1. Phylogeny  
   Kinase suppressor of Ras 2 (KSR2) is a member of the KSR family of signaling regulators that, together with its close paralog KSR1, forms a conserved component of the Ras/RAF/MEK/ERK cascade. KSR2 is evolutionarily conserved in metazoans and has been documented in vertebrate species, where its sequence shares approximately 61% amino acid similarity with KSR1, thereby indicating its divergence into functionally specialized roles within the MAPK signaling network (zhang2014identificationofksr1 pages 229-230). The KSR proteins, originally identified in invertebrates such as Caenorhabditis elegans and Drosophila melanogaster, are part of an evolutionarily ancient signaling apparatus that can be traced back to the early eukaryotic lineage; indeed, phylogenetic analyses have suggested that the core MAPK regulators, including KSR, are components of an ancestral signaling module present in the Last Eukaryotic Common Ancestor (costanzogarvey2009ksr2isan pages 1-2, udell2011mechanisticprinciplesof pages 1-2). In mammals, while both KSR1 and KSR2 maintain the ability to act as scaffolds for MAP kinase assembly, KSR2 possesses unique structural elements—notably a 63–amino acid insertion located between the CA2 and CA3 domains—that further distinguish its regulatory properties and protein–protein interaction profile (costanzogarvey2009ksr2isan pages 2-4, udell2011mechanisticprinciplesof pages 2-4). Moreover, the evolutionary kinship of KSR2 with the RAF kinase family underscores the shared ancestry of these signaling proteins, even though KSR2 functions primarily as a scaffold rather than as a fully active kinase (martinvega2023navigatingtheerk12 pages 14-16, kolch2005coordinatingerkmapksignalling pages 2-3).
2. Reaction Catalyzed  
   KSR2, although classified as a pseudokinase due to its very low intrinsic catalytic activity, is capable of catalyzing phosphorylation under defined in vitro conditions. The reaction it mediates can be summarized by the following stoichiometry: ATP + MAP2K1 (MEK1) → ADP + phosphorylated MAP2K1 + H⁺ (roskoski2012mek12dualspecificityprotein pages 5-6). In this context, KSR2 specifically phosphorylates several serine and threonine residues on its substrate, MAP2K1/MEK1, albeit with a catalytic efficiency much lower than that of conventional active kinases. This weak kinase activity plays a supplementary role to its primary function as a scaffold by contributing to the allosteric activation of BRAF when KSR2 is engaged in a heteromeric complex with MEK1 (dar2016smallmoleculestabilization pages 1-2, mckay2011complexityinksr pages 3-4). Thus, while the net phosphotransfer reaction conforms to the canonical kinase mechanism—utilizing ATP as the phosphoryl donor—the overall contribution of KSR2 to the phosphorylation of MAP2K1 is minimal in quantitative terms, serving instead to fine-tune the signaling output of the MAPK cascade (zhang2014identificationofksr1 pages 197-199).
3. Cofactor Requirements  
   The phosphorylation reaction catalyzed by KSR2 is dependent on the presence of divalent metal ions, with Mg²⁺ being essential for optimal ATP binding and for facilitating the transfer of the phosphate group during catalysis. In vitro studies have demonstrated that, similar to many serine/threonine kinases, the enzymatic (or pseudoenzymatic) function of KSR2 is contingent upon Mg²⁺ ions, which coordinate with ATP to properly orient the phosphoryl group within the active site (roskoski2012mek12dualspecificityprotein pages 5-6, dar2016smallmoleculestabilization pages 6-7). The requirement for ATP itself is also evident, as ATP binding supports the stabilization of KSR2’s architecture in the kinase domain and aids in maintaining the conformation necessary for its scaffolding function, even though the intrinsic phosphotransfer activity remains very low (udell2011mechanisticprinciplesof pages 2-4).
4. Substrate Specificity  
   KSR2 exhibits a high degree of functional specificity toward the MAP kinase kinase pathway, with its substrate specificity being primarily directed at MAP2K1, also known as MEK1. In vitro experiments have shown that KSR2 phosphorylates several serine and threonine residues on MEK1, although the overall phosphorylation efficiency is very weak compared to dedicated catalytically active kinases (mckay2011complexityinksr pages 3-4, zhang2014identificationofksr1 pages 197-199). The substrate engagement is facilitated by the direct binding of MEK1 to KSR2 within a heterodimeric complex, an interaction that aligns the activation loops of the two proteins in a face‐to‐face orientation. This precise spatial arrangement is critical for the specificity of the phosphorylation reaction, even if a distinct consensus motif for substrate recognition by KSR2 is not well established due to the predominant reliance on scaffold-mediated interactions (roskoski2012mek12dualspecificityprotein pages 5-6). Consequently, the substrate specificity of KSR2 is defined functionally more by its ability to form stable complexes with MEK1 than by recognition of a short linear peptide motif.
5. Structure  
   KSR2 is organized into a modular structure characterized by a series of conserved regions designated CA1 through CA5. Unlike its close paralog KSR1, KSR2 lacks the N-terminal CA1 domain; instead, it features a unique insertion of approximately 63 amino acids between the CA2 and CA3 domains that is not present in KSR1 (zhang2014identificationofksr1 pages 229-230, costanzogarvey2009ksr2isan pages 2-4). The CA2 region is proline-rich, although its precise functional contributions remain to be fully clarified. The CA3 domain contains a cysteine-rich region (CRD) that plays a crucial role in membrane recruitment and mediates interactions with regulatory partners such as AMP-activated protein kinase (AMPK) (martinvega2023navigatingtheerk12 pages 14-16, costanzogarvey2009ksr2isan pages 2-4). Following CA3, the CA4 region is notable for its serine/threonine-rich sequence and for harboring motifs that facilitate interactions with ERK, thereby contributing to KSR2’s scaffolding capacity within the MAPK module. The CA5 domain constitutes the pseudokinase domain of KSR2; despite containing motifs that resemble those found in catalytically active protein kinases—such as a glycine-rich P-loop, a β3 strand with a conserved arginine (substituted in lieu of the canonical lysine), an activation loop with potential phosphorylation sites, and a DFG motif—structural analyses reveal that the configuration of these elements supports only very low-level kinase activity (roskoski2012mek12dualspecificityprotein pages 5-6, endicott2012thestructuralbasis pages 16-18). X-ray crystallography and AlphaFold modeling have demonstrated that the kinase domain of KSR2 adopts the typical bilobal architecture, with an N-terminal lobe composed predominantly of β-sheets and a C-terminal lobe rich in α-helices, bridged by a nucleotide-binding cleft that accommodates ATP (mckay2011complexityinksr pages 3-4). Key regulatory features include an ordered, albeit noncanonical, activation loop and a relatively short αC-helix; these elements are positioned in a manner that favors the scaffolding role of KSR2 rather than robust catalytic turnover (dar2016smallmoleculestabilization pages 4-6).
6. Regulation  
   The regulatory mechanisms governing KSR2 are multifaceted, integrating post-translational modifications, protein–protein interactions, and allosteric conformational changes. One of the primary modes of regulation is via phosphorylation; several serine and threonine residues within KSR2 are subject to phosphorylation, a modification that influences both its subcellular localization and its ability to interact with regulatory proteins such as the 14-3-3 family (dougherty2009ksr2isa pages 7-8, morrison2003regulationofmap pages 5-7). In resting cells, phosphorylated KSR2 may bind 14-3-3 proteins, resulting in sequestration within the cytosol; upon stimulation by growth factors or Ca²⁺ signals, dephosphorylation events—often mediated by phosphatases such as calcineurin—trigger the translocation of KSR2 to the plasma membrane, where it can effectively assemble with MEK1 and BRAF (dougherty2009ksr2isa pages 8-9, dougherty2009ksr2isa pages 9-11). In addition to this phosphorylation/dephosphorylation cycle, KSR2 interacts with AMPK through unique sequence motifs, linking its regulatory functions to cellular energy homeostasis; this interaction further modulates its capacity to assemble and activate MAPK signaling complexes, as evidenced by metabolic disturbances observed in KSR2 knockout models (costanzogarvey2009ksr2isan pages 23-26, martinvega2023navigatingtheerk12 pages 14-16). Moreover, an allosteric regulatory mechanism is provided by KSR2’s interaction with BRAF: upon binding to MEK1, KSR2 dimerizes with BRAF, thereby promoting an allosteric activation of BRAF that enhances its ability to phosphorylate MEK1 (dar2016smallmoleculestabilization pages 2-4, mckay2011complexityinksr pages 3-4). Pharmacological modulation of KSR2 has also been demonstrated; for instance, the small molecule APS-2-79 has been shown to bind within the ATP-binding pocket of KSR2, stabilizing an inactive conformation and thus attenuating its ability to facilitate Raf-dependent signaling (dar2016smallmoleculestabilization pages 33-37, kung2019prospectsforpharmacological pages 14-16).
7. Function  
   KSR2 functions predominantly as a location‐regulated scaffold that bridges MEK to RAF, thereby organizing the assembly of the MAP kinase cascade and modulating signaling efficiency. By binding constitutively to MEK1 and forming stimulus‐dependent complexes with RAF kinases such as BRAF, KSR2 facilitates the effective propagation of Ras‐dependent signaling through the ERK cascade (costanzogarvey2009ksr2isan pages 2-4, mckay2011complexityinksr pages 1-3). Despite its classification as a pseudokinase, KSR2 possesses measurable yet very low catalytic activity, allowing it to phosphorylate MAP2K1/MEK1 on multiple serine and threonine residues in vitro. This low-level enzymatic function is thought to complement its allosteric role in activating BRAF, thus contributing to an overall amplification of MAPK signaling (roskoski2012mek12dualspecificityprotein pages 5-6, zhang2014identificationofksr1 pages 197-199). Beyond its role in canonical MAPK signaling, KSR2 is integrally involved in the regulation of cellular energy metabolism. Experimental evidence from knockout mouse models indicates that loss of KSR2 leads to significant metabolic dysregulation, manifesting as obesity, insulin resistance, and reduced energy expenditure (costanzogarvey2009ksr2isan pages 23-26, martinvega2023navigatingtheerk12 pages 14-16). In addition, KSR2 exerts a regulatory influence on alternative signaling pathways by negatively modulating the activity of MAP3K8 and MAP3K3, thereby inhibiting downstream activation of ERK, JNK, NF-κB, and the production of interleukin-8 (costanzogarvey2009ksr2isan pages 2-4, dar2016smallmoleculestabilization pages 7-9). In oncogenic contexts, particularly in Ras-mutant cancers, KSR2 functions as a MEK-dependent allosteric activator of BRAF; through its dimerization with BRAF, KSR2 enhances RAF-mediated phosphorylation of MEK, thereby contributing to tumor cell transformation and proliferation (dar2016smallmoleculestabilization pages 2-4, mckay2011complexityinksr pages 3-4). Furthermore, tissue-specific expression patterns indicate that KSR2 is enriched in neuroendocrine tissues, implicating it in processes such as self-renewal and clonogenicity in certain tumor-propagating cells, particularly in subtypes of small-cell lung carcinoma (martinvega2023navigatingtheerk12 pages 14-16, mckay2011complexityinksr pages 1-3).
8. Other Comments  
   Additional aspects of KSR2’s biology underscore its emerging role as both a regulator and potential therapeutic target. Several missense mutations in KSR2, including P662L, E667V, R684C, I801L, G816D, R818Q, R823H, D843N, and S904L, have been documented and are associated with metabolic disorders such as obesity and insulin resistance, thereby emphasizing its clinical relevance (kung2019prospectsforpharmacological pages 14-16). Moreover, KSR2’s regulation of MAP3K8 and MAP3K3 signaling pathways—resulting in the attenuation of ERK, JNK, and NF-κB activation and the suppression of interleukin-8 production—further broadens its functional repertoire beyond the classical MAPK cascade (costanzogarvey2009ksr2isan pages 2-4, dar2016smallmoleculestabilization pages 7-9). Pharmacologically, the identification of small molecule inhibitors such as APS-2-79, which binds within the ATP-binding pocket of KSR2 and stabilizes an inactive conformation, represents an important advancement; such compounds have the potential to modulate KSR2-mediated scaffolding activity and, consequently, the downstream Ras/ERK signaling pathway in oncogenic contexts (dar2016smallmoleculestabilization pages 33-37, kung2019prospectsforpharmacological pages 27-28). In light of these multifaceted roles, KSR2 is a pivotal node that not only integrates growth factor signals with metabolic status through its interactions with AMPK and calcineurin but also influences tumorigenesis via its support of Raf-mediated MEK activation. This dual functionality positions KSR2 as a unique target for therapeutic intervention in both metabolic disorders and Ras-driven cancers (costanzogarvey2009ksr2isan pages 23-26, mckay2011complexityinksr pages 3-4).
9. References
10. costanzogarvey2009ksr2isan pages 1-2 – Costanzo-Garvey, D., Pfluger, P., Dougherty, M.K., et al. “Ksr2 is an essential regulator of amp kinase, energy expenditure, and insulin sensitivity.” Cell Metabolism, 2009.
11. costanzogarvey2009ksr2isan pages 2-4 – Costanzo-Garvey, D., Pfluger, P., Dougherty, M.K., et al. “Ksr2 is an essential regulator of amp kinase, energy expenditure, and insulin sensitivity.” Cell Metabolism, 2009.
12. costanzogarvey2009ksr2isan pages 23-26 – Costanzo-Garvey, D., Pfluger, P., Dougherty, M.K., et al. “Ksr2 is an essential regulator of amp kinase, energy expenditure, and insulin sensitivity.” Cell Metabolism, 2009.
13. dar2016smallmoleculestabilization pages 1-2 – Dar, A.C., Dhawan, A.P., Scopton, A.P. “Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling.” Nature, 2016.
14. dar2016smallmoleculestabilization pages 4-6 – Dar, A.C., Dhawan, A.P., Scopton, A.P. “Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling.” Nature, 2016.
15. dar2016smallmoleculestabilization pages 6-7 – Dar, A.C., Dhawan, A.P., Scopton, A.P. “Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling.” Nature, 2016.
16. dar2016smallmoleculestabilization pages 33-37 – Dar, A.C., Dhawan, A.P., Scopton, A.P. “Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling.” Nature, 2016.
17. dar2016smallmoleculestabilization pages 7-9 – Dar, A.C., Dhawan, A.P., Scopton, A.P. “Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling.” Nature, 2016.
18. dougherty2009ksr2isa pages 7-8 – Dougherty, M.K., Ritt, D.A., Zhou, M., et al. “Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals.” Molecular Cell, 2009.
19. dougherty2009ksr2isa pages 8-9 – Dougherty, M.K., Ritt, D.A., Zhou, M., et al. “Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals.” Molecular Cell, 2009.
20. dougherty2009ksr2isa pages 9-11 – Dougherty, M.K., Ritt, D.A., Zhou, M., et al. “Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals.” Molecular Cell, 2009.
21. dougherty2009ksr2isa pages 13-19 – Dougherty, M.K., Ritt, D.A., Zhou, M., et al. “Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals.” Molecular Cell, 2009.
22. dougherty2009ksr2isa pages 19-21 – Dougherty, M.K., Ritt, D.A., Zhou, M., et al. “Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals.” Molecular Cell, 2009.
23. endicott2012thestructuralbasis pages 16-18 – Endicott, J.A., Noble, M.E.M., Johnson, L.N. “The structural basis for control of eukaryotic protein kinases.” Annual Review of Biochemistry, 2012.
24. martinvega2023navigatingtheerk12 pages 14-16 – Martin-Vega, A. and Cobb, M.H. “Navigating the erk1/2 mapk cascade.” Biomolecules, 2023.
25. martinvega2023navigatingtheerk12 pages 39-41 – Martin-Vega, A. and Cobb, M.H. “Navigating the erk1/2 mapk cascade.” Biomolecules, 2023.
26. mckay2011complexityinksr pages 1-3 – McKay, M.M., Freeman, A.K., Morrison, D.K. “Complexity in ksr function revealed by raf inhibitor and ksr structure studies.” Small GTPases, 2011.
27. mckay2011complexityinksr pages 3-4 – McKay, M.M., Freeman, A.K., Morrison, D.K. “Complexity in ksr function revealed by raf inhibitor and ksr structure studies.” Small GTPases, 2011.
28. roskoski2012mek12dualspecificityprotein pages 5-6 – Roskoski, R. “Mek1/2 dual-specificity protein kinases: structure and regulation.” Biochemical and Biophysical Research Communications, 2012.
29. takacsvellai2014themetastasissuppressor pages 2-4 – Takács-Vellai, K. “The metastasis suppressor nm23 as a modulator of ras/erk signaling.” Journal of Molecular Signaling, 2014.
30. takacsvellai2014themetastasissuppressor pages 7-7 – Takács-Vellai, K. “The metastasis suppressor nm23 as a modulator of ras/erk signaling.” Journal of Molecular Signaling, 2014.
31. udell2011mechanisticprinciplesof pages 1-2 – Udell, C.M., Rajakulendran, T., Sicheri, F., Therrien, M. “Mechanistic principles of raf kinase signaling.” Cellular and Molecular Life Sciences, 2011.
32. udell2011mechanisticprinciplesof pages 2-4 – Udell, C.M., Rajakulendran, T., Sicheri, F., Therrien, M. “Mechanistic principles of raf kinase signaling.” Cellular and Molecular Life Sciences, 2011.
33. kolch2005coordinatingerkmapksignalling pages 2-3 – Kolch, W. “Coordinating erk/mapk signalling through scaffolds and inhibitors.” Nature Reviews Molecular Cell Biology, 2005.
34. kolch2005coordinatingerkmapksignalling pages 3-4 – Kolch, W. “Coordinating erk/mapk signalling through scaffolds and inhibitors.” Nature Reviews Molecular Cell Biology, 2005.
35. kung2019prospectsforpharmacological pages 14-16 – Kung, J.E. and Jura, N. “Prospects for pharmacological targeting of pseudokinases.” Nature Reviews Drug Discovery, 2019.
36. kung2019prospectsforpharmacological pages 27-28 – Kung, J.E. and Jura, N. “Prospects for pharmacological targeting of pseudokinases.” Nature Reviews Drug Discovery, 2019.
37. kung2019prospectsforpharmacological pages 47-48 – Kung, J.E. and Jura, N. “Prospects for pharmacological targeting of pseudokinases.” Nature Reviews Drug Discovery, 2019.
38. maloney2022themechanismof pages 1-2 – Maloney, R.C., Zhang, M., Liu, Y., Jang, H., Nussinov, R. “The mechanism of activation of mek1 by b-raf and ksr1.” Cellular and Molecular Life Sciences, 2022.
39. mckay2011rafinhibitorinducedksr1braf pages 2-4 – McKay, M.M., Ritt, D.A., Morrison, D.K. “Raf inhibitor-induced ksr1/b-raf binding and its effects on erk cascade signaling.” Current Biology, 2011.

References

1. (costanzogarvey2009ksr2isan pages 2-4): Diane Costanzo-Garvey, P. Pfluger, M. K. Dougherty, J. Stock, M. Boehm, O. Chaika, Mario R. Fernandez, K. Fisher, R. Kortum, Eun-Gyoung Hong, J. Jun, H. Ko, Aimee Schreiner, D. J. Volle, T. Treece, Amy L. Swift, Mike Winer, Denise Chen, Min Wu, L. Leon, A. Shaw, J. Mcneish, Jason K. Kim, D. Morrison, M. Tschöp, and Robert E. Lewis. Ksr2 is an essential regulator of amp kinase, energy expenditure, and insulin sensitivity. Cell metabolism, 10 5:366-78, Nov 2009. URL: https://doi.org/10.1016/j.cmet.2009.09.010, doi:10.1016/j.cmet.2009.09.010. This article has 171 citations and is from a highest quality peer-reviewed journal.
2. (costanzogarvey2009ksr2isan pages 23-26): Diane Costanzo-Garvey, P. Pfluger, M. K. Dougherty, J. Stock, M. Boehm, O. Chaika, Mario R. Fernandez, K. Fisher, R. Kortum, Eun-Gyoung Hong, J. Jun, H. Ko, Aimee Schreiner, D. J. Volle, T. Treece, Amy L. Swift, Mike Winer, Denise Chen, Min Wu, L. Leon, A. Shaw, J. Mcneish, Jason K. Kim, D. Morrison, M. Tschöp, and Robert E. Lewis. Ksr2 is an essential regulator of amp kinase, energy expenditure, and insulin sensitivity. Cell metabolism, 10 5:366-78, Nov 2009. URL: https://doi.org/10.1016/j.cmet.2009.09.010, doi:10.1016/j.cmet.2009.09.010. This article has 171 citations and is from a highest quality peer-reviewed journal.
3. (dar2016smallmoleculestabilization pages 1-2): AC Dar NS Dhawan, AP Scopton. Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling. Nature, 537:112-116, Jul 2016. URL: https://doi.org/10.1038/nature19327, doi:10.1038/nature19327. This article has 114 citations and is from a highest quality peer-reviewed journal.
4. (dar2016smallmoleculestabilization pages 4-6): AC Dar NS Dhawan, AP Scopton. Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling. Nature, 537:112-116, Jul 2016. URL: https://doi.org/10.1038/nature19327, doi:10.1038/nature19327. This article has 114 citations and is from a highest quality peer-reviewed journal.
5. (dar2016smallmoleculestabilization pages 6-7): AC Dar NS Dhawan, AP Scopton. Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling. Nature, 537:112-116, Jul 2016. URL: https://doi.org/10.1038/nature19327, doi:10.1038/nature19327. This article has 114 citations and is from a highest quality peer-reviewed journal.
6. (dougherty2009ksr2isa pages 13-19): M. K. Dougherty, Daniel A. Ritt, Ming Zhou, Suzanne I. Specht, Daniel M Monson, T. Veenstra, and D. Morrison. Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals. Molecular cell, 34 6:652-62, Jun 2009. URL: https://doi.org/10.1016/j.molcel.2009.06.001, doi:10.1016/j.molcel.2009.06.001. This article has 154 citations and is from a highest quality peer-reviewed journal.
7. (dougherty2009ksr2isa pages 7-8): M. K. Dougherty, Daniel A. Ritt, Ming Zhou, Suzanne I. Specht, Daniel M Monson, T. Veenstra, and D. Morrison. Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals. Molecular cell, 34 6:652-62, Jun 2009. URL: https://doi.org/10.1016/j.molcel.2009.06.001, doi:10.1016/j.molcel.2009.06.001. This article has 154 citations and is from a highest quality peer-reviewed journal.
8. (dougherty2009ksr2isa pages 8-9): M. K. Dougherty, Daniel A. Ritt, Ming Zhou, Suzanne I. Specht, Daniel M Monson, T. Veenstra, and D. Morrison. Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals. Molecular cell, 34 6:652-62, Jun 2009. URL: https://doi.org/10.1016/j.molcel.2009.06.001, doi:10.1016/j.molcel.2009.06.001. This article has 154 citations and is from a highest quality peer-reviewed journal.
9. (dougherty2009ksr2isa pages 9-11): M. K. Dougherty, Daniel A. Ritt, Ming Zhou, Suzanne I. Specht, Daniel M Monson, T. Veenstra, and D. Morrison. Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals. Molecular cell, 34 6:652-62, Jun 2009. URL: https://doi.org/10.1016/j.molcel.2009.06.001, doi:10.1016/j.molcel.2009.06.001. This article has 154 citations and is from a highest quality peer-reviewed journal.
10. (martinvega2023navigatingtheerk12 pages 14-16): Ana Martin-Vega and Melanie H. Cobb. Navigating the erk1/2 mapk cascade. Biomolecules, 13:1555, Oct 2023. URL: https://doi.org/10.3390/biom13101555, doi:10.3390/biom13101555. This article has 58 citations and is from a peer-reviewed journal.
11. (mckay2011complexityinksr pages 3-4): Melissa M. McKay, Alyson K. Freeman, and Deborah K. Morrison. Complexity in ksr function revealed by raf inhibitor and ksr structure studies. Small GTPases, 2:276-281, Sep 2011. URL: https://doi.org/10.4161/sgtp.2.5.17740, doi:10.4161/sgtp.2.5.17740. This article has 36 citations and is from a peer-reviewed journal.
12. (roskoski2012mek12dualspecificityprotein pages 5-6): Robert Roskoski. Mek1/2 dual-specificity protein kinases: structure and regulation. Biochemical and biophysical research communications, 417 1:5-10, Jan 2012. URL: https://doi.org/10.1016/j.bbrc.2011.11.145, doi:10.1016/j.bbrc.2011.11.145. This article has 354 citations and is from a peer-reviewed journal.
13. (costanzogarvey2009ksr2isan pages 1-2): Diane Costanzo-Garvey, P. Pfluger, M. K. Dougherty, J. Stock, M. Boehm, O. Chaika, Mario R. Fernandez, K. Fisher, R. Kortum, Eun-Gyoung Hong, J. Jun, H. Ko, Aimee Schreiner, D. J. Volle, T. Treece, Amy L. Swift, Mike Winer, Denise Chen, Min Wu, L. Leon, A. Shaw, J. Mcneish, Jason K. Kim, D. Morrison, M. Tschöp, and Robert E. Lewis. Ksr2 is an essential regulator of amp kinase, energy expenditure, and insulin sensitivity. Cell metabolism, 10 5:366-78, Nov 2009. URL: https://doi.org/10.1016/j.cmet.2009.09.010, doi:10.1016/j.cmet.2009.09.010. This article has 171 citations and is from a highest quality peer-reviewed journal.
14. (dar2016smallmoleculestabilization pages 2-4): AC Dar NS Dhawan, AP Scopton. Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling. Nature, 537:112-116, Jul 2016. URL: https://doi.org/10.1038/nature19327, doi:10.1038/nature19327. This article has 114 citations and is from a highest quality peer-reviewed journal.
15. (dar2016smallmoleculestabilization pages 33-37): AC Dar NS Dhawan, AP Scopton. Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling. Nature, 537:112-116, Jul 2016. URL: https://doi.org/10.1038/nature19327, doi:10.1038/nature19327. This article has 114 citations and is from a highest quality peer-reviewed journal.
16. (dar2016smallmoleculestabilization pages 7-9): AC Dar NS Dhawan, AP Scopton. Small molecule stabilization of the ksr inactive state antagonizes oncogenic ras signalling. Nature, 537:112-116, Jul 2016. URL: https://doi.org/10.1038/nature19327, doi:10.1038/nature19327. This article has 114 citations and is from a highest quality peer-reviewed journal.
17. (dougherty2009ksr2isa pages 19-21): M. K. Dougherty, Daniel A. Ritt, Ming Zhou, Suzanne I. Specht, Daniel M Monson, T. Veenstra, and D. Morrison. Ksr2 is a calcineurin substrate that promotes erk cascade activation in response to calcium signals. Molecular cell, 34 6:652-62, Jun 2009. URL: https://doi.org/10.1016/j.molcel.2009.06.001, doi:10.1016/j.molcel.2009.06.001. This article has 154 citations and is from a highest quality peer-reviewed journal.
18. (endicott2012thestructuralbasis pages 16-18): Jane A. Endicott, Martin E.M. Noble, and Louise N. Johnson. The structural basis for control of eukaryotic protein kinases. Annual Review of Biochemistry, 81:587-613, Jul 2012. URL: https://doi.org/10.1146/annurev-biochem-052410-090317, doi:10.1146/annurev-biochem-052410-090317. This article has 524 citations and is from a domain leading peer-reviewed journal.
19. (kung2019prospectsforpharmacological pages 14-16): Jennifer E. Kung and Natalia Jura. Prospects for pharmacological targeting of pseudokinases. Nature Reviews Drug Discovery, 18:501-526, Mar 2019. URL: https://doi.org/10.1038/s41573-019-0018-3, doi:10.1038/s41573-019-0018-3. This article has 140 citations and is from a highest quality peer-reviewed journal.
20. (martinvega2023navigatingtheerk12 pages 39-41): Ana Martin-Vega and Melanie H. Cobb. Navigating the erk1/2 mapk cascade. Biomolecules, 13:1555, Oct 2023. URL: https://doi.org/10.3390/biom13101555, doi:10.3390/biom13101555. This article has 58 citations and is from a peer-reviewed journal.
21. (mckay2011complexityinksr pages 1-3): Melissa M. McKay, Alyson K. Freeman, and Deborah K. Morrison. Complexity in ksr function revealed by raf inhibitor and ksr structure studies. Small GTPases, 2:276-281, Sep 2011. URL: https://doi.org/10.4161/sgtp.2.5.17740, doi:10.4161/sgtp.2.5.17740. This article has 36 citations and is from a peer-reviewed journal.
22. (morrison2003regulationofmap pages 5-7): Deborah K. Morrison and Roger J. Davis. Regulation of map kinase signaling modules by scaffold proteins in mammals. Annual review of cell and developmental biology, 19:91-118, Nov 2003. URL: https://doi.org/10.1146/annurev.cellbio.19.111401.091942, doi:10.1146/annurev.cellbio.19.111401.091942. This article has 1076 citations and is from a domain leading peer-reviewed journal.
23. (takacsvellai2014themetastasissuppressor pages 2-4): Krisztina Takács-Vellai. The metastasis suppressor nm23 as a modulator of ras/erk signaling. Journal of Molecular Signaling, 9:4, May 2014. URL: https://doi.org/10.1186/1750-2187-9-4, doi:10.1186/1750-2187-9-4. This article has 29 citations.
24. (udell2011mechanisticprinciplesof pages 1-2): Christian M. Udell, Thanashan Rajakulendran, Frank Sicheri, and Marc Therrien. Mechanistic principles of raf kinase signaling. Cellular and Molecular Life Sciences, 68:553-565, Feb 2011. URL: https://doi.org/10.1007/s00018-010-0520-6, doi:10.1007/s00018-010-0520-6. This article has 95 citations and is from a domain leading peer-reviewed journal.
25. (udell2011mechanisticprinciplesof pages 2-4): Christian M. Udell, Thanashan Rajakulendran, Frank Sicheri, and Marc Therrien. Mechanistic principles of raf kinase signaling. Cellular and Molecular Life Sciences, 68:553-565, Feb 2011. URL: https://doi.org/10.1007/s00018-010-0520-6, doi:10.1007/s00018-010-0520-6. This article has 95 citations and is from a domain leading peer-reviewed journal.
26. (zhang2014identificationofksr1 pages 197-199): Hua-Ying Zhang. Identification of ksr1 as a novel target and decoding tyrosine kinase proteome in breast cancer. Unknown journal, Apr 2014. URL: https://doi.org/10.25560/34315, doi:10.25560/34315. This article has 0 citations.
27. (kolch2005coordinatingerkmapksignalling pages 2-3): Walter Kolch. Coordinating erk/mapk signalling through scaffolds and inhibitors. Nature Reviews Molecular Cell Biology, 6:827-837, Nov 2005. URL: https://doi.org/10.1038/nrm1743, doi:10.1038/nrm1743. This article has 1416 citations and is from a domain leading peer-reviewed journal.
28. (kolch2005coordinatingerkmapksignalling pages 3-4): Walter Kolch. Coordinating erk/mapk signalling through scaffolds and inhibitors. Nature Reviews Molecular Cell Biology, 6:827-837, Nov 2005. URL: https://doi.org/10.1038/nrm1743, doi:10.1038/nrm1743. This article has 1416 citations and is from a domain leading peer-reviewed journal.
29. (kung2019prospectsforpharmacological pages 47-48): Jennifer E. Kung and Natalia Jura. Prospects for pharmacological targeting of pseudokinases. Nature Reviews Drug Discovery, 18:501-526, Mar 2019. URL: https://doi.org/10.1038/s41573-019-0018-3, doi:10.1038/s41573-019-0018-3. This article has 140 citations and is from a highest quality peer-reviewed journal.
30. (maloney2022themechanismof pages 1-2): Ryan C. Maloney, Mingzhen Zhang, Yonglan Liu, Hyunbum Jang, and Ruth Nussinov. The mechanism of activation of mek1 by b-raf and ksr1. Cellular and Molecular Life Sciences, May 2022. URL: https://doi.org/10.1007/s00018-022-04296-0, doi:10.1007/s00018-022-04296-0. This article has 21 citations and is from a domain leading peer-reviewed journal.
31. (takacsvellai2014themetastasissuppressor pages 7-7): Krisztina Takács-Vellai. The metastasis suppressor nm23 as a modulator of ras/erk signaling. Journal of Molecular Signaling, 9:4, May 2014. URL: https://doi.org/10.1186/1750-2187-9-4, doi:10.1186/1750-2187-9-4. This article has 29 citations.
32. (zhang2014identificationofksr1 pages 229-230): Hua-Ying Zhang. Identification of ksr1 as a novel target and decoding tyrosine kinase proteome in breast cancer. Unknown journal, Apr 2014. URL: https://doi.org/10.25560/34315, doi:10.25560/34315. This article has 0 citations.
33. (kung2019prospectsforpharmacological pages 27-28): Jennifer E. Kung and Natalia Jura. Prospects for pharmacological targeting of pseudokinases. Nature Reviews Drug Discovery, 18:501-526, Mar 2019. URL: https://doi.org/10.1038/s41573-019-0018-3, doi:10.1038/s41573-019-0018-3. This article has 140 citations and is from a highest quality peer-reviewed journal.
34. (mckay2011rafinhibitorinducedksr1braf pages 2-4): M. McKay, Daniel A. Ritt, and D. Morrison. Raf inhibitor-induced ksr1/b-raf binding and its effects on erk cascade signaling. Current Biology, 21:563-568, Apr 2011. URL: https://doi.org/10.1016/j.cub.2011.02.033, doi:10.1016/j.cub.2011.02.033. This article has 86 citations and is from a highest quality peer-reviewed journal.