Insilico Structural Annotation of Human Cyclin Dependent Kinase2

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Abstract

CDK2 is a member of the cyclin-dependent protein kinase family that is ubiquitously expressed. its catalytic subunit of the cyclin-dependent protein kinase complex, whose activity is restricted to the G1-S phase, and essential for cell cycle G1/S phase transition. It is associated with and is regulated by the regulatory subunits of the complex including cyclin A or E, CDK inhibitor p21Cip1 (CDKN1A) and p27Kip1 (CDKN1B). it phosphorylates multiple cellular substrates including SMAD3 and FOXO1. Phosphorylation of FOXO1 leads to its inhibition.

Keywords: Biological Process, cell cycle,cellular component cytoplasm,ligand ATP binding, PTM, acytilation, phospoprotein

CDK2 Subcellular location is Cytoplasm › cytoskeleton › microtubule organizing center › centrosome. Nucleus › Cajal body. Cytoplasm. Endosome. Localized at the centrosomes in late G2 phase after separation of the centrosomes but before the start of prophase. Nuclear-cytoplasmic trafficking is mediated during the inhibition by 1,25-(OH)2D3. Serine/threonine-protein kinase involved in the control of the cell cycle.CDK2 full name is Cell Division Protein Kinase2, its aliases is p33 (CDK2), its group is CMGC, its family is CDK, it is a Recombinant full-length human CDK2 and CyclinA1were co-expressed by baculovirus in Sf9 insect cells using an N-terminal GST tag on both proteins.its Uniport id is P24941, its OMIM record is 1E+05,gene record 1017, its genebank code is NM_001798, it has 298 amino acids,its recombinant molecular mass is 58kDa.

Annotation

Serine/threonine-protein kinase involved in the control of the cell cycle; essential for meiosis, but dispensable for mitosis. Phosphorylates CTNNB1, USP37, p53/

TP53, NPM1, CDK7, RB1, BRCA2, MYC, NPAT, EZH2. Interacts with cyclins A, B1, B3, D, or E. Triggers duplication of centrosomes and DNA. Acts at the G1-S transition to promote the E2F transcriptional program and the initiation of DNA synthesis, and modulates G2 progression; controls the timing of entry into mitosis/meiosis by controlling the subsequent activation of cyclin B/CDK1 by phosphorylation, and coordinates the activation of cyclin B/CDK1 at the centrosome and in the nucleus. Crucial role in orchestrating a fine balance between cellular proliferation, cell death, and DNA repair in human embryonic stem cells (hESCs). Activity of CDK2 is maximal during S phase and G2; activated by interaction with cyclin E during the early stages of DNA synthesis to permit G1-S transition, and subsequently activated by cyclin A2 (cyclin A1 in germ cells) during the late stages of DNA replication to drive the transition from S phase to mitosis, the G2 phase. EZH2 phosphorylation promotes H3K27me3 maintenance and epigenetic gene silencing. Phosphorylates CABLES1 By similarity. Cyclin E/CDK2 prevents oxidative stress-mediated Ras-induced senescence by phosphorylating MYC. Involved in G1-S phase DNA damage checkpoint that prevents cells with damaged DNA from initiating mitosis, it regulates homologous recombination-dependent repair by phosphorylating BRCA2, this phosphorylation is low in S phase when recombination is active, but increases as cells progress towards mitosis. In response to DNA damage, double-strand break repair by homologous recombination a reduction of CDK2-mediated BRCA2 phosphorylation. Phosphorylation of RB1 disturbs its interaction with E2F1. NPM1 phosphorylation by cyclin E/CDK2 promotes its dissociates from unduplicated centrosomes, thus initiating centrosome duplication. Cyclin E/CDK2-mediated phosphorylation of NPAT at G1-S transition and until prophase stimulates the NPAT-mediated activation of histone gene transcription during S phase. Required for vitamin D-mediated growth inhibition by being itself inactivated. Involved in the nitric oxide- (NO) mediated signaling in a nitrosylation/activation-dependent manner. USP37 is activated by phosphorylation and thus triggers G1-S transition. CTNNB1 phosphorylation regulates insulin internalization

CDK's active site annotaion

Sites	Position	Description
Active site	127	Proton acceptor
Metal Binding	132	Magnesium catalytic
Metal Binding	145	Magnesium catalytic
Binding site	33	ATP
Binding site	86	ATP
Binding site	145	ATP
Site	9	CDK7 Binding
Site	88	CDK7 Binding

>1HCK:A|PDBID|CHAIN|SEQUENCE

MENFQKVEKIGEGTYGVVYKARNKLTGEVVALKKIRLDTETE
GVPSTAIREISLLKELNHPNIVKLLDVIHTENKLYLVFEFLHQDLKK
FMDASALTGIPLPLIKSYLFQLLQGLAFCHSHRVLHRDLKPQNLLINTEGA
IKLADFGLARAFGVPVRTYTHEVVTLWYRAPEILLGCKYYSTAVDIWSLG
CIFAEMVTRRALFPGDSEIDQLFRIFRTLGTPDEVVWPGVTSMPDYKPSFP
KWARQDFSKVVPPLDEDGRSLLSQMLHYDPNKRISAKAALAHPFFQDVT
KPVPHLRL

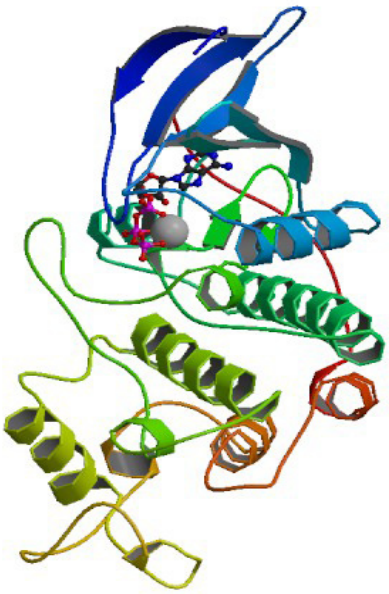
Sequence and Secondary Structure for 1HCK chain A Secondary Structure

```
        *           *           *           *           *
Query 1   MENFQKVEKIGEGTYGVVYKARNKLTGEVVALKKIRLDTETEGV
          PSTAI REISLLKELNH                                60
Helix 1   HHHHHHHHHHHH HHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
          HHHHHHH                                          60
Sheet 1   EEEEEEE EEEEEEEEE EEEEEEEEEEEEEEEE EEEEEEEEEEEEE 60
Turns 1   T TT T T T                                       60
        *           *           *           *           *
Query 61  PNIVKLLDVIHTENKLYLVFEFLHQDLKKFMDASALTGIPLPLIKSYLFQ
          LLQGLAFCHS                                       120
Helix 61  HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
          HHHHHHHHHHHHHHHHH                                120
Sheet 61  EEEEEEEEEEEEEEEEEEEEEEEEEE EEEEEEEEEEEEEEEEE
          EEEE                                             120
Turns 61  T T                                              120
        *           *           *           *           *
Query 121 HRVLHRDLKPQNLLINTEGAIKLADFGLARAFGVPVRTYTHEVV
          TLWYRAPEILLGCKYY                                 180
Helix 121 HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
          HHHHHHHHHHHHH                                    180
Sheet 121 EEEEEEEEEEEEE EEEEEE EEEEEEEEEEEEEEEEEEEEEE     180
Turns 121 T TT T T                                         180
        *           *           *           *           *
Query 181 STAVDIWSLGCIFAEMVTRRALFPGDSEIDQLFRIFRTLGTPDEV
          VWPG VTSMPDYKPSF                                 240
Helix 181 HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
          HHHH                                             240
Sheet 181 EEEEEEEEEEEEEEEEEEE EEEEEEEEEEEEEEEEEEEEE       240
Turns 181 TT T T T T                                       240
        *           *           *           *           *
Query 241 PKWARQDFSKVVPPLDEDGRSLLSQMLHYDPNKRISAKAALAH
          PFFQ DVTKPVPHLRL                                 298
Helix 241 HHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHHH
          HHHHHHHHH                                        298
Sheet 241 EEEEEEEEEEEE EEEEEEE EEEEEEEEEEEEEEE            298
Turns 241 TT T T T T T                                     298
```

Total Residues: H: 247 E: 220 T: 26
Percent: H: 82.9 E: 73.8 T: 8.7

The Secondary structure predicted by the Chou Fasman, Secondery Structure prediction server

As per the prediction method the helices are 82.9% Extended sheets are 73.8% and turns are 8.7%



3 D Structure of the CDK2

Results and Discussion

It has 298 Amino acids, it belongs to protein kinase super family it has catalytic activity as ATP + a protein = ADP + a phosphoprotein. CDK2 has active site amino acid at 127 position, magnesium catalytic site at 132 and 145, its ATP binding site is at 33,86,145, it plays a role in Post Translation Modefication as acetylation of the Phospoprotein this work may be useful to drug designing and for understanding the cancer disease in development.

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