## Phylogeny

Cyclin-dependent kinase 20 (CDK20, a.k.a. CCRK or CDCH) belongs to the serine/threonine protein-kinase family of CDKs and is evolutionarily conserved from yeast to mammals, including amphibians, fish, rodents and Old-World monkeys (Cheung & Lin, 2011; Guo & Stiller, 2004; Malumbres, 2014). It shares ~43 % sequence identity with CDK7, grouping it with CDKs that control both cell-cycle progression and transcription (Lai, Shin, & Qiu, 2020; Malumbres et al., 2009).

## Reaction Catalyzed

ATP + protein-Ser/Thr-OH ⇌ ADP + protein-Ser/Thr-O-PO₃²⁻ + H⁺  
A key physiological reaction is phosphorylation of CDK2 on Thr160 within its activation loop (Tian, Wan, & Tan, 2012; Cheung & Lin, 2011).

## Cofactor Requirements

Mg²⁺ is required for catalytic activity and proper ATP positioning (Tian et al., 2012; Malumbres, 2014).

## Substrate Specificity

CDK20 efficiently phosphorylates CDK2-Thr160, a modification essential for CDK2 activation and G1→S transition (Cheung & Lin, 2011; Tian et al., 2012). Additional reported targets include MAK-related kinase (MRK/ICK) and other cell-cycle or cilia-associated proteins, but a definitive consensus motif remains undefined (Fu et al., 2006; Lai et al., 2020).

## Structure

The 346-residue (~42 kDa) kinase contains the conserved bilobal CDK core (residues 4–288), with a glycine-rich loop in the N-lobe and an activation segment in the C-lobe that includes the regulatory Thr160 (Cheung & Lin, 2011; Tian et al., 2012). Eleven canonical kinase subdomains, the catalytic lysine, and the C-helix are present (Lai et al., 2020; Wohlbold et al., 2006). At least four splice variants exist, including a cardiac-specific isoform with reduced CDK2-activating capacity (Lai et al., 2020). No experimental crystal structure is yet available; homology models are based on CDK7 and CDK2 templates (Wood & Endicott, 2018; Endicott & Noble, 2013).

## Regulation

Activity is modulated by multiple mechanisms:  
• Phosphorylation of its substrates (e.g., CDK2-Thr160) is pivotal for downstream cell-cycle control (Tian et al., 2012).  
• Alternative splicing yields isoforms with distinct activation potentials (Lai et al., 2020; Wohlbold et al., 2006).  
• Promoter CpG hyper-methylation correlates with elevated expression in adult brain cortex (Cheung & Lin, 2011).  
• Protein–protein interactions with cyclins and other regulators appear necessary because CDK20 lacks strong intrinsic CAK activity and may require co-regulators for full function (Wohlbold et al., 2006; Tian et al., 2012).

## Function

CDK20 activates CDK2 to drive the G1/S transition (Cheung & Lin, 2011; Tian et al., 2012). Beyond proliferation, it is crucial for Sonic Hedgehog signalling during neural-tube development by coordinating primary-cilium assembly with TBC1D32, enabling GLI2 activation (Lai et al., 2020; Tian et al., 2012). High expression is observed in brain, kidney, liver, heart and placenta (Cheung & Lin, 2011; Lai et al., 2020). Over-expression is reported in glioblastoma, ovarian and colorectal cancers, linking CDK20 dysregulation to tumorigenesis (Cheung & Lin, 2011; Tian et al., 2012).

## Inhibitors

Small-molecule inhibitor RGB-286147 suppresses cell proliferation by targeting CDK20-dependent signalling (Cheung & Lin, 2011; Tian et al., 2012).

## Other Comments

Multiple splice variants, including a cardiac-specific form that poorly activates CDK2, underscore functional diversity (Lai et al., 2020; Wohlbold et al., 2006). While disease-linked mutations are not yet defined, CDK20 over-expression consistently associates with aggressive tumour phenotypes. Ongoing studies aim to map its substrate repertoire and develop selective inhibitors (Cheung & Lin, 2011; Guo & Stiller, 2004).

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