo like kinases exhibit important roles in key cellular events regulating cell cycle progression and cell division such as centrosome maturation, cdc2 activation, mitotic spindle formation, regulation of the anaphase promoting complex, chromosome segregation, cytokinesis, DNA damage response pathways and apoptosis.

DNA/RNA

Description

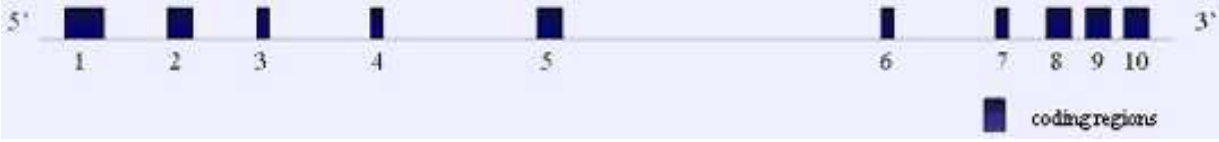
PLK1 mRNA spans approximately 11.5 kb and has 10 exons. The sizes of the exons 1 to 10 are 461, 169, 145, 94, 220, 156, 78, 155, 183 and 508 bps.

Transcription

PLK1 mRNA (NM_005030) is 2204 bp. PLK1 expression is believed to reach its peak value in mitosis in the cell cycle. It is highly expressed in actively proliferating tissues such as those in the placenta, spleen, ovary, and testis. High expression of PLK1 is also detected in various neoplastic tissues. Northern blot analysis reveals low or undetectable levels of PLK1 transcript in most other adult tissues (e.g.: brain, thymus, liver, lung, pancreas, heart, kidney, stomach, intestine and skin).

Pseudogene

Mouse Plk gene maps to Chromosome 7 and the processed pseudogene to mouse Chromosome 5. No human pseudogene for PLK1 has been reported.



The alignment of PLK1 mRNA (NM_005030) to its genomic sequence NC_000016).

Protein

Description

Protein consists of 603 amino acids and is 66kDa. In addition to the N-terminus kinase domain, there are two conserved polo-box regions of 30 amino acids at the C-terminus. Kinase activity is regulated at least in part, by the polo-boxes that are functionally important for both auto-inhibition and sub-cellular localization.

Expression

PLK1 protein becomes a target of the anaphase-promoting complex/cyclosome and is degraded by the ubiquitin-proteasome pathway as cells exit mitosis.

Localisation

During interphase, PLK1 localizes to centrosomes. In early mitosis, it associates with mitotic spindle poles. A recombinant GFP-PLK1 protein localizes to centromere/kinetochore region, suggesting a possible role for chromosome separation.

Function

PLK1 is believed to be involved in the regulation of key steps during cell division, DNA damage repair pathways, apoptosis, and the progression of the cell cycle.

PLK1 has roles in the activation of cdc2 through cdc25 and direct phosphorylation of cyclin B1, through which MPF (mitosis promoting factor) is activated so that mitosis can start.

Microinjection of PLK1 antibodies causes failure of g-tubulin recruitment to the centrosomes. This failure results in immature centrosomes and monopolar spindle formation. Similar microinjection experiments in cell lines (transformed HeLa and non-immortalized Hs68 fibroblasts) result in a marked inhibition of cell cycle progression.

PLK1 also has a possible role during cytokinesis based on the observation that PLK1 interacts and co-localizes with a kinesin related motor protein (CHO1/MKLP-1) at the interzone during anaphase and the mid-body during telophase and cytokinesis.

Evidence suggests that BRCA2 is a substrate of PLK1 both in response to DNA damage and during normal cell cycle progression. This suggests a role for PLK1 in regulating DNA damage repair.

Other studies have shown that the loss of PLK1 expression can induce pro-apoptotic pathways and inhibit growth.

Based on yeast and murine studies of meiosis, human PLK1 may also have a regulatory function in meiosis. S. cerevisiae polo kinase CDC5 is required to phosphorylate and remove meiotic cohesion during the first cell division. In CDC5 depleted cells, kinetochores are bioriented during meiosis I, and Mam1, a protein essential for coorientation, fails to associate with kinetochores. CDC5 is believed to have roles in sister-kinetochore coorientation and chromosome segregation during meiosis I.

Homology

P.troglodytes: PLK1, polo-like kinase, XP_510879.1, 735 aa.
M.musculus: Plk1, polo-like kinase 1 (Drosophila), NP_035251.2, 603 aa.
R.norvegicus: Plk1, polo-like kinase 1 (Drosophila), NP_058796.1, 603 aa.
D.melanogaster: polo, polo, NP_524179.2, 576 aa
C.elegans: plk-1 PoLo Kinase, NP_741243.1, 649 aa.
S.cerevisiae: CDC5, NP_013714.1, 705 aa.

Implicated in

Note

Increased PLK1 levels are detected in a variety of cancers.

Disease

Increased PLK1 transcript has been detected in a variety of tumor types including esophageal, head and neck squamous cell, liver, lung and breast carcinomas. Immunohistochemical studies also demonstrate increased PLK1 protein levels in melanomas, breast, ovarian, prostate cancers, and head, neck squamous cell carcinomas.

Prognosis

Statistically significant correlations between increased PLK1 expression and decreased patient survival suggest that PLK1 is a negative prognostic indicator for some types of cancer.

For example,

- In prostate cancer, PLK1 overexpression is linked to higher tumor grades;
- In non-Hodgkin's lymphomas, PLK1 overexpression reflects malignancy potentials. In hepatoblastomas, ovarian, colorectal cancers and melanomas, PLK1 overexpression suggests PLK1 to be a poor-prognostic indicator.

Oncogenesis

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.
In addition to PLK1¹s role in normal cell cycle regulation, its connection to such known tumor suppressors may be crucial for the tumorigenesis processes.

To be noted

Note
A study also suggests that PLK1 protein cannot be detected in normal brain tissue but it can be detected in brain tissues from Alzheimer¹s disease patients.

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