## Phylogeny

CDK20/CCRK is a serine/threonine kinase of the CMGC group, positioned within the transcription-associated CDK subfamily and clearly separated from canonical cell-cycle CDKs such as CDK1/2/4/6 (malumbres2014cyclindependentkinases pages 1-2, wood2018structuralinsightsinto pages 1-2).  
Comprehensive kinome surveys derived from the Manning classification cluster CDK20 together with atypical CDKs (CDK10, CDK11) on the CMGC/CDK branch (chowdhury2023cmgckinasesin pages 2-4, lim2013cdkscyclinsand pages 15-15).  
Verified orthologs span diverse taxa:  
– Mus musculus: Cdk20 (chowdhury2023cmgckinasesin pages 2-4)  
– Danio rerio: ccrk (lim2013cdkscyclinsand pages 15-15)  
– Caenorhabditis elegans: DYF-5 (fu2019ciliogenesisassociatedkinase pages 2-4)  
– Drosophila melanogaster: CG14964 (lim2013cdkscyclinsand pages 15-15)  
– Chlamydomonas reinhardtii: LF2/LF4 (fu2019ciliogenesisassociatedkinase pages 2-4)  
– Leishmania mexicana: LmxMPK9 (unknownauthorsUnknownyearúlohacdk13během pages 37-40)

## Reaction Catalyzed

ATP + [protein]-Ser/Thr → ADP + [protein]-O-phospho-Ser/Thr (fu2019ciliogenesisassociatedkinase pages 2-4).

## Cofactor Requirements

Catalytic turnover requires a divalent metal ion, typically Mg²⁺, to coordinate ATP in the active site, consistent with CMGC-group kinases (wood2018structuralinsightsinto pages 20-20).

## Substrate Specificity

Experimental peptide-library profiling defined a preferred motif R-P-X-S/T-P/A/S/T with a stringent Arg at −3 and Pro at −2; Pro at +1 is not obligatory (fu2019ciliogenesisassociatedkinase pages 2-4).  
Documented physiological substrates include:  
– CDK2 Thr160 (malumbres2014cyclindependentkinases pages 1-2)  
– ICK/MRK Thr157 (fu2006identificationofyinyang pages 1-2)  
– KIF3A at a consensus RPXS motif (fu2019ciliogenesisassociatedkinase pages 2-4).  
A kinase-wide specificity atlas entry for CDK20 is not yet available (chen2022integrativemultiomicsanalysis pages 5-7).

## Structure

Domain organisation: an N-terminal bilobal kinase domain (~residues 1–300) followed by a large intrinsically disordered C-terminal segment required for substrate docking and subcellular localisation (fu2019ciliogenesisassociatedkinase pages 2-4).  
3-D information: high-confidence AlphaFold model AF-Q8IZL9-F1 predicts a canonical CDK fold with conserved β-sheet N-lobe, α-helix C-lobe and an ordered activation loop (wood2018structuralinsightsinto pages 20-20).  
Key catalytic elements:  
– Catalytic Lys (β3) forms a salt bridge with the αC-helix Glu to stabilise ATP binding (wood2018structuralinsightsinto pages 2-3).  
– Activation loop contains the regulatory Thr157; phosphorylation promotes alignment of the hydrophobic spine for full activity (wood2018structuralinsightsinto pages 18-19).  
– A PKKRP motif centred on Arg272 supports active-state stabilisation; R272 mutations abolish kinase function (fu2019ciliogenesisassociatedkinase pages 2-4).

## Regulation

Post-translational modifications  
– Activation-loop phosphorylation at Thr157 by an upstream CAK (fu2019ciliogenesisassociatedkinase pages 2-4).  
– CCRK autophosphorylates Tyr within the ICK activation motif when acting as an upstream kinase for ICK (fu2006identificationofyinyang pages 1-2).  
Protein–protein interactions  
– Associates with cyclin H for activation, characteristic of transcriptional CDKs (malumbres2014cyclindependentkinases pages 1-2).  
– Stabilised by BRO/Broadminded (snouffer2017cellcyclerelatedkinase pages 12-14).  
Transcriptional and genomic control  
– Direct androgen-receptor target in hepatocytes, driving transcriptional up-regulation (malumbres2014cyclindependentkinases pages 9-10).  
– Frequently amplified and promoter-demethylated across multiple tumour types, leading to overexpression (chen2022integrativemultiomicsanalysis pages 11-16).

## Function

Ciliogenesis and Hedgehog signalling  
– Coordinates assembly of ciliary membrane and axoneme with TBC1D32, enabling high-level Shh/GLI2 responses in the neural tube (snouffer2017cellcyclerelatedkinase pages 2-4).  
– Restricts primary cilium length and promotes import of Hedgehog components Gli2 and Smoothened (fu2019ciliogenesisassociatedkinase pages 2-4).  
Cell-cycle regulation  
– Functions as a CDK-activating kinase for CDK2 by phosphorylating Thr160, thereby supporting G1/S progression (malumbres2014cyclindependentkinases pages 1-2).  
Additional signalling nodes  
– Phosphorylates ICK and KIF3A, linking CCRK to autophagy and mTORC1 regulation (fu2019ciliogenesisassociatedkinase pages 2-4).  
Expression pattern  
– Enriched in proliferative compartments such as intestinal crypt epithelium and regenerating tissues (fu2019ciliogenesisassociatedkinase pages 2-4).

## Other Comments

Disease associations  
– Loss-of-function mutations, especially within the PKKRP motif, cause ciliopathy phenotypes (e.g., ECO syndrome) and epilepsy (fu2019ciliogenesisassociatedkinase pages 2-4).  
– Oncogenic roles include β-catenin/TCF-driven hepatocarcinogenesis and cilium-dependent glioblastoma proliferation (malumbres2014cyclindependentkinases pages 9-10).  
– High CDK20 expression correlates with resistance to several anticancer drugs in pan-cancer analyses (chen2022integrativemultiomicsanalysis pages 11-16).

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