## Phylogeny

• Member of the CMGC kinase superfamily, cyclin-dependent kinase (CDK) group, PFTAIRE (also termed PCTAIRE) subfamily as mapped in the human kinome tree established by Manning et al. 2002 (chowdhury2023cmgckinasesin pages 19-21).  
• Forms an evolutionary branch with CDK16–18, distinct from canonical cell-cycle CDKs and transcriptional CDKs; characteristic replacement of the PSTAIRE helix with a PFTAIRE motif (pluta2024cyclin‐dependentkinasesmasters pages 14-15, pellarin2025cyclindependentproteinkinases pages 16-17).  
• Orthology is conserved across vertebrates, reflecting the high conservation reported for CMGC kinases (chowdhury2023cmgckinasesin pages 2-4).

## Reaction Catalyzed

ATP + [protein]-L-Ser/Thr → ADP + [protein]-L-Ser/Thr-phosphate; exemplified by phosphorylation of BIRC5 (survivin) at Thr34 (park2014als2cr7(cdk15)attenuates pages 1-2).

## Cofactor Requirements

No cofactor requirement has been explicitly reported for CDK15 in the cited literature (chowdhury2023cmgckinasesin pages 19-21).

## Substrate Specificity

• Kinome-wide motif analyses place CDK15 among proline-directed serine/threonine kinases that favour S/T-P at the +1 position (chowdhury2023cmgckinasesin pages 2-4, pluta2024cyclin‐dependentkinasesmasters pages 23-25).  
• Verified cellular substrate: survivin, phosphorylated at Thr34 where the +1 residue is Pro (park2014als2cr7(cdk15)attenuates pages 3-4).

## Structure

• Predicted bilobal kinase fold with canonical N-lobe β-sheet/αC-helix and C-lobe α-helical bundle; retains VAIK (β3), HRD (catalytic loop) and DFG (activation segment) motifs essential for catalysis (chowdhury2023cmgckinasesin pages 19-21).  
• Contains a CMGC-insert in the C-lobe implicated in substrate selection (chowdhury2023cmgckinasesin pages 19-21).  
• αC-helix harbours the distinctive PFTAIRE sequence that modulates cyclin interaction (pluta2024cyclin-dependentkinasesmasters pages 14-15).  
• AlphaFold model provides full-length structural prediction, showing an intact regulatory and catalytic hydrophobic spine and a flexible activation loop (pluta2024cyclin-dependentkinasesmasters pages 23-25).  
• No experimentally determined crystal or cryo-EM structure has been reported in the cited sources.

## Regulation

• Activation-loop phosphorylation is described as a post-translational regulatory mechanism, although specific sites and upstream kinases are not detailed (chowdhury2023cmgckinasesin pages 19-21).  
• Interacts with regulatory subunits/cyclins typical of CDKs; precise cyclin partner(s) remain to be identified (chowdhury2023cmgckinasesin pages 18-19).  
• Binds mitotic regulators Mad2, Plk1, Aurora B and Survivin, associations that link CDK15 to spindle assembly checkpoint control (unknownauthors2022ubiquitylationandphosphorylation pages 107-150).

## Function

• Expression is tissue-variable with notable enrichment in brain and muscle; dysregulated expression reported in several cancers (pluta2024cyclin-dependentkinasesmasters pages 23-25, chowdhury2023cmgckinasesin pages 2-4).  
• Anti-apoptotic role: phosphorylation of survivin Thr34 stabilises survivin, up-regulates survivin and Bcl-2, suppresses caspase-3/-8/-9 activation and PARP cleavage, thereby conferring resistance to TRAIL/TNFSF10-induced apoptosis (park2014als2cr7(cdk15)attenuates pages 1-2, park2014als2cr7(cdk15)attenuates pages 4-5).  
• Cell-cycle control: knock-down studies implicate CDK15 in spindle assembly checkpoint integrity via interactions with SAC components (unknownauthors2022ubiquitylationandphosphorylation pages 107-150).

## Other Comments

• Over-expression correlates with TRAIL resistance and poor prognosis in multiple tumor types (park2014als2cr7(cdk15)attenuates pages 5-6, chowdhury2023cmgckinasesin pages 19-21).  
• Gene resides in the chromosomal region linked to amyotrophic lateral sclerosis 2, suggesting neurological relevance, although functional data are limited (zhou2016theemergingroles pages 11-12).  
• Functional or disease-associated mutations have been noted but remain sparsely characterized (chowdhury2023cmgckinasesin pages 19-21, pluta2024cyclin-dependentkinasesmasters pages 23-25).

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