## Proposed EC/sub-subclass:

Not specified in the provided material.

## Accepted name:

Cyclin-dependent kinase 10

## Synonyms:

CDK10; cdc2-related kinase (cdc2rk in Drosophila); CDK10/Cyclin M complex.

## Phylogeny

Member of the CMGC group of serine/threonine kinases and, within it, of the transcriptional CDK subfamily alongside CDK7, 8, 9, 11, 12 and 13 (Malumbres, 2014; Pellarin et al., 2025). CDK10 forms a distinct subfamily with its closest paralogue CDK11, sharing 53 % sequence identity and 82 % similarity (Düster et al., 2022). Orthologues are present in Drosophila but absent from yeast and C. elegans (Guen et al., 2017; Düster et al., 2022).

## Reaction Catalyzed

ATP + [a protein] ⇌ ADP + [a phosphoprotein] (Malumbres, 2014).

## Cofactor Requirements

Mg²⁺ is required for ATP coordination (Guen et al., 2017).

## Substrate Specificity

Generally classed as a Pro-directed kinase that favours Ser/Thr followed by Pro (S/T-P) (Johnson et al., 2023), although one study reports the motif is not strictly Pro-directed (Düster et al., 2022). Verified substrates include:  
• RNA polymerase II CTD (Ser2, Ser5, Ser7; activity enhanced when Ser7→Lys) (Unknown Authors, 2021; Düster et al., 2022).  
• c-Myc at multiple (S/T)-P sites (Unknown Authors, 2021).  
• ETS2, PKN2 (Thr121/Thr124), RB1, HDGF and ARGLU1 (Bazzi & Tai, 2021; Düster et al., 2022).

## Structure

Full-length human CDK10 is a 360-residue protein with the canonical bilobal CDK fold; a shorter splice isoform lacks the ATP-binding lobe and is catalytically inactive (Bazzi & Tai, 2021; Düster et al., 2022). Key elements include the variant αC-helix PISSLRE motif, gatekeeper Met117, catalytic Asp163 and regulatory Thr133/Thr196 (Düster et al., 2022). A bipartite C-terminal nuclear-localisation signal is present (Guen et al., 2017). No experimental structure of the CDK10/Cyclin M complex is available; AlphaFold modelling supports the typical CDK architecture (Düster et al., 2022; Unknown Authors, 2021).

## Regulation

• Cyclin binding – Kinase activity requires stoichiometric complex formation with Cyclin M; binding also protects CDK10 from proteasomal degradation (Düster et al., 2022; Guen et al., 2013).  
• Activating phosphorylation – Thr196 in the activation loop is essential for full activity (Düster et al., 2022; Guen et al., 2017).  
• Degradation signal – Thr133 phosphorylation promotes Pin1-mediated ubiquitin-proteasome degradation (Düster et al., 2022; Pellarin et al., 2025).  
• Additional modifications – Tyr50 and Tyr54 are phosphorylated; CDK1/Cyclin B1 and CDK5/p35 can modify sites other than Thr196 (Guen et al., 2017; Düster et al., 2022).  
• Protein partners – Interacts with HSP90 and Pin1, influencing stability and activity (Bazzi & Tai, 2021; Unknown Authors, 2021).

## Function

Kinase activity peaks in G2/M (Guen et al., 2017). Documented roles include:  
• Transcription and co-transcriptional splicing via phosphorylation of RNA Pol II CTD; present in spliceosomal C complexes (Guen et al., 2017; Pellarin et al., 2025).  
• Negative regulation of ciliogenesis and control of actin cytoskeleton through phosphorylation of PKN2 in a RhoA-dependent pathway; the CDK10/Cyclin M complex localises to basal bodies (Bazzi & Tai, 2021; Guen et al., 2017).  
• Suppression of MAPK signalling by phosphorylating ETS2, promoting its COP1/DET1-mediated degradation and reducing c-RAF expression (Guen et al., 2013; Düster et al., 2022).  
• Additional substrates (RB1, c-Myc, HDGF, ARGLU1) link CDK10 to cell-cycle progression and transcriptional regulation (Düster et al., 2022).  
Cyclin M lacks an NLS and relies on CDK10’s C-terminal NLS for nuclear import (Düster et al., 2022; Guen et al., 2017).

## Inhibitors

ATP-competitive but non-selective inhibitors include flavopiridol (IC50 ≈ 298 nM), dinaciclib, SNS-032, NVP-2 and the CDK11 inhibitor OTS964 (IC50 ≈ 1.5 µM). No CDK10-selective small molecules are available (Düster et al., 2022).

## Other Comments

Loss-of-function mutations in FAM58A (Cyclin M) cause STAR syndrome, attributed to impaired CDK10/Cyclin M activity and defective ciliogenesis (Guen et al., 2013; Guen et al., 2017). Pathogenic splice-site mutations in CDK10 lead to developmental abnormalities; complete knockout is embryonic lethal in mice (Düster et al., 2022; Unknown Authors, 2021). CDK10 shows context-dependent roles in cancer, acting as a tumour suppressor in breast, gastric, liver cancers and glioma but displaying oncogenic behaviour in colorectal cancer; low CDK10 correlates with tamoxifen resistance in ER-positive breast cancer (Düster et al., 2022; Guen et al., 2013).

## References

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