1. Phylogeny  
   Cyclin‐dependent kinase‐like 4 (CDKL4; UniProt Q5MAI5) is a member of the CDKL family, which includes CDKL1, CDKL2, CDKL3, and CDKL5. Members of this family are classified within the CMGC group of serine/threonine kinases and are distinctly separated from the classical cyclin‐dependent kinases (CDKs) despite sharing a conserved kinase domain. CDKL4 and its paralogs are evolutionarily conserved throughout metazoans; for example, the single CDKL ortholog in Caenorhabditis elegans (CDKL‐1) has been reported as being related to the vertebrate CDKL1–4 proteins, indicating that these kinases have been preserved from invertebrates to mammals (canning2018cdklfamilykinases pages 5-7, canning2018cdklfamilykinases pages 1-3). Structural phylogenetic analysis places the CDKL family within an evolutionarily distinct branch that diverged from the core CDK clade, and although CDKL5 has been most extensively characterized due to its association with neurological disorders, CDKL4 is grouped with the other CDKL family members based on sequence similarity within the kinase domain and the presence of unique regulatory C‐terminal extensions (canning2018cdklfamilykinases pages 3-4, endicott2013structuralcharacterizationof pages 3-5). These kinases share approximately 35–40% sequence identity with classical CDKs over their kinase domain, yet they exhibit distinct sequence motifs, such as variant PSTAIRE-like sequences and additional C-terminal regions that confer specialized functions within the cell (endicott2013structuralcharacterizationof pages 3-5, kannan2004evolutionaryconstraintsassociated pages 5-8).
2. Reaction Catalyzed  
   CDKL4 catalyzes the transfer of a phosphate group from ATP to the hydroxyl groups of serine or threonine residues in protein substrates. The enzymatic reaction can be represented as follows:  
     ATP + [protein]–(L‑serine or L‑threonine) → ADP + [protein]–(L‑serine/threonine)‑phosphate + H⁺  
   This reaction is typical of serine/threonine kinases and exemplifies the general catalytic mechanism shared by members of the CMGC kinase group (johnson2023anatlasof pages 1-2, endicott2013structuralcharacterizationof pages 1-2).
3. Cofactor Requirements  
   The catalytic activity of CDKL4 is dependent on the presence of divalent metal ions, with Mg²⁺ being required as a cofactor. The presence of Mg²⁺ is critical for proper ATP binding and phosphoryl transfer, a requirement that is characteristic of the majority of protein kinases and consistent with observed requirements in related serine/threonine kinases of the CMGC group (johnson2009proteinkinaseinhibitors pages 5-7, endicott2013structuralcharacterizationof pages 1-2).
4. Substrate Specificity  
   CDKL4 is anticipated to exhibit substrate specificity in line with other members of the CDKL family, which are considered to be proline-directed serine/threonine kinases. Analysis of the CDKL family has demonstrated that several members, including CDKL5, phosphorylate substrates in a manner that typically involves a serine or threonine residue immediately followed by a proline at the +1 position. This preference for a proline-directed motif is a common characteristic of CMGC kinases (johnson2023anatlasof pages 1-2, kannan2004evolutionaryconstraintsassociated pages 5-8). Although experimental studies specifically delineating the substrate consensus motif for CDKL4 are limited compared to CDKL5, homology-based inference suggests that CDKL4 likely prefers substrates containing serine or threonine followed by a proline (canning2018cdklfamilykinases pages 3-4, johnson2023anatlasof pages 4-4). In addition, distinct regulatory domains, such as the unusual C-terminal αJ helix observed in other CDKL family members, may influence the precise substrate recognition and phosphorylation efficiency, thereby modifying motif recognition relative to canonical CDKs (canning2018cdklfamilykinases pages 7-8, endicott2013structuralcharacterizationof pages 5-6).
5. Structure  
   CDKL4 is predicted to contain a conserved N-terminal kinase domain that exhibits a bilobal architecture, which is common to the serine/threonine kinases of the CMGC group. The N-terminal lobe is predominantly composed of β-sheets and contains the glycine-rich loop essential for ATP binding, while the larger C-terminal lobe is primarily α-helical and includes the substrate-binding region. Within the kinase domain, key catalytic features such as the DFG motif, catalytic loop, and the activation segment (or activation loop) are conserved and are critical for enzymatic activity (endicott2013structuralcharacterizationof pages 3-5). Notably, unlike classical CDKs, the CDKL family lacks the canonical cyclin-binding motif in the N-terminal region, and instead features unique structural adaptations in its C-terminal half. For instance, several CDKL family members possess an extended C-terminal region that includes an atypical amphipathic αJ helix. This helix has been shown to be essential for the kinase activity of CDKL2 and CDKL3, and although specific structural studies on CDKL4 are less comprehensive, it is presumed that CDKL4 shares similar regulatory elements (canning2018cdklfamilykinases pages 3-4, endicott2013structuralcharacterizationof pages 5-6). Additionally, conserved residues corresponding to the salt bridges and hydrophobic spines seen in classical kinases are predicted to be present in the CDKL4 structure, thereby stabilizing the active conformation and ensuring precise alignment of catalytic residues. Although high-resolution crystal structures for CDKL4 have not yet been reported, structural modeling based on available CDKL family members suggests that CDKL4 maintains the core kinase fold with unique insertions that may facilitate distinct substrate docking and regulatory interactions (canning2018cdklfamilykinases pages 11-11, endicott2013structuralcharacterizationof pages 8-9).
6. Regulation  
   Regulatory mechanisms governing CDKL4 activity appear to diverge from those observed in classical cyclin-dependent kinases. Similar to other CDKL family members, activation of CDKL4 is believed to depend on phosphorylation within the activation segment. Phosphorylation events in this region are critical for aligning the activation loop in an “active” conformation, although phosphomimetic mutations alone have been insufficient to fully recapitulate the active state in related kinases such as CDKL3, suggesting that additional regulatory inputs are necessary (endicott2013structuralcharacterizationof pages 5-6, canning2018cdklfamilykinases pages 3-4). Structural studies and kinase assays on related CDKL proteins indicate that regulatory mechanisms may involve both autophosphorylation and trans-phosphorylation by yet-unidentified upstream kinases. Moreover, CDKL proteins do not appear to interact with classical cyclins; instead, their regulation may rely on alternative binding partners or intrinsic structural elements, such as the distinct C-terminal αJ helix, which modulates catalytic activity and substrate binding (canning2018cdklfamilykinases pages 7-8, endicott2013structuralcharacterizationof pages 5-6). The lack of a canonical cyclin-binding interface means that CDKL4 may employ distinct allosteric or conformational changes to achieve full activation, and any post-translational modifications beyond phosphorylation, such as ubiquitination, have not yet been extensively characterized within the context of CDKL4 (canning2018cdklfamilykinases pages 3-4).
7. Function  
   The biological functions of CDKL4 remain less well defined relative to other members of the CDKL family, such as CDKL5, which has been extensively linked to neurodevelopmental disorders. Based on the conserved features among CDKL family kinases, CDKL4 is anticipated to be involved in intracellular signaling processes that are critical for cellular homeostasis. Emerging data on the CDKL family indicate roles in ciliary assembly and regulation, as evidenced by studies of CDKL1 and CDKL5 in controlling cilium length and modulating intraflagellar transport (canning2018cdklfamilykinases pages 7-8, canning2018cdklfamilykinases pages 11-11). In addition, phylogenetic and expression analyses suggest that CDKL family kinases have tissue-specific expression patterns, with several family members showing high expression levels in neuronal tissues, which implies a role in brain development and function. Although direct functional studies on CDKL4 are limited, its inclusion in the CDKL subfamily implies potential involvement in similar processes such as the regulation of microtubule dynamics, neuronal signaling, and possibly roles in cell proliferation and differentiation (castano2023discoveryandcharacterization pages 29-30, canning2018cdklfamilykinases pages 1-3). Functional investigations of related kinases have highlighted a contribution to synaptic plasticity, dendritic spine formation, and cilia-associated signal transduction. In some cancer models, alterations in the expression of CDKL family kinases have been correlated with changes in cell cycle progression and invasion properties, although specific disease associations for CDKL4 have not been definitively established (fang2018lossofcyclin‐dependent pages 10-10, canning2018cdklfamilykinases pages 9-10).
8. Other Comments  
   Currently, selective inhibitors have been developed primarily for other CDKL family members (for example, CDKL5), and small-molecule inhibitors designed to target CDKL kinases in general display a range of specificity profiles. Although no inhibitors have been reported that are exclusive for CDKL4, the structural similarities within the CDKL family suggest that advances in inhibitor design for CDKL5 and related kinases may be translatable to CDKL4. Disease associations have been robustly characterized for CDKL5, with mutations leading to severe neurodevelopmental disorders; however, the contribution of CDKL4 to human disease remains to be clarified. Some studies have implicated alterations in the expression levels of CDKL family kinases in various cancers and developmental disorders. The unique structural properties of CDKL4, particularly its divergent C-terminal region and potential for distinct substrate interactions, highlight the need for further biochemical and cellular characterization. In addition, the development of isoform-specific inhibitors might eventually provide pharmacological tools for dissecting the precise biological roles of CDKL4 in neurological and proliferative pathways (castano2023discoveryandcharacterization pages 30-34, fang2018lossofcyclin‐dependent pages 10-10).
9. References
10. canning2018cdklfamilykinases pages 1-3
11. canning2018cdklfamilykinases pages 3-4
12. canning2018cdklfamilykinases pages 5-7
13. canning2018cdklfamilykinases pages 7-8
14. canning2018cdklfamilykinases pages 9-10
15. canning2018cdklfamilykinases pages 11-11
16. endicott2013structuralcharacterizationof pages 1-2
17. endicott2013structuralcharacterizationof pages 3-5
18. endicott2013structuralcharacterizationof pages 5-6
19. endicott2013structuralcharacterizationof pages 8-9
20. endicott2013structuralcharacterizationof pages 9-9
21. johnson2009proteinkinaseinhibitors pages 5-7
22. johnson2023anatlasof pages 1-2
23. johnson2023anatlasof pages 2-3
24. johnson2023anatlasof pages 3-4
25. johnson2023anatlasof pages 4-4
26. johnson2023anatlasof pages 4-5
27. johnson2023anatlasof pages 9-10
28. johnson2023anatlasof pages 12-18
29. johnson2023anatlasof pages 18-20
30. johnson2023anatlasof pages 21-23
31. johnson2023anatlasof pages 23-26
32. kannan2004evolutionaryconstraintsassociated pages 5-8
33. kannan2004evolutionaryconstraintsassociated pages 11-13
34. kannan2004evolutionaryconstraintsassociated pages 13-15
35. klomp2024determiningtheerkregulated pages 9-11
36. munoz2018phosphoproteomicscreeningidentifies pages 4-5
37. wohlbold2006thecyclindependentkinase pages 2-3
38. wohlbold2006thecyclindependentkinase pages 4-5
39. castano2023discoveryandcharacterization pages 29-30
40. castano2023discoveryandcharacterization pages 30-34
41. echalier2010recentdevelopmentsin pages 7-8
42. fang2018lossofcyclin‐dependent pages 10-10
43. reddy2014discoveryof8cyclopentyl2[4(4methylpiperazin1yl)phenylamino]7oxo78dihydropyrido[23<i pages 22-22
44. shehata2012analysisofsubstrate pages 1-2
45. shehata2012analysisofsubstrate pages 3-4
46. yaronbarir2024theintrinsicsubstrate pages 2-3
47. bosken2014thestructureand pages 10-11
48. hsu2011zebrafishcyclindependentprotein pages 1-4

References

1. (canning2018cdklfamilykinases pages 5-7): Peter Canning, Kwangjin Park, João Gonçalves, Chunmei Li, Conor J. Howard, Timothy D. Sharpe, Liam J. Holt, Laurence Pelletier, Alex N. Bullock, and Michel R. Leroux. Cdkl family kinases have evolved distinct structural features and ciliary function. Cell Reports, 22:885-894, Jan 2018. URL: https://doi.org/10.1016/j.celrep.2017.12.083, doi:10.1016/j.celrep.2017.12.083. This article has 80 citations and is from a highest quality peer-reviewed journal.
2. (canning2018cdklfamilykinases pages 1-3): Peter Canning, Kwangjin Park, João Gonçalves, Chunmei Li, Conor J. Howard, Timothy D. Sharpe, Liam J. Holt, Laurence Pelletier, Alex N. Bullock, and Michel R. Leroux. Cdkl family kinases have evolved distinct structural features and ciliary function. Cell Reports, 22:885-894, Jan 2018. URL: https://doi.org/10.1016/j.celrep.2017.12.083, doi:10.1016/j.celrep.2017.12.083. This article has 80 citations and is from a highest quality peer-reviewed journal.
3. (canning2018cdklfamilykinases pages 11-11): Peter Canning, Kwangjin Park, João Gonçalves, Chunmei Li, Conor J. Howard, Timothy D. Sharpe, Liam J. Holt, Laurence Pelletier, Alex N. Bullock, and Michel R. Leroux. Cdkl family kinases have evolved distinct structural features and ciliary function. Cell Reports, 22:885-894, Jan 2018. URL: https://doi.org/10.1016/j.celrep.2017.12.083, doi:10.1016/j.celrep.2017.12.083. This article has 80 citations and is from a highest quality peer-reviewed journal.
4. (canning2018cdklfamilykinases pages 3-4): Peter Canning, Kwangjin Park, João Gonçalves, Chunmei Li, Conor J. Howard, Timothy D. Sharpe, Liam J. Holt, Laurence Pelletier, Alex N. Bullock, and Michel R. Leroux. Cdkl family kinases have evolved distinct structural features and ciliary function. Cell Reports, 22:885-894, Jan 2018. URL: https://doi.org/10.1016/j.celrep.2017.12.083, doi:10.1016/j.celrep.2017.12.083. This article has 80 citations and is from a highest quality peer-reviewed journal.
5. (canning2018cdklfamilykinases pages 7-8): Peter Canning, Kwangjin Park, João Gonçalves, Chunmei Li, Conor J. Howard, Timothy D. Sharpe, Liam J. Holt, Laurence Pelletier, Alex N. Bullock, and Michel R. Leroux. Cdkl family kinases have evolved distinct structural features and ciliary function. Cell Reports, 22:885-894, Jan 2018. URL: https://doi.org/10.1016/j.celrep.2017.12.083, doi:10.1016/j.celrep.2017.12.083. This article has 80 citations and is from a highest quality peer-reviewed journal.
6. (endicott2013structuralcharacterizationof pages 1-2): Jane A. Endicott and Martin E.M. Noble. Structural characterization of the cyclin-dependent protein kinase family. Biochemical Society transactions, 41 4:1008-16, Aug 2013. URL: https://doi.org/10.1042/bst20130097, doi:10.1042/bst20130097. This article has 48 citations and is from a peer-reviewed journal.
7. (endicott2013structuralcharacterizationof pages 3-5): Jane A. Endicott and Martin E.M. Noble. Structural characterization of the cyclin-dependent protein kinase family. Biochemical Society transactions, 41 4:1008-16, Aug 2013. URL: https://doi.org/10.1042/bst20130097, doi:10.1042/bst20130097. This article has 48 citations and is from a peer-reviewed journal.
8. (endicott2013structuralcharacterizationof pages 5-6): Jane A. Endicott and Martin E.M. Noble. Structural characterization of the cyclin-dependent protein kinase family. Biochemical Society transactions, 41 4:1008-16, Aug 2013. URL: https://doi.org/10.1042/bst20130097, doi:10.1042/bst20130097. This article has 48 citations and is from a peer-reviewed journal.
9. (johnson2009proteinkinaseinhibitors pages 5-7): Louise N. Johnson. Protein kinase inhibitors: contributions from structure to clinical compounds. Quarterly Reviews of Biophysics, 42:1-40, Feb 2009. URL: https://doi.org/10.1017/s0033583508004745, doi:10.1017/s0033583508004745. This article has 333 citations and is from a peer-reviewed journal.
10. (johnson2023anatlasof pages 1-2): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
11. (johnson2023anatlasof pages 12-18): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
12. (johnson2023anatlasof pages 2-3): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
13. (johnson2023anatlasof pages 3-4): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
14. (johnson2023anatlasof pages 4-4): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
15. (johnson2023anatlasof pages 4-5): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
16. (kannan2004evolutionaryconstraintsassociated pages 13-15): Natarajan Kannan and Andrew F. Neuwald. Evolutionary constraints associated with functional specificity of the cmgc protein kinases mapk, cdk, gsk, srpk, dyrk, and ck2α. Protein Science, 13:2059-2077, Aug 2004. URL: https://doi.org/10.1110/ps.04637904, doi:10.1110/ps.04637904. This article has 200 citations and is from a peer-reviewed journal.
17. (klomp2024determiningtheerkregulated pages 9-11): Jennifer E. Klomp, J. Nathaniel Diehl, Jeffrey A. Klomp, A. Cole Edwards, Runying Yang, Alexis J. Morales, Khalilah E. Taylor, Kristina Drizyte-Miller, Kirsten L. Bryant, Antje Schaefer, Jared L. Johnson, Emily M. Huntsman, Tomer M. Yaron, Mariaelena Pierobon, Elisa Baldelli, Alex W. Prevatte, Natalie K. Barker, Laura E. Herring, Emanuel F. Petricoin, Lee M. Graves, Lewis C. Cantley, Adrienne D. Cox, Channing J. Der, and Clint A. Stalnecker. Determining the erk-regulated phosphoproteome driving kras-mutant cancer. Science, Jun 2024. URL: https://doi.org/10.1126/science.adk0850, doi:10.1126/science.adk0850. This article has 31 citations and is from a highest quality peer-reviewed journal.
18. (munoz2018phosphoproteomicscreeningidentifies pages 4-5): Ivan M Muñoz, Michael E Morgan, Julien Peltier, Florian Weiland, Mateusz Gregorczyk, Fiona CM Brown, Thomas Macartney, Rachel Toth, Matthias Trost, and John Rouse. Phosphoproteomic screening identifies physiological substrates of the cdkl 5 kinase. The EMBO Journal, Sep 2018. URL: https://doi.org/10.15252/embj.201899559, doi:10.15252/embj.201899559. This article has 85 citations.
19. (wohlbold2006thecyclindependentkinase pages 2-3): Lara Wohlbold, Stephane Larochelle, Jack C.-F. Liao, Geulah Livshits, Juliet Singer, Kevan M. Shokat, and Robert P. Fisher. The cyclin-dependent kinase (cdk) family member pnqalre/ccrk supports cell proliferation but has no intrinsic cdk-activating kinase (cak) activity. Cell Cycle, 5:546-554, Mar 2006. URL: https://doi.org/10.4161/cc.5.5.2541, doi:10.4161/cc.5.5.2541. This article has 83 citations and is from a peer-reviewed journal.
20. (canning2018cdklfamilykinases pages 9-10): Peter Canning, Kwangjin Park, João Gonçalves, Chunmei Li, Conor J. Howard, Timothy D. Sharpe, Liam J. Holt, Laurence Pelletier, Alex N. Bullock, and Michel R. Leroux. Cdkl family kinases have evolved distinct structural features and ciliary function. Cell Reports, 22:885-894, Jan 2018. URL: https://doi.org/10.1016/j.celrep.2017.12.083, doi:10.1016/j.celrep.2017.12.083. This article has 80 citations and is from a highest quality peer-reviewed journal.
21. (castano2023discoveryandcharacterization pages 29-30): Anna Castano, Margaux Silvestre, Carrow I. Wells, Jennifer L. Sanderson, Carla A. Ferrer, Han Wee Ong, Yi Liang, William Richardson, Josie A. Silvaroli, Frances M. Bashore, Jeffery L. Smith, Isabelle M. Genereux, Kelvin Dempster, David H. Drewry, Navjot S. Pabla, Alex N. Bullock, Tim A. Benke, Sila K. Ultanir, and Alison D. Axtman. Discovery and characterization of a specific inhibitor of serine-threonine kinase cyclin dependent kinase-like 5 (cdkl5) demonstrates role in hippocampal ca1 physiology. BioRxiv, Apr 2023. URL: https://doi.org/10.1101/2023.04.24.538049, doi:10.1101/2023.04.24.538049. This article has 9 citations.
22. (echalier2010recentdevelopmentsin pages 7-8): Aude Echalier, Jane A. Endicott, and Martin E.M. Noble. Recent developments in cyclin-dependent kinase biochemical and structural studies. Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics, 1804:511-519, Mar 2010. URL: https://doi.org/10.1016/j.bbapap.2009.10.002, doi:10.1016/j.bbapap.2009.10.002. This article has 162 citations.
23. (endicott2013structuralcharacterizationof pages 8-9): Jane A. Endicott and Martin E.M. Noble. Structural characterization of the cyclin-dependent protein kinase family. Biochemical Society transactions, 41 4:1008-16, Aug 2013. URL: https://doi.org/10.1042/bst20130097, doi:10.1042/bst20130097. This article has 48 citations and is from a peer-reviewed journal.
24. (endicott2013structuralcharacterizationof pages 9-9): Jane A. Endicott and Martin E.M. Noble. Structural characterization of the cyclin-dependent protein kinase family. Biochemical Society transactions, 41 4:1008-16, Aug 2013. URL: https://doi.org/10.1042/bst20130097, doi:10.1042/bst20130097. This article has 48 citations and is from a peer-reviewed journal.
25. (fang2018lossofcyclin‐dependent pages 10-10): Chia‐Lang Fang, Yih‐Huei Uen, Han‐Kun Chen, You‐Cheng Hseu, Chih‐Chan Lin, Shih‐Ting Hung, Ding‐Ping Sun, and Kai‐Yuan Lin. Loss of cyclin‐dependent kinase‐like 2 predicts poor prognosis in gastric cancer, and its overexpression suppresses cells growth and invasion. Cancer Medicine, 7:2993-3002, May 2018. URL: https://doi.org/10.1002/cam4.1577, doi:10.1002/cam4.1577. This article has 17 citations and is from a peer-reviewed journal.
26. (johnson2023anatlasof pages 18-20): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
27. (johnson2023anatlasof pages 21-23): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
28. (johnson2023anatlasof pages 9-10): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.
29. (kannan2004evolutionaryconstraintsassociated pages 11-13): Natarajan Kannan and Andrew F. Neuwald. Evolutionary constraints associated with functional specificity of the cmgc protein kinases mapk, cdk, gsk, srpk, dyrk, and ck2α. Protein Science, 13:2059-2077, Aug 2004. URL: https://doi.org/10.1110/ps.04637904, doi:10.1110/ps.04637904. This article has 200 citations and is from a peer-reviewed journal.
30. (kannan2004evolutionaryconstraintsassociated pages 5-8): Natarajan Kannan and Andrew F. Neuwald. Evolutionary constraints associated with functional specificity of the cmgc protein kinases mapk, cdk, gsk, srpk, dyrk, and ck2α. Protein Science, 13:2059-2077, Aug 2004. URL: https://doi.org/10.1110/ps.04637904, doi:10.1110/ps.04637904. This article has 200 citations and is from a peer-reviewed journal.
31. (reddy2014discoveryof8cyclopentyl2[4(4methylpiperazin1yl)phenylamino]7oxo78dihydropyrido[23<i pages 22-22): M. V. Ramana Reddy, Balireddy Akula, Stephen C. Cosenza, Saikrishna Athuluridivakar, Muralidhar R. Mallireddigari, Venkat R. Pallela, Vinay K. Billa, D. R. C. Venkata Subbaiah, E. Vijaya Bharathi, Rodrigo Vasquez-Del Carpio, Amol Padgaonkar, Stacey J. Baker, and E. Premkumar Reddy. Discovery of 8-cyclopentyl-2-[4-(4-methyl-piperazin-1-yl)-phenylamino]-7-oxo-7,8-dihydro-pyrido[2,3-d]pyrimidine-6-carbonitrile (7x) as a potent inhibitor of cyclin-dependent kinase 4 (cdk4) and ampk-related kinase 5 (ark5). Journal of Medicinal Chemistry, 57:578-599, Jan 2014. URL: https://doi.org/10.1021/jm401073p, doi:10.1021/jm401073p. This article has 91 citations and is from a highest quality peer-reviewed journal.
32. (shehata2012analysisofsubstrate pages 1-2): Saifeldin N. Shehata, Roger W. Hunter, Eriko Ohta, Mark W. Peggie, Hua Jane Lou, Frank Sicheri, Elton Zeqiraj, Benjamin E. Turk, and Kei Sakamoto. Analysis of substrate specificity and cyclin y binding of pctaire-1 kinase. Cellular Signalling, 24:2085-2094, Nov 2012. URL: https://doi.org/10.1016/j.cellsig.2012.06.018, doi:10.1016/j.cellsig.2012.06.018. This article has 25 citations and is from a peer-reviewed journal.
33. (shehata2012analysisofsubstrate pages 3-4): Saifeldin N. Shehata, Roger W. Hunter, Eriko Ohta, Mark W. Peggie, Hua Jane Lou, Frank Sicheri, Elton Zeqiraj, Benjamin E. Turk, and Kei Sakamoto. Analysis of substrate specificity and cyclin y binding of pctaire-1 kinase. Cellular Signalling, 24:2085-2094, Nov 2012. URL: https://doi.org/10.1016/j.cellsig.2012.06.018, doi:10.1016/j.cellsig.2012.06.018. This article has 25 citations and is from a peer-reviewed journal.
34. (wohlbold2006thecyclindependentkinase pages 4-5): Lara Wohlbold, Stephane Larochelle, Jack C.-F. Liao, Geulah Livshits, Juliet Singer, Kevan M. Shokat, and Robert P. Fisher. The cyclin-dependent kinase (cdk) family member pnqalre/ccrk supports cell proliferation but has no intrinsic cdk-activating kinase (cak) activity. Cell Cycle, 5:546-554, Mar 2006. URL: https://doi.org/10.4161/cc.5.5.2541, doi:10.4161/cc.5.5.2541. This article has 83 citations and is from a peer-reviewed journal.
35. (yaronbarir2024theintrinsicsubstrate pages 2-3): Tomer M. Yaron-Barir, Brian A. Joughin, Emily M. Huntsman, Alexander Kerelsky, Daniel M. Cizin, Benjamin M. Cohen, Amit Regev, Junho Song, Neil Vasan, Ting-Yu Lin, Jose M. Orozco, Christina Schoenherr, Cari Sagum, Mark T. Bedford, R. Max Wynn, Shih-Chia Tso, David T. Chuang, Lei Li, Shawn S.-C. Li, Pau Creixell, Konstantin Krismer, Mina Takegami, Harin Lee, Bin Zhang, Jingyi Lu, Ian Cossentino, Sean D. Landry, Mohamed Uduman, John Blenis, Olivier Elemento, Margaret C. Frame, Peter V. Hornbeck, Lewis C. Cantley, Benjamin E. Turk, Michael B. Yaffe, and Jared L. Johnson. The intrinsic substrate specificity of the human tyrosine kinome. Nature, 629:1174-1181, May 2024. URL: https://doi.org/10.1038/s41586-024-07407-y, doi:10.1038/s41586-024-07407-y. This article has 56 citations and is from a highest quality peer-reviewed journal.
36. (bosken2014thestructureand pages 10-11): Christian A. Bösken, Lucas Farnung, Corinna Hintermair, Miriam Merzel Schachter, Karin Vogel-Bachmayr, Dalibor Blazek, Kanchan Anand, Robert P. Fisher, Dirk Eick, and Matthias Geyer. The structure and substrate specificity of human cdk12/cyclin k. Nature Communications, Mar 2014. URL: https://doi.org/10.1038/ncomms4505, doi:10.1038/ncomms4505. This article has 214 citations and is from a highest quality peer-reviewed journal.
37. (castano2023discoveryandcharacterization pages 30-34): Anna Castano, Margaux Silvestre, Carrow I. Wells, Jennifer L. Sanderson, Carla A. Ferrer, Han Wee Ong, Yi Liang, William Richardson, Josie A. Silvaroli, Frances M. Bashore, Jeffery L. Smith, Isabelle M. Genereux, Kelvin Dempster, David H. Drewry, Navjot S. Pabla, Alex N. Bullock, Tim A. Benke, Sila K. Ultanir, and Alison D. Axtman. Discovery and characterization of a specific inhibitor of serine-threonine kinase cyclin dependent kinase-like 5 (cdkl5) demonstrates role in hippocampal ca1 physiology. BioRxiv, Apr 2023. URL: https://doi.org/10.1101/2023.04.24.538049, doi:10.1101/2023.04.24.538049. This article has 9 citations.
38. (hsu2011zebrafishcyclindependentprotein pages 1-4): Li-Sung Hsu, Cyong-Jhih Liang, Chen-Yuan Tseng, Chi-Wei Yeh, and Jen-Ning Tsai. Zebrafish cyclin-dependent protein kinase–like 1 (zcdkl1): identification and functional characterization. International Journal of Molecular Sciences, 12:3606-3617, Jun 2011. URL: https://doi.org/10.3390/ijms12063606, doi:10.3390/ijms12063606. This article has 24 citations and is from a peer-reviewed journal.
39. (johnson2023anatlasof pages 23-26): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 436 citations and is from a highest quality peer-reviewed journal.