## 1. Phylogeny

Mitogen‐activated protein kinase 4 (MAPK4), commonly designated as ERK4 or MAP kinase isoform p63, is a member of the atypical MAP kinase (MAPK) subfamily that diverges significantly from canonical MAPKs such as ERK1/2, p38, and JNK. Unlike classical MAPKs that are activated via a three‐tier phosphorylation cascade involving MAP kinase kinase kinases (MAPKKKs) and MAP kinase kinases (MAPKKs) targeting a dual Thr–Xaa–Tyr (TXY) motif, MAPK4 evolved with an atypical activation loop characterized by a single phosphorylatable serine embedded within a Ser–Glu–Gly (SEG) motif (aberg2006regulationofmapkactivated pages 1-2). Phylogenetic analyses indicate that MAPK4 is evolutionarily linked to ERK3 (MAPK6); these kinases share approximately 73% amino acid identity within their kinase domains, which suggests that an ancestral gene duplication event gave rise to the ERK3/ERK4 subfamily (al2015identificationofnovelb pages 19-23). This evolutionarily derived subfamily appears to be largely confined to vertebrates, with orthologs of MAPK4 identified in mammals, fish, and other chordates. Structural sequence analyses further indicate that MAPK4 bears additional unique motifs—most notably a Ser–Pro–Arg (SPR) sequence in subdomain VIII instead of the canonical Ala–Pro–Glu (APE) sequence, which is rarely observed in human kinases (kant2006characterizationofthe pages 1-2). Such substitutions are thought to underlie distinctive regulatory and substrate binding properties not found in classical MAPKs. Furthermore, while conventional MAPKs are subject to activation by dual phosphorylation of a TXY motif, MAPK4’s fixation of the SEG motif implies that its activation has been uncoupled from traditional MAPKK input, favoring alternative regulatory mechanisms such as autophosphorylation or phosphorylation mediated by upstream p21-activated kinases (PAKs) (huang2024reconstructingthedeep pages 14-16). Collectively, MAPK4 is situated within the atypical MAPK group, a set that includes ERK3, ERK7, and NLK, and is defined by critical structural deviations that reflect a unique evolutionary trajectory and specialized cellular functions (coulombe2007atypicalmitogenactivatedprotein pages 2-4).

## 2. Reaction Catalyzed

MAPK4 functions as a serine/threonine protein kinase and catalyzes reaction events typical of protein kinases that involve the transfer of a phosphate group from ATP to the hydroxyl group of serine or threonine residues present in substrate proteins. The overall chemical reaction that MAPK4 mediates is represented by:  
  ATP + [protein]–(L-serine/threonine) → ADP + [protein]–(L-serine/threonine)-phosphate + H⁺ (jiang2022mitogenactivatedproteinkinase pages 1-2).

A distinctive feature of MAPK4’s catalytic activity lies in its reciprocal phosphorylation cascade with its physiological binding partner, MAPKAPK5 (also known as PRAK). When MAPK4 interacts with MAPKAPK5, it undergoes phosphorylation at a critical residue, Ser-186, within its atypical activation loop; this phosphorylation event is necessary not only to achieve full catalytic activation of MAPK4 but also to facilitate its subsequent function in the phosphorylation of MAPKAPK5 (deleris2008activationloopphosphorylation pages 318-322). Once MAPKAPK5 becomes phosphorylated and activated by the action of MAPK4, it, in turn, phosphorylates MAPK4, thereby establishing a tightly regulated loop of reciprocal phosphorylation. This bidirectional phosphorylation serves to sustain and fine-tune the signaling output of the MAPK4–MAPKAPK5 complex—in essence, reinforcing the active states of both kinases (aberg2006regulationofmapkactivated pages 1-2, deleris2011activationloopphosphorylation pages 1-2). Although detailed kinetic parameters and transient intermediate conformations remain under further investigation, the fundamental enzymatic mechanism employed by MAPK4 is consistent with other serine/threonine protein kinases that depend on ATP hydrolysis for phosphotransfer, while its reciprocal phosphorylation with MAPKAPK5 distinguishes its role in noncanonical MAPK pathways from those of conventional kinases.

## 3. Cofactor Requirements

The phosphotransfer reaction catalyzed by MAPK4 is dependent on the presence of divalent metal ions, which play a critical role in coordinating ATP binding and subsequent catalysis within the kinase active site. Like most serine/threonine kinases, MAPK4 is believed to require Mg²⁺ ions as the primary cofactor to stabilize the negative charges on the phosphoryl group of ATP, thus facilitating the phosphorylation process (jiang2022mitogenactivatedproteinkinase pages 1-2). Although explicit experimental data regarding the substitution of Mg²⁺ with other divalent cations such as Mn²⁺ is not detailed in the current reports, precedent in other kinase systems suggests that, under certain in vitro conditions, Mn²⁺ could serve as an alternative cofactor if required (coulombe2007atypicalmitogenactivatedprotein pages 1-2). In addition to metal ions, no evidence points to the requirement for any other small-molecule or protein cofactors beyond the modulation provided by protein–protein interactions, particularly those with MAPKAPK5, which significantly influences MAPK4 phosphorylation and activation status (dahm2025atypicalmapksin pages 1-3). The well-established dependence on Mg²⁺ is considered a hallmark of serine/threonine kinase catalysis and is thus assumed to be true for MAPK4.

## 4. Substrate Specificity

MAPK4 exhibits highly selective substrate specificity that sets it apart from canonical MAPKs, and this specificity plays a defining role in its function as an atypical kinase. Experimental data have consistently identified two primary physiological substrates for MAPK4: microtubule-associated protein 2 (MAP2) and MAPK-activated protein kinase 5 (MAPKAPK5) (aberg2006regulationofmapkactivated pages 1-2). MAP2 is a critical component of the cytoskeletal framework, contributing to the stabilization and organization of the microtubule network—a function that is essential for maintaining cellular integrity, particularly in neuronal cells. Meanwhile, MAPKAPK5 is not only a substrate but also acts as a binding partner in a reciprocal phosphorylation circuit with MAPK4, thereby propagating intracellular signals that are linked with cell cycle entry and other downstream effects (al2015identificationofnovelb pages 19-23).

The substrate recognition mechanism of MAPK4 is intricately related to its atypical activation loop structure. Instead of a dual phospho-acceptor motif found in conventional MAPKs, MAPK4 harbors an SEG motif that contains only one phosphorylatable serine residue (Ser-186). This atypical configuration is thought to create unique docking sites for substrates as well as to determine the conformational dynamics of the active site, thereby modulating the accessibility and recognition of substrates such as MAPKAPK5 and MAP2 (coulombe2007atypicalmitogenactivatedprotein pages 4-6). Although a universally agreed-upon consensus phosphorylation motif for MAPK4 substrates has not been fully established, it appears that selective substrate recognition by MAPK4 depends on both the specific amino acid context around the phosphorylation site and additional docking interactions mediated by specialized protein interfaces. For instance, the direct interactions between MAPK4 and MAPKAPK5 not only ensure the accuracy of the phosphotransfer but also enhance the affinity between the kinase and its substrate, thereby promoting a tightly controlled signaling output (dyrseth2013asearchfor pages 76-78). This high degree of substrate specificity is critical for ensuring that MAPK4-mediated phosphorylation events are precisely directed toward cellular processes that involve cytoskeletal regulation and cell cycle progression.

## 5. Structure

The structural organization of MAPK4 is reflective of its dual roles in catalytic activity and regulatory protein–protein interactions. MAPK4 is composed of an estimated 587 amino acids that collectively result in a molecular mass of approximately 70 kDa (kant2006characterizationofthe pages 1-2). Central to its structure is a highly conserved catalytic kinase domain that features the classical bilobal architecture commonly found in protein kinases. The N-terminal lobe primarily facilitates ATP binding, whereas the C-terminal lobe contains the catalytic machinery responsible for substrate phosphorylation (coulombe2007atypicalmitogenactivatedprotein pages 2-4).

A key hallmark of MAPK4’s structure is its atypical activation loop. Rather than containing the canonical dual phosphorylation motif (TXY) characteristic of conventional MAPKs, MAPK4’s activation loop is marked by a solitary phosphorylatable serine residue embedded within an SEG motif, specifically at position Ser-186. The phosphorylation of Ser-186 is essential for attaining full catalytic activity and is a prerequisite for the kinase’s interaction with downstream substrates, particularly MAPKAPK5 (deleris2011activationloopphosphorylation pages 1-2). High-resolution structural details are currently limited by the absence of an experimentally determined crystal structure; however, homology models based on related MAPKs, including ERK2, and computational predictions (e.g., AlphaFold models) suggest that MAPK4 maintains a typical bilobal kinase fold with several distinctive loop regions and extensions that likely contribute to its unique regulatory functions (coulombe2007atypicalmitogenactivatedprotein pages 2-4).

In addition to the kinase domain, MAPK4 features a long C-terminal extension that is not observed in classical MAPKs. Although the precise function of this extension remains to be fully elucidated, it is hypothesized to serve as a platform for further protein–protein interactions and may contribute to the stability or subcellular localization of the kinase (al2015identificationofnovela pages 19-23). Another unique structural element is found in subdomain VIII of the kinase domain, where the conventional Ala–Pro–Glu (APE) motif has been replaced by an S–P–R motif. This substitution is unusual in that it replaces a negatively charged glutamic acid with an arginine, which likely alters local electrostatic interactions and may influence substrate docking or the stability of the kinase’s active conformation (kant2006characterizationofthe pages 1-2). Overall, while detailed three-dimensional data are still emerging, the available structural insights position MAPK4 as a kinase with both shared features of the MAPK fold and distinctive modifications that provide the molecular basis for its atypical enzymatic behavior and regulatory interactions.

## 6. Regulation

MAPK4 is subject to regulation through phosphorylation-dependent mechanisms that set it apart from classical MAPK signaling paradigms. In canonical MAPK cascades, activation typically requires dual phosphorylation of threonine and tyrosine residues by upstream MAPKKs; however, MAPK4 is activated via phosphorylation of a single serine residue (Ser-186) located in its atypical activation loop, marking it as distinct (aberg2006regulationofmapkactivated pages 1-2). This phosphorylation event is not solely an on/off switch; rather, it is integral to the functional interplay between MAPK4 and its known binding partner, MAPKAPK5. When MAPK4 forms a complex with MAPKAPK5, it is phosphorylated on Ser-186—a prerequisite for subsequent activity. Following this, MAPK4 mediates the phosphorylation and activation of MAPKAPK5. In return, MAPKAPK5 phosphorylates MAPK4, thereby establishing a reciprocal regulatory loop that sustains the active state of both kinases (deleris2008activationloopphosphorylation pages 318-322).

Upstream of these reciprocal phosphorylation events, group I p21-activated kinases (PAKs) have been implicated in catalyzing the phosphorylation of the activation loop in MAPK4, thereby contributing to its basal activation state. This link to PAKs suggests that MAPK4 activity may be modulated by signals that influence cytoskeletal dynamics and cellular motility—processes in which PAKs are key regulatory nodes (huang2024reconstructingthedeep pages 14-16). In addition to phosphorylation, evidence points to the role of dephosphorylation events mediated by dual-specificity phosphatases (such as DUSP2) in fine-tuning MAPK4 activity; these phosphatases remove phosphate groups from the activation loop, potentially serving to downregulate MAPK4 signaling and thereby control the duration and intensity of its catalytic output (elkhadragy2017regulationofthe pages 35-39).

This unique autoregulatory and reciprocal phosphorylation mechanism, which establishes a feedback loop between MAPK4 and MAPKAPK5, is central to the modulation of cellular signaling cascades that influence cell cycle entry and cytoskeletal reorganization. The phosphorylation state of MAPK4—principally defined by the phosphorylation status of Ser-186—thus serves as a critical molecular switch that integrates upstream signals from PAKs with downstream effects mediated by MAPKAPK5, ensuring that the kinase complex operates within a tightly controlled regulatory framework.

## 7. Function

The biological roles of MAPK4 are intimately connected to its ability to phosphorylate substrates that are central to intracellular signaling processes. One of the most well-characterized substrates of MAPK4 is microtubule-associated protein 2 (MAP2), a key player in the stabilization and organization of the microtubule network. This function is particularly critical in neuronal cells, where MAP2 is essential for maintaining dendritic architecture and facilitating proper cytoskeletal dynamics; however, MAP2 also serves important roles in other cell types where microtubule integrity is required (aberg2006regulationofmapkactivated pages 1-2).

In addition to MAP2, MAPK4 phosphorylates and activates MAPK-activated protein kinase 5 (MAPKAPK5 or PRAK). The reciprocal phosphorylation cycle between MAPK4 and MAPKAPK5 is believed to form a regulatory module that plays an important role in promoting cell cycle entry. In this module, MAPK4 phosphorylates its binding partner on specific target residues, leading to the activation of MAPKAPK5, which then feeds back by phosphorylating MAPK4. This mutual reinforcement ensures a robust and sustained signal that can drive signaling processes essential for cellular proliferation (deleris2008activationloopphosphorylation pages 318-322, deleris2011activationloopphosphorylation pages 1-2).

Beyond these direct phosphorylation targets, MAPK4 is implicated in broader signaling events that coordinate cytoskeletal reorganization with cell cycle progression. The ability of MAPK4 to integrate signals from cytoskeletal regulators—such as PAKs—and to engage in reciprocal phosphorylation with MAPKAPK5 suggests that it plays a pivotal role in orchestrating events that lead to controlled cell division. Such regulatory control is of particular interest in the context of oncogenesis, where dysregulated cell proliferation and altered cytoskeletal dynamics are frequently observed. Although definitive causal links between aberrant MAPK4 signaling and specific disease states remain to be fully established, preliminary data suggest that the unique MAPK4–MAPKAPK5 module may represent an attractive target for therapeutic intervention in disorders of uncontrolled proliferation (al2015identificationofnovelb pages 19-23).

Expression patterns of MAPK4 appear to be relatively restricted compared to conventional MAPKs, with evidence indicating tissue-specific expression profiles in mammals and other vertebrates. This context-dependent expression implies that MAPK4’s activity is likely tailored to particular cellular environments where fine-tuned control over cytoskeletal dynamics and cell cycle entry is paramount. The coupling of MAPK4’s phosphorylative activity with key cellular processes underscores its role as an integrator of signals that coordinate cellular architecture and proliferative responses, establishing it as a unique signaling node within the atypical MAPK cascade.

## 8. Other Comments

Despite its discovery over a decade ago, MAPK4 remains less extensively characterized than many classical MAP kinases and is frequently cited among “dark kinases” due to gaps in our comprehensive understanding of its structure–function relationship. Its atypical regulatory behavior and the reciprocal phosphorylation feedback loop with MAPKAPK5 have garnered significant research attention as models of noncanonical kinase regulation. Ongoing investigations are aimed at elucidating the full spectrum of MAPK4’s substrates, as well as the detailed kinetics and structural dynamics of its activation loop phosphorylation. This includes efforts to leverage advanced phosphoproteomic techniques and computational modeling to better capture the transient conformational changes that underlie its distinct signaling properties (ghose2019natureofthe pages 1-6).

The particular configuration of MAPK4’s activation loop, especially the presence of the SEG motif and the unique S–P–R substitution in subdomain VIII, presents promising opportunities for the development of targeted chemical probes or inhibitors. Although current inhibitor development for MAPK4 lags behind that for conventional MAPKs, the distinctive attributes of MAPK4’s catalytic and regulatory domains suggest that novel small-molecule inhibitors could be designed to selectively perturb its activity without affecting off-target kinases. Such specific inhibitors may prove beneficial in exploring MAPK4’s potential roles in cell cycle control and in diseases characterized by dysregulated proliferation, such as certain cancers (dahm2025atypicalmapksin pages 1-3).

Furthermore, the evolutionary divergence seen in MAPK4 raises important questions regarding its tissue-specific regulation and function. Comparative studies across vertebrate species could illuminate how selective pressures have shaped the unique regulatory features of MAPK4, particularly its autophosphorylation dynamics and reciprocal interactions with MAPKAPK5. As high-resolution structural techniques (including cryo-electron microscopy and deep-learning-based structure prediction) continue to advance, they hold the promise to reveal previously unappreciated aspects of MAPK4’s three-dimensional conformation, substrate binding pockets, and allosteric regulatory sites (huang2024reconstructingthedeep pages 7-10).

These emerging insights into MAPK4’s regulatory machinery underscore the importance of integrating evolutionary phylogeny with biochemical analyses to fully understand its role within the broader MAPK signaling network. In addition to its established functions in cytoskeletal regulation and cell cycle progression, future studies may uncover additional roles in developmental signaling pathways and stress responses. Given the complexity of its regulatory feedback with MAPKAPK5 and the possibility that MAPK4 activity is modulated by upstream signals via PAKs, there is significant potential for MAPK4 to serve as a nexus point integrating multiple signaling inputs to coordinate cellular behavior (elkhadragy2017regulationofthe pages 17-22, huang2024reconstructingthedeep pages 14-16).

In summary, MAPK4 represents a distinct branch of the MAPK family that has evolved unique catalytic, structural, and regulatory mechanisms. Its specialized mode of operation, characterized by a single serine phosphorylation event within its atypical SEG activation loop and its reciprocal interaction with MAPKAPK5, distinguishes it from conventional MAPKs and underscores its potential as a critical regulator of cytoskeletal organization and cell cycle progression. Continued research is expected to further uncover the molecular intricacies of MAPK4 function, paving the way for targeted therapeutic strategies in diseases linked to its dysregulation.

## 9. References

aberg2006regulationofmapkactivated pages 1-2; aberg2006regulationofmapkactivated pages 10-11; kant2006characterizationofthe pages 1-2; al2015identificationofnovelb pages 19-23; coulombe2007atypicalmitogenactivatedprotein pages 2-4; coulombe2007atypicalmitogenactivatedprotein pages 4-6; deleris2008activationloopphosphorylation pages 318-322; deleris2011activationloopphosphorylation pages 1-2; dahm2025atypicalmapksin pages 1-3; dyrseth2013asearchfor pages 76-78; elkhadragy2017regulationofthe pages 17-22; elkhadragy2017regulationofthe pages 35-39; ghose2019natureofthe pages 1-6; huang2024reconstructingthedeep pages 7-10; huang2024reconstructingthedeep pages 14-16; huang2024reconstructingthedeep pages 1-3; jiang2022mitogenactivatedproteinkinase pages 1-2.

References

1. (aberg2006regulationofmapkactivated pages 1-2): Espen Åberg, Maria Perander, Bjarne Johansen, Catherine Julien, Sylvain Meloche, Stephen M. Keyse, and Ole-Morten Seternes. Regulation of mapk-activated protein kinase 5 activity and subcellular localization by the atypical mapk erk4/mapk4. Journal of Biological Chemistry, 281:35499-35510, Nov 2006. URL: https://doi.org/10.1074/jbc.m606225200, doi:10.1074/jbc.m606225200. This article has 106 citations and is from a domain leading peer-reviewed journal.
2. (aberg2006regulationofmapkactivated pages 10-11): Espen Åberg, Maria Perander, Bjarne Johansen, Catherine Julien, Sylvain Meloche, Stephen M. Keyse, and Ole-Morten Seternes. Regulation of mapk-activated protein kinase 5 activity and subcellular localization by the atypical mapk erk4/mapk4. Journal of Biological Chemistry, 281:35499-35510, Nov 2006. URL: https://doi.org/10.1074/jbc.m606225200, doi:10.1074/jbc.m606225200. This article has 106 citations and is from a domain leading peer-reviewed journal.
3. (al2015identificationofnovela pages 19-23): R Al. Identification of novel roles and new modes of regulation for the atypical map kinases erk3 and erk4. Unknown journal, 2015.
4. (al2015identificationofnovelb pages 19-23): R Al. Identification of novel roles and new modes of regulation for the atypical map kinases erk3 and erk4. Unknown journal, 2015.
5. (coulombe2007atypicalmitogenactivatedprotein pages 1-2): Phillipe Coulombe and Sylvain Meloche. Atypical mitogen-activated protein kinases: structure, regulation and functions. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research, 1773:1376-1387, Aug 2007. URL: https://doi.org/10.1016/j.bbamcr.2006.11.001, doi:10.1016/j.bbamcr.2006.11.001. This article has 462 citations.
6. (coulombe2007atypicalmitogenactivatedprotein pages 2-4): Phillipe Coulombe and Sylvain Meloche. Atypical mitogen-activated protein kinases: structure, regulation and functions. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research, 1773:1376-1387, Aug 2007. URL: https://doi.org/10.1016/j.bbamcr.2006.11.001, doi:10.1016/j.bbamcr.2006.11.001. This article has 462 citations.
7. (coulombe2007atypicalmitogenactivatedprotein pages 4-6): Phillipe Coulombe and Sylvain Meloche. Atypical mitogen-activated protein kinases: structure, regulation and functions. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research, 1773:1376-1387, Aug 2007. URL: https://doi.org/10.1016/j.bbamcr.2006.11.001, doi:10.1016/j.bbamcr.2006.11.001. This article has 462 citations.
8. (dahm2025atypicalmapksin pages 1-3): Katrin Dahm, Parthiban Vijayarangakannan, Hans‐Peter Wollscheid, Hansjörg Schild, and Krishnaraj Rajalingam. Atypical mapks in cancer. The FEBS Journal, Sep 2025. URL: https://doi.org/10.1111/febs.17283, doi:10.1111/febs.17283. This article has 1 citations.
9. (deleris2008activationloopphosphorylation pages 318-322): Paul Déléris, Justine Rousseau, Philippe Coulombe, Geneviève Rodier, Pierre‐Luc Tanguay, and Sylvain Meloche. Activation loop phosphorylation of the atypical map kinases erk3 and erk4 is required for binding, activation and cytoplasmic relocalization of mk5. Journal of Cellular Physiology, Dec 2008. URL: https://doi.org/10.1002/jcp.21560, doi:10.1002/jcp.21560. This article has 94 citations and is from a peer-reviewed journal.
10. (deleris2011activationloopphosphorylation pages 1-2): Paul Déléris, Matthias Trost, Ivan Topisirovic, Pierre-Luc Tanguay, Katherine L.B. Borden, Pierre Thibault, and Sylvain Meloche. Activation loop phosphorylation of erk3/erk4 by group i p21-activated kinases (paks) defines a novel pak-erk3/4-mapk-activated protein kinase 5 signaling pathway. Journal of Biological Chemistry, 286:6470-6478, Feb 2011. URL: https://doi.org/10.1074/jbc.m110.181529, doi:10.1074/jbc.m110.181529. This article has 108 citations and is from a domain leading peer-reviewed journal.
11. (dyrseth2013asearchfor pages 76-78): T Dyrseth. A search for mirnas that regulates the expression of the atypical kinases erk3, erk4 and mk5. Unknown journal, 2013.
12. (elkhadragy2017regulationofthe pages 17-22): L Elkhadragy. Regulation of the expression and activity of extracellular signal-regulated kinase 3 (erk3). Unknown journal, 2017.
13. (elkhadragy2017regulationofthe pages 35-39): L Elkhadragy. Regulation of the expression and activity of extracellular signal-regulated kinase 3 (erk3). Unknown journal, 2017.
14. (ghose2019natureofthe pages 1-6): Ranajeet Ghose. Nature of the pre-chemistry ensemble in mitogen-activated protein kinases. Journal of Molecular Biology, 431:145-157, Jan 2019. URL: https://doi.org/10.1016/j.jmb.2018.12.007, doi:10.1016/j.jmb.2018.12.007. This article has 13 citations and is from a domain leading peer-reviewed journal.
15. (huang2024reconstructingthedeep pages 1-3): EJ Huang, Jeeun Parksong, Amy F. Peterson, Fernando Torres, Sergi Regot, and Gabriel S. Bever. Reconstructing the deep phylogeny of the mapk signaling network: functional specialization via multi-tier coevolutionary expansion. BioRxiv, Oct 2024. URL: https://doi.org/10.1101/2024.10.01.616093, doi:10.1101/2024.10.01.616093. This article has 0 citations.
16. (huang2024reconstructingthedeep pages 14-16): EJ Huang, Jeeun Parksong, Amy F. Peterson, Fernando Torres, Sergi Regot, and Gabriel S. Bever. Reconstructing the deep phylogeny of the mapk signaling network: functional specialization via multi-tier coevolutionary expansion. BioRxiv, Oct 2024. URL: https://doi.org/10.1101/2024.10.01.616093, doi:10.1101/2024.10.01.616093. This article has 0 citations.
17. (huang2024reconstructingthedeep pages 7-10): EJ Huang, Jeeun Parksong, Amy F. Peterson, Fernando Torres, Sergi Regot, and Gabriel S. Bever. Reconstructing the deep phylogeny of the mapk signaling network: functional specialization via multi-tier coevolutionary expansion. BioRxiv, Oct 2024. URL: https://doi.org/10.1101/2024.10.01.616093, doi:10.1101/2024.10.01.616093. This article has 0 citations.
18. (jiang2022mitogenactivatedproteinkinase pages 1-2): Min Jiang, You-tao Zhang, Peng Li, Jinjing Jian, Changling Zhao, and Guosong Wen. Mitogen-activated protein kinase and substrate identification in plant growth and development. International Journal of Molecular Sciences, 23:2744, Mar 2022. URL: https://doi.org/10.3390/ijms23052744, doi:10.3390/ijms23052744. This article has 48 citations and is from a peer-reviewed journal.
19. (kant2006characterizationofthe pages 1-2): Shashi Kant, Stefanie Schumacher, Manvendra Kumar Singh, Andreas Kispert, Alexey Kotlyarov, and Matthias Gaestel. Characterization of the atypical mapk erk4 and its activation of the mapk-activated protein kinase mk5\*. Journal of Biological Chemistry, 281:35511-35519, Nov 2006. URL: https://doi.org/10.1074/jbc.m606693200, doi:10.1074/jbc.m606693200. This article has 142 citations and is from a domain leading peer-reviewed journal.