## 1. Phylogeny

Tyrosine‐protein kinase TXK, also known as Protein‐tyrosine kinase 4 (PTK4) or Resting lymphocyte kinase (RLK), is classified within the non‐receptor tyrosine kinase superfamily and, more specifically, the Tec family of kinases. Comparative phylogenetic analyses consistently group TXK alongside other Tec family members such as interleukin‐2 inducible T‐cell kinase (ITK), Bruton’s tyrosine kinase (BTK), TEC, and Bmx, all of which are involved in intracellular signaling in lymphocytes and have evolved specialized regulatory features to mediate immune responses (bradshaw2010thesrcsyk pages 3-5). Molecular phylogenetics based on kinase domain sequences has revealed that the Tec family arose from a common ancestral kinase that existed early in vertebrate evolution, with gene duplication events later giving rise to the distinct family members. In the context of the kinome, TXK is positioned in a clade that exhibits a conserved catalytic core common to cytoplasmic tyrosine kinases, but distinguishes itself by unique protein modules that are not present in other Tec kinases. For instance, while most Tec family kinases harbor an N-terminal pleckstrin homology (PH) domain and Tec homology (TH) domain, TXK is divergent in that its N-terminal region is replaced by a unique cysteine-rich string motif which undergoes palmitoylation; this divergence is evolutionarily conserved and indicative of its specialized role in T-cell signaling (eshaq2024nonreceptortyrosinekinases pages 9-12).  
Analyses performed using maximum likelihood and Bayesian methodologies have demonstrated that the Tec family members, including TXK, maintain a high degree of orthology across vertebrate species; orthologs of TXK have been identified in mammals ranging from rodents to primates, attesting to its integral role in adaptive immunity (bhanumathy2021proteintyrosinekinases pages 2-4, yeung2021evolutionoffunctional pages 3-6). In broader kinome surveys, TXK belongs to the cytoplasmic branch of tyrosine kinases and appears as part of an evolutionarily conserved set of kinases that participate in immune receptor signaling. Furthermore, comparative studies of protein domain organization among Tec family kinases have highlighted that while most family members follow a canonical modular layout, TXK’s distinct N-terminal structure marks it as a specialized member within this group and suggests that selective pressures during vertebrate evolution have tailored its regulatory properties to suit particular signaling functions in T lymphocytes (santos2016paralogspecificpatternsof pages 1-1). Recent genomic surveys and orthology analyses further indicate that the Tec family, with TXK as a representative member, emerged early in the evolution of adaptive immunity and that the conservation of its catalytic domain coupled with innovative regulatory motifs has ensured its functional preservation over millions of years (liu2017identificationandcharacterization pages 2-4). Together, these phylogenetic insights underscore the evolutionary importance of TXK and its close relationship with other Tec kinases that coordinate T-cell activation and differentiation.

## 2. Reaction Catalyzed

TXK catalyzes the transfer of the γ‐phosphate from ATP to a specific tyrosine residue on target protein substrates, an essential modification that modulates protein function and initiates downstream signaling cascades in lymphocytes (xu2019pf06651600adual pages 7-8). In the catalytic mechanism of TXK, ATP binds within a conserved kinase domain where it is properly oriented by key residues of the glycine-rich loop and ATP-binding pocket; this precise arrangement facilitates the nucleophilic attack by the hydroxyl oxygen of a tyrosine residue on the substrate (vargas2013inhibitorsofbtk pages 1-3). The reaction is described by the general kinase-catalyzed equation: ATP + substrate protein (with a free tyrosine hydroxyl group) yields ADP plus the phosphorylated protein, with the newly incorporated phosphate group inducing conformational changes that regulate protein–protein interactions and enzymatic activity (xu2019pf06651600adual pages 7-8).  
In the context of T-cell receptor (TCR) signaling, TXK plays a pivotal role by phosphorylating substrates such as phospholipase C gamma 1 (PLCG1), thereby driving its recruitment to lipid rafts and subsequent activation. The phosphorylation of PLCG1 triggers the hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP2) into diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP3), which in turn facilitates calcium mobilization from the endoplasmic reticulum and leads to the activation of downstream transcription factors including NFAT (bhanumathy2021proteintyrosinekinases pages 1-2).  
This phosphorylation event by TXK is reversible and is subject to tight regulation by protein tyrosine phosphatases, ensuring that the signaling cascades remain transient and accurately calibrated according to physiological needs (gocek2014nonreceptorproteintyrosine pages 1-2). Thus, TXK acts as a molecular switch in T cells, whereby its catalytic activity directly converts extracellular receptor engagement into intracellular phosphorylation signals that ultimately regulate gene expression, cytokine production, and other cellular processes necessary for effective immune responses.

## 3. Cofactor Requirements

The enzymatic activity of TXK depends critically on the coordination of ATP with divalent metal ions that act as essential cofactors. Magnesium ions (Mg²⁺) are the primary cofactors required for TXK activity, as they stabilize the binding of ATP via coordination with the phosphate groups, thereby lowering the activation energy for the enzymatic reaction (xu2019pf06651600adual pages 7-8). Mg²⁺ ions interact with residues in the ATP-binding pocket of the kinase domain to ensure that ATP is precisely oriented for efficient phosphotransfer to the tyrosine residue on substrate proteins (castelosoccio2023proteinkinasesdrug pages 1-2).  
Experimental studies on related tyrosine kinases, such as those in the Tec family, have noted that under non-physiological conditions other divalent cations like Mn²⁺ can functionally substitute for Mg²⁺; however, in physiological conditions, TXK activity is predominantly magnesium-dependent (fu2024largescaleanalysisof pages 1-3). In addition to the metal cofactor, although accessory molecules (e.g., phosphatidylinositols) are influential in directing membrane localization and protein interactions within Tec kinases, they do not directly contribute to the catalytic mechanism of phosphotransfer. Therefore, Mg²⁺ remains the critical cofactor that underpins the efficient catalytic cycle of TXK, a requirement that is characteristic of most protein kinases and essential for its role in intracellular signaling.

## 4. Substrate Specificity

TXK exhibits a finely tuned substrate specificity that is central to its role in orchestrating signaling networks within T cells. One of the primary substrates of TXK is phospholipase C gamma 1 (PLCG1). Post-phosphorylation by TXK, PLCG1 undergoes a localization shift into lipid rafts where it then catalyzes the hydrolysis of PIP2 into the second messengers IP3 and DAG, which subsequently trigger Ca²⁺ release from the endoplasmic reticulum and activate the NFAT transcription factor (bhanumathy2021proteintyrosinekinases pages 1-2).  
In addition to PLCG1, TXK phosphorylates components of a multiprotein complex that regulates interferon-gamma (IFNG) transcription in T-helper 1 (Th1) cells. Within this promoter-binding complex, TXK targets poly(ADP-ribose) polymerase 1 (PARP1) and eukaryotic translation elongation factor 1A1 (EEF1A1), resulting in enhanced transcriptional activation of IFNG—a critical cytokine in anti-microbial and anti-tumor immune responses (bhanumathy2021proteintyrosinekinases pages 2-4).  
TXK further modulates T-cell function by phosphorylating the adaptor protein LCP2; this phosphorylation event is linked to the up-regulation of interleukin-2 (IL-2), a cytokine vital for T-cell survival, proliferation, and differentiation. Moreover, TXK phosphorylates CTLA4 at Tyr-201, a modification that creates a binding interface for phosphatidylinositol 3-kinase (PI3K) and integrates inhibitory signaling into the overall T-cell activation network (xu2019pf06651600adual pages 7-8).  
Structural determinants of substrate specificity in TXK arise from its modular domain composition. The SH2 domain of TXK is specialized in recognizing phosphotyrosine-containing motifs on target proteins, ensuring that substrates which have been pre-phosphorylated by upstream kinases or other signaling events are efficiently engaged. In parallel, the SH3 domain facilitates interactions with proline-rich sequences within regulatory proteins. These binding modules work concertedly with the catalytic kinase domain to ensure that phosphorylation occurs within precise spatial and temporal contexts, thereby reinforcing the fidelity of T-cell receptor (TCR) signaling (vargas2013inhibitorsofbtk pages 1-3).  
Although comprehensive peptide library studies have suggested potential consensus sequences around the phosphorylation sites preferred by TXK, a singular consensus motif for TXK has yet to be definitively established; rather, its substrate recognition appears to be an emergent property of the integrated contributions from its catalytic and regulatory domains.

## 5. Structure

The structural organization of TXK is emblematic of the Tec family kinases, yet it is marked by unique features that differentiate it from its relatives. Unlike typical Tec kinases that commence with an N-terminal pleckstrin homology (PH) domain coupled with a Tec homology (TH) domain, TXK is characterized by an atypical N-terminal region lacking these domains. Instead, TXK contains a cysteine-rich string motif whose residues are prime candidates for palmitoylation, thereby facilitating membrane association—a critical function given TXK’s role in T-cell signaling (eshaq2024nonreceptortyrosinekinases pages 9-12).  
Following this unconventional N-terminal extension, TXK exhibits conserved modular domains that include the Src Homology 3 (SH3) domain, which mediates interactions with proline-rich sequences from other signaling proteins. The SH3 domain plays an integral role in transient protein–protein interactions that are essential for the assembly of multiprotein complexes at the plasma membrane (bradshaw2010thesrcsyk pages 3-5). Adjacent to the SH3 domain is the Src Homology 2 (SH2) domain, which is specialized in recognizing phosphotyrosine motifs in target proteins. This domain is critical for the recruitment of phosphorylated substrates and adaptor proteins to TXK during TCR signaling (bradshaw2010thesrcsyk pages 3-5).  
Central to TXK’s function is its kinase catalytic domain, which conforms to the canonical bilobal structure observed in eukaryotic protein kinases. The N-terminal lobe of this catalytic domain consists of a five-stranded β-sheet and includes a glycine-rich loop that is central to nucleotide binding, while the predominantly α-helical C-terminal lobe houses the subdomains responsible for substrate catalysis. A key feature within this catalytic domain is the activation loop, whose phosphorylation at Tyr-420 is indispensable for full kinase activation; phosphorylation at this site triggers a conformational realignment that opens the substrate-binding cleft and permits efficient catalysis (xu2019pf06651600adual pages 7-8).  
Although no full-length crystal structure of TXK has been reported to date, homology models generated using computational algorithms such as those underlying the AlphaFold predictions have provided substantial insights into its three-dimensional architecture. These models corroborate the conservation of key catalytic motifs juxtaposed with the divergent architecture of the N-terminal regulatory region, thereby suggesting alternative mechanisms for membrane recruitment and substrate recognition in TXK compared to other Tec kinases (andreotti2018multidomaincontrolover pages 6-8). Structural studies of related kinases further indicate that critical residues in the active site—particularly those involved in coordinating ATP and facilitating phosphotransfer—are strictly conserved, underscoring the evolutionary pressure to maintain enzymatic function despite divergence in regulatory modules.

## 6. Regulation

Regulation of TXK is achieved through an intricate network of post-translational modifications and protein–protein interactions that together fine-tune its activity in the immune cell. A central regulatory event is the phosphorylation of the activation loop at Tyr-420. This modification, which can be catalyzed by upstream Src family kinases or occur via autophosphorylation, is essential for relieving the autoinhibited conformation of TXK and transitioning the enzyme into a fully active state capable of substrate phosphorylation (bhanumathy2021proteintyrosinekinases pages 1-2, amatya2019dynamicregulatoryfeatures pages 7-9).  
TXK regulation is further modulated through its dynamic interactions mediated by its SH2 and SH3 domains. The SH2 domain enables TXK to bind transiently to phosphotyrosine residues on activated receptors or adaptor proteins, thereby participating in the spatial organization of signaling complexes. Meanwhile, the SH3 domain engages binding partners that harbor proline-rich motifs; such interactions not only influence the localization of TXK but can also modulate its catalytic activity by altering conformational equilibria within the kinase (andreotti2018multidomaincontrolover pages 3-4).  
In addition to positive regulatory mechanisms, negative regulation is accomplished by protein tyrosine phosphatases that dephosphorylate critical tyrosine residues such as Tyr-420, thereby returning TXK to an inactive or autoinhibited state. This reversible phosphorylation ensures that TXK activity remains tightly controlled and temporally restricted to periods of antigen stimulation (eshaq2024nonreceptortyrosinekinases pages 1-2).  
Membrane association is another key regulatory layer; despite the absence of the conventional PH domain, TXK’s unique N-terminal cysteine-rich motif undergoes palmitoylation—a lipid modification that promotes its targeting to the plasma membrane during T-cell receptor engagement. This membrane localization is essential for positioning TXK in proximity to its substrates and other components of the TCR signaling cascade (bradshaw2010thesrcsyk pages 3-5, eshaq2024nonreceptortyrosinekinases pages 9-12).  
Furthermore, regulatory redundancy within the Tec family is evident in that TXK and ITK display overlapping functions; when the activity of one kinase is compromised, the other can partially compensate to ensure that downstream signaling events, particularly those leading to cytokine production and cellular activation, are maintained (hsu2023selectiveinhibitionof pages 16-20). This crosstalk between family members underscores the evolutionary conservation of regulatory mechanisms and highlights the elaborate control network that governs T-cell activation.

## 7. Function

TXK plays a vital role in adaptive immunity by acting as a molecular switch in T-cell signaling. Expressed constitutively in resting lymphocytes, TXK is rapidly recruited to the plasma membrane following T-cell receptor (TCR) engagement by antigen-presenting cells. This recruitment is accompanied by its phosphorylation at Tyr-420, an event critical for full activation of the kinase and the initiation of downstream signaling pathways (bhanumathy2021proteintyrosinekinases pages 1-2, xu2019pf06651600adual pages 7-8).  
One of the most important functions of TXK is its ability to phosphorylate phospholipase C gamma 1 (PLCG1). Once phosphorylated, PLCG1 translocates to lipid rafts where it catalyzes the hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP2) into diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP3); IP3, in turn, stimulates calcium release from intracellular stores, thereby promoting the activation of transcription factors such as NFAT (bhanumathy2021proteintyrosinekinases pages 1-2).  
Beyond its effects on calcium signaling, TXK has a significant impact on T-cell differentiation and cytokine production. In T-helper 1 (Th1) cells, TXK is an essential component of a transcriptional regulatory complex that enhances the expression of interferon-gamma (IFNG). Within this complex, TXK phosphorylates both PARP1 and eukaryotic translation elongation factor 1A1 (EEF1A1), thereby promoting IFNG gene transcription and reinforcing Th1-mediated immune responses (bhanumathy2021proteintyrosinekinases pages 2-4).  
Additionally, TXK modulates the activity of the adaptor protein LCP2, a key molecule in TCR signaling; phosphorylation of LCP2 by TXK is associated with the up-regulation of interleukin-2 (IL-2), which is central to T-cell clonal expansion and survival. Moreover, TXK phosphorylates the immunoregulatory receptor CTLA4 at Tyr-201, facilitating the recruitment of phosphatidylinositol 3-kinase (PI3K). This modification is thought to integrate inhibitory signals with positive activation cues, thereby fine-tuning the amplitude of T-cell responses (xu2019pf06651600adual pages 7-8).  
TXK is also implicated in the regulation of the actin cytoskeleton, which is crucial for the dynamic remodeling of T cells during migration, the formation of the immunological synapse, and stable cell–cell contact during antigen recognition. This contribution further underscores the multifunctional nature of TXK in directing both biochemical signaling events and biophysical changes within immune cells (dievart2020originanddiversity pages 12-14).  
Overall, the functions mediated by TXK underscore its role as a central hub in the adaptive immune response. Its ability to orchestrate a range of signaling events—from calcium mobilization and transcriptional activation to cytoskeletal rearrangements—ensures that T cells can mount rapid and robust responses upon encountering antigenic stimuli, thereby maintaining immune surveillance and host defense.

## 8. Other Comments

Given its central role in T-cell activation and regulation of cytokine production, TXK has garnered significant interest as a potential therapeutic target in conditions characterized by dysregulated immune responses, including autoimmune diseases and T-cell malignancies (yaron2020thefdaapproveddrug pages 1-4). Efforts to develop small molecule inhibitors that specifically target TXK—or that modulate the activity of multiple Tec family kinases—are ongoing and represent a promising avenue for immunomodulatory therapies. Inhibitors that selectively target TXK may offer advantages by minimizing off-target effects while preserving critical functions mediated by related kinases such as ITK (xu2019pf06651600adual pages 8-8, castelosoccio2023proteinkinasesdrug pages 1-2).  
TXK’s unique structural features, most notably its divergent N-terminal cysteine-rich region instead of a canonical PH/TH domain, provide potential opportunities for the design of novel inhibitors that could exploit these differences. Such compounds might be developed to interfere selectively with TXK’s membrane association or to modulate its interactions with specific adaptor proteins. Although disease-associated mutations in TXK have not yet been widely characterized, alterations in critical residues—such as the activation loop Tyr-420—could feasibly impair its function and contribute to immune pathologies, making these sites potential biomarkers for diagnostic or prognostic applications (joseph2011controllingtheactivity pages 8-9).  
Recent advances in structural biology, including efforts to determine the full-length three-dimensional structure of TXK using X-ray crystallography or cryo-electron microscopy, promise to shed further light on its regulatory mechanisms and facilitate the rational design of highly specific inhibitors (andreotti2018multidomaincontrolover pages 6-8). Additionally, ongoing research into the functional redundancy and compensatory interplay between TXK and ITK holds substantial promise for refining therapeutic strategies that aim to selectively modulate T-cell responses. For instance, selective inhibition of ITK while sparing TXK activity has been shown to preserve key anti-tumor functions of T cells, highlighting the potential benefits of targeting these kinases in a coordinated yet specific manner (hsu2023selectiveinhibitionof pages 16-20).  
Beyond its roles in T-cell receptor signaling and cytokine gene transcription, TXK is increasingly recognized as a key regulator of the actin cytoskeleton, influencing not only immune cell activation but also cellular migration and intercellular communication. This multifaceted regulatory capacity positions TXK as a particularly attractive target for immunotherapeutic interventions aimed at modulating both biochemical signaling pathways and the biophysical properties of immune cells.  
Overall, TXK continues to be an active subject of investigation in the fields of immunology and cancer biology. As our understanding of its structure–function relationships deepens, there is considerable potential for the development of next-generation therapeutics that exploit its unique regulatory features to correct aberrant immune signaling. The continued integration of phylogenetic, structural, and biochemical data will be essential for translating these insights into clinically effective strategies for diseases where T-cell signaling is disrupted.

## 9. References

1. amatya2019dynamicregulatoryfeatures pages 7-9
2. bhanumathy2021proteintyrosinekinases pages 1-2
3. bhanumathy2021proteintyrosinekinases pages 2-4
4. bradshaw2010thesrcsyk pages 3-5
5. eshaq2024nonreceptortyrosinekinases pages 9-12
6. fu2024largescaleanalysisof pages 1-3
7. hsu2023selectiveinhibitionof pages 16-20
8. vargas2013inhibitorsofbtk pages 1-3
9. xu2019pf06651600adual pages 7-8
10. xu2019pf06651600adual pages 8-8
11. yaron2020thefdaapproveddrug pages 1-4
12. santos2016paralogspecificpatternsof pages 1-1
13. yeung2021evolutionoffunctional pages 3-6
14. joseph2011controllingtheactivity pages 8-9
15. dievart2020originanddiversity pages 12-14

References

1. (amatya2019dynamicregulatoryfeatures pages 7-9): Neha Amatya, David Yin-wei Lin, and Amy H. Andreotti. Dynamic regulatory features of the protein tyrosine kinases. Biochemical Society Transactions, 47:1101-1116, Aug 2019. URL: https://doi.org/10.1042/bst20180590, doi:10.1042/bst20180590. This article has 31 citations and is from a peer-reviewed journal.
2. (bhanumathy2021proteintyrosinekinases pages 1-2): Kalpana K. Bhanumathy, Amrutha Balagopal, Frederick S. Vizeacoumar, Franco J. Vizeacoumar, Andrew Freywald, and Vincenzo Giambra. Protein tyrosine kinases: their roles and their targeting in leukemia. Cancers, 13:184, Jan 2021. URL: https://doi.org/10.3390/cancers13020184, doi:10.3390/cancers13020184. This article has 73 citations and is from a peer-reviewed journal.
3. (bhanumathy2021proteintyrosinekinases pages 2-4): Kalpana K. Bhanumathy, Amrutha Balagopal, Frederick S. Vizeacoumar, Franco J. Vizeacoumar, Andrew Freywald, and Vincenzo Giambra. Protein tyrosine kinases: their roles and their targeting in leukemia. Cancers, 13:184, Jan 2021. URL: https://doi.org/10.3390/cancers13020184, doi:10.3390/cancers13020184. This article has 73 citations and is from a peer-reviewed journal.
4. (bradshaw2010thesrcsyk pages 3-5): J. M. Bradshaw. The src, syk, and tec family kinases: distinct types of molecular switches. Cellular signalling, 22 8:1175-84, Aug 2010. URL: https://doi.org/10.1016/j.cellsig.2010.03.001, doi:10.1016/j.cellsig.2010.03.001. This article has 364 citations and is from a peer-reviewed journal.
5. (eshaq2024nonreceptortyrosinekinases pages 1-2): Abdulaziz M. Eshaq, Thomas W. Flanagan, Sofie-Yasmin Hassan, Sara A. Al Asheikh, Waleed A. Al-Amoudi, Simeon Santourlidis, Sarah-Lilly Hassan, Maryam O. Alamodi, Marcelo L. Bendhack, Mohammed O. Alamodi, Youssef Haikel, Mossad Megahed, and Mohamed Hassan. Non-receptor tyrosine kinases: their structure and mechanistic role in tumor progression and resistance. Cancers, 16:2754, Aug 2024. URL: https://doi.org/10.3390/cancers16152754, doi:10.3390/cancers16152754. This article has 6 citations and is from a peer-reviewed journal.
6. (eshaq2024nonreceptortyrosinekinases pages 9-12): Abdulaziz M. Eshaq, Thomas W. Flanagan, Sofie-Yasmin Hassan, Sara A. Al Asheikh, Waleed A. Al-Amoudi, Simeon Santourlidis, Sarah-Lilly Hassan, Maryam O. Alamodi, Marcelo L. Bendhack, Mohammed O. Alamodi, Youssef Haikel, Mossad Megahed, and Mohamed Hassan. Non-receptor tyrosine kinases: their structure and mechanistic role in tumor progression and resistance. Cancers, 16:2754, Aug 2024. URL: https://doi.org/10.3390/cancers16152754, doi:10.3390/cancers16152754. This article has 6 citations and is from a peer-reviewed journal.
7. (fu2024largescaleanalysisof pages 1-3): Qiong Fu, Qian Liu, Rensen Zhang, Jia Chen, Hengchang Guo, Zhenhua Ming, Feng Yu, and Heping Zheng. Large-scale analysis of the n-terminal regulatory elements of the kinase domain in plant receptor-like kinase family. BMC Plant Biology, Mar 2024. URL: https://doi.org/10.1186/s12870-024-04846-7, doi:10.1186/s12870-024-04846-7. This article has 2 citations and is from a peer-reviewed journal.
8. (hsu2023selectiveinhibitionof pages 16-20): Lih-Yun Hsu, James T Rosenbaum, Erik Verner, William B Jones, Craig M. Hill, James W. Janc, Joseph J. Buggy, Ning Ding, John C. Reneau, Michael S. Khodadoust, Youn H. Kim, Ryan A. Wilcox, and Richard A. Miller. Selective inhibition of interleukin-2 inducible t cell kinase (itk) enhances anti-tumor immunity in association with th1-skewing, cytotoxic t cell activation, and reduced t cell exhaustion. BioRxiv, Jul 2023. URL: https://doi.org/10.1101/2023.07.05.547822, doi:10.1101/2023.07.05.547822. This article has 2 citations.
9. (liu2017identificationandcharacterization pages 2-4): Ake Liu, Funan He, and Xun Gu. Identification and characterization of tyrosine kinases in anole lizard indicate the conserved tyrosine kinase repertoire in vertebrates. Molecular Genetics and Genomics, 292:1405-1418, Aug 2017. URL: https://doi.org/10.1007/s00438-017-1356-7, doi:10.1007/s00438-017-1356-7. This article has 6 citations and is from a peer-reviewed journal.
10. (santos2016paralogspecificpatternsof pages 1-1): Helena G. Dos Santos and Jessica Siltberg-Liberles. Paralog-specific patterns of structural disorder and phosphorylation in the vertebrate sh3–sh2–tyrosine kinase protein family. Genome Biology and Evolution, 8:2806-2825, Aug 2016. URL: https://doi.org/10.1093/gbe/evw194, doi:10.1093/gbe/evw194. This article has 9 citations and is from a domain leading peer-reviewed journal.
11. (vargas2013inhibitorsofbtk pages 1-3): Leonardo Vargas, A. Hamasy, A. Hamasy, B. Nore, B. Nore, and C. I. E. Smith. Inhibitors of btk and itk: state of the new drugs for cancer, autoimmunity and inflammatory diseases. Scandinavian Journal of Immunology, Aug 2013. URL: https://doi.org/10.1111/sji.12069, doi:10.1111/sji.12069. This article has 91 citations and is from a peer-reviewed journal.
12. (xu2019pf06651600adual pages 7-8): Hua Xu, Michael I. Jesson, Uthpala I. Seneviratne, Tsung H. Lin, M. Nusrat Sharif, Liang Xue, Chuong Nguyen, Robert A. Everley, John I. Trujillo, Douglas S. Johnson, Gary R. Point, Atli Thorarensen, Iain Kilty, and Jean-Baptiste Telliez. Pf-06651600, a dual jak3/tec family kinase inhibitor. ACS Chemical Biology, 14:1235-1242, May 2019. URL: https://doi.org/10.1021/acschembio.9b00188, doi:10.1021/acschembio.9b00188. This article has 137 citations and is from a domain leading peer-reviewed journal.
13. (xu2019pf06651600adual pages 8-8): Hua Xu, Michael I. Jesson, Uthpala I. Seneviratne, Tsung H. Lin, M. Nusrat Sharif, Liang Xue, Chuong Nguyen, Robert A. Everley, John I. Trujillo, Douglas S. Johnson, Gary R. Point, Atli Thorarensen, Iain Kilty, and Jean-Baptiste Telliez. Pf-06651600, a dual jak3/tec family kinase inhibitor. ACS Chemical Biology, 14:1235-1242, May 2019. URL: https://doi.org/10.1021/acschembio.9b00188, doi:10.1021/acschembio.9b00188. This article has 137 citations and is from a domain leading peer-reviewed journal.
14. (yaron2020thefdaapproveddrug pages 1-4): Tomer M. Yaron, Brook E. Heaton, Tyler M. Levy, Jared L. Johnson, Tristan X. Jordan, Benjamin M. Cohen, Alexander Kerelsky, Ting-Yu Lin, Katarina M. Liberatore, Danielle K. Bulaon, Edward R. Kastenhuber, Marisa N. Mercadante, Kripa Shobana-Ganesh, Long He, Robert E. Schwartz, Shuibing Chen, Harel Weinstein, Olivier Elemento, Elena Piskounova, Benjamin E. Nilsson-Payant, Gina Lee, Joseph D. Trimarco, Kaitlyn N. Burke, Cait E. Hamele, Ryan R. Chaparian, Alfred T. Harding, Aleksandra Tata, Xinyu Zhu, Purushothama Rao Tata, Clare M. Smith, Anthony P. Possemato, Sasha L. Tkachev, Peter V. Hornbeck, Sean A. Beausoleil, Shankara K. Anand, François Aguet, Gad Getz, Andrew D. Davidson, Kate Heesom, Maia Kavanagh-Williamson, David Matthews, Benjamin R. tenOever, Lewis C. Cantley, John Blenis, and Nicholas S. Heaton. The fda-approved drug alectinib compromises sars-cov-2 nucleocapsid phosphorylation and inhibits viral infection in vitro. BioRxiv, Aug 2020. URL: https://doi.org/10.1101/2020.08.14.251207, doi:10.1101/2020.08.14.251207. This article has 38 citations.
15. (yeung2021evolutionoffunctional pages 3-6): Wayland Yeung, Annie Kwon, Rahil Taujale, Claire Bunn, Aarya Venkat, and Natarajan Kannan. Evolution of functional diversity in the holozoan tyrosine kinome. Molecular Biology and Evolution, 38:5625-5639, Sep 2021. URL: https://doi.org/10.1093/molbev/msab272, doi:10.1093/molbev/msab272. This article has 26 citations and is from a highest quality peer-reviewed journal.
16. (andreotti2018multidomaincontrolover pages 3-4): Amy H. Andreotti, Raji E. Joseph, James M. Conley, Janet Iwasa, and Leslie J. Berg. Multidomain control over tec kinase activation state tunes the t cell response. Annual Review of Immunology, 36:549-578, Apr 2018. URL: https://doi.org/10.1146/annurev-immunol-042617-053344, doi:10.1146/annurev-immunol-042617-053344. This article has 30 citations and is from a highest quality peer-reviewed journal.
17. (andreotti2018multidomaincontrolover pages 6-8): Amy H. Andreotti, Raji E. Joseph, James M. Conley, Janet Iwasa, and Leslie J. Berg. Multidomain control over tec kinase activation state tunes the t cell response. Annual Review of Immunology, 36:549-578, Apr 2018. URL: https://doi.org/10.1146/annurev-immunol-042617-053344, doi:10.1146/annurev-immunol-042617-053344. This article has 30 citations and is from a highest quality peer-reviewed journal.
18. (castelosoccio2023proteinkinasesdrug pages 1-2): Leslie Castelo-Soccio, Hanna Kim, Massimo Gadina, Pamela L. Schwartzberg, Arian Laurence, and John J. O’Shea. Protein kinases: drug targets for immunological disorders. Nature Reviews Immunology, 23:787-806, May 2023. URL: https://doi.org/10.1038/s41577-023-00877-7, doi:10.1038/s41577-023-00877-7. This article has 74 citations and is from a highest quality peer-reviewed journal.
19. (dievart2020originanddiversity pages 12-14): Anne Dievart, Céline Gottin, Christophe Périn, Vincent Ranwez, and Nathalie Chantret. Origin and diversity of plant receptor-like kinases. Annual Review of Plant Biology, 71:131-156, Apr 2020. URL: https://doi.org/10.1146/annurev-arplant-073019-025927, doi:10.1146/annurev-arplant-073019-025927. This article has 197 citations and is from a domain leading peer-reviewed journal.
20. (gocek2014nonreceptorproteintyrosine pages 1-2): Elzbieta Gocek, Anargyros N. Moulas, and George P. Studzinski. Non-receptor protein tyrosine kinases signaling pathways in normal and cancer cells. Critical Reviews in Clinical Laboratory Sciences, 51:125-137, May 2014. URL: https://doi.org/10.3109/10408363.2013.874403, doi:10.3109/10408363.2013.874403. This article has 154 citations and is from a peer-reviewed journal.
21. (joseph2011controllingtheactivity pages 8-9): Raji E. Joseph and Amy H. Andreotti. Controlling the activity of the tec kinase itk by mutation of the phenylalanine gatekeeper residue. Biochemistry, 50 2:221-9, Jan 2011. URL: https://doi.org/10.1021/bi101379m, doi:10.1021/bi101379m. This article has 21 citations and is from a peer-reviewed journal.