1. Phylogeny  
   Beta‐adrenergic receptor kinase 1 (GRK2, also known as ADRBK1 or BARK1) is a member of the G protein–coupled receptor kinase (GRK) family, which is itself a subgroup within the large AGC serine/threonine kinase superfamily that emerged early in eukaryotic evolution (belmonte2011gproteincoupled pages 1-2). GRK2 is classified in the GRK2 subfamily together with GRK3; these kinases share a high degree of amino acid sequence similarity and conserved domain architecture, a feature that is evident in all mammalian orthologs and to a large extent is preserved among vertebrates (gurevich2012gproteincoupledreceptor pages 1-2, watari2014multiplefunctionsof pages 1-2). Orthologs of GRK2 have been identified in a wide range of species from mammals to lower vertebrates, signifying that the function of GRK2 in modulating receptor activity is an evolutionarily conserved mechanism that predates the divergence of many eukaryotic lineages (belmonte2011gproteincoupled pages 1-2, homan2014structuralinsightsinto pages 1-2). In evolutionary analyses, GRK2 is grouped with kinases that govern receptor desensitization and cellular responsiveness, and its conservation among species underscores its essential role in maintaining cellular homeostasis via precise control of G protein–coupled receptor signaling (gurevich2012gproteincoupledreceptor pages 1-2, penela2019gproteincoupledreceptor pages 2-3). The presence of both an N‐terminal RH domain and a C‐terminal pleckstrin homology (PH) domain that are preserved across different species indicates that these domains are indispensable for GRK2’s interactions with regulatory proteins such as the G protein βγ subunits, which are integral to its function (belmonte2011gproteincoupled pages 2-4, penela2019gproteincoupledreceptor pages 2-3). Comparative genomic studies have positioned GRK2 alongside other key kinases regulating receptor signaling—revealing that the mechanisms for agonist-dependent receptor phosphorylation and subsequent desensitization have deep evolutionary roots (gurevich2012gproteincoupledreceptor pages 1-2, homan2014structuralinsightsinto pages 1-2). Thus, the phylogenetic context of GRK2 not only demonstrates its conservation from lower eukaryotes to mammals but also establishes its evolutionary relationship with other AGC kinases that coordinate essential cellular processes (belmonte2011gproteincoupled pages 11-13).
2. Reaction Catalyzed  
   GRK2 catalyzes the transfer of the γ‐phosphate group from ATP to specific serine or threonine residues on its substrates, which are primarily agonist-occupied G protein–coupled receptors (GPCRs) such as beta‐adrenergic receptors (belmonte2011gproteincoupled pages 1-2). In biochemical terms, the reaction can be formally written as:  
     ATP + [protein]–(L‐serine or L‐threonine) → ADP + [protein]–(L‐serine/threonine‐phosphate) + H⁺  
   This phosphorylation event is the initial step that leads to receptor desensitization because it promotes the recruitment of beta‐arrestin proteins that sterically block further G protein coupling and trigger receptor internalization (belmonte2011gproteincoupled pages 4-5, cato2019structuralandbiochemical pages 133-136). The reaction is tightly coupled to agonist binding, as GRK2 specifically phosphorylates receptors that have adopted the activated conformation upon ligand binding (cato2019structuralandbiochemical pages 63-67).
3. Cofactor Requirements  
   The kinase activity of GRK2 is strictly dependent on ATP, which acts as the phosphate donor in the phosphorylation reaction, and on divalent metal ion cofactors, with Mg²⁺ being the primary requirement (cato2019structuralandbiochemical pages 133-136). The binding of Mg²⁺ is essential for coordinating the phosphates of ATP within the catalytic site, thereby enabling efficient transfer of the phosphate group to the substrate protein (belmonte2011gproteincoupled pages 1-2). This cofactor dependence aligns GRK2 with other serine/threonine kinases within the AGC family, which similarly require Mg²⁺ for optimal catalytic activity (cato2019structuralandbiochemical pages 133-136).
4. Substrate Specificity  
   GRK2 displays a high substrate specificity for G protein–coupled receptors that have been activated by an agonist. It preferentially phosphorylates serine/threonine residues within the intracellular loops and the C-terminal tail of these receptors, particularly beta‐adrenergic receptors, to which its activity is essential for terminating G protein signaling (belmonte2011gproteincoupled pages 1-2, belmonte2011gproteincoupled pages 4-5). Although the strict consensus motif for substrates phosphorylated by GRK2 is not as clearly defined as that of some other serine/threonine kinases, its substrate preference is largely determined by the conformation of the activated receptor rather than a specific linear amino acid motif (cato2019structuralandbiochemical pages 63-67, gurevich2012gproteincoupledreceptor pages 50-51). In addition to beta‐adrenergic receptors, GRK2 has been implicated in the regulation of other receptors including the lysophosphatidic acid receptors LPAR1 and LPAR2. For LPAR1, GRK2 plays a key role in the phosphorylation-dependent desensitization process, whereas desensitization of LPAR2 may occur by mechanisms that do not strictly rely on its kinase activity (belmonte2011gproteincoupled pages 4-5). Such dual modalities of action further illustrate GRK2’s versatility as a regulator of receptor signaling (cato2019structuralandbiochemical pages 63-67).
5. Structure  
   GRK2 is composed of several distinct structural domains that collectively determine its catalytic activity, substrate recognition, and regulatory interactions. The amino‐terminal region, although partially unstructured when isolated, contains an αN helix that adopts a defined conformation upon binding to activated GPCRs and is crucial for receptor docking (homan2014structuralinsightsinto pages 6-9, belmonte2011gproteincoupled pages 1-2). This region is immediately followed by the regulator of G protein signaling (RGS) homology (RH) domain, which contributes to the interaction with Gα subunits and may facilitate phosphorylation‐independent regulatory functions (gurevich2012gproteincoupledreceptor pages 1-2, hullmann2016theexpandinggrk pages 3-5).  
   Central to GRK2 is its catalytic kinase domain, which exhibits the classical bilobal architecture characteristic of AGC kinases. The N-terminal lobe is composed primarily of β-sheets while the C-terminal lobe is predominantly α-helical; these two lobes form a distinct catalytic cleft that binds ATP and the substrate (cato2019structuralandbiochemical pages 17-21, homan2015crystalstructureof pages 11-11). Within this domain, key catalytic features such as the ATP-binding pocket, the conserved catalytic lysine (essential for activity), and a hydrophobic spine that stabilizes the active conformation are present (cato2019structuralandbiochemical pages 17-21, gurevich2012gproteincoupledreceptor pages 13-15). Notably, unlike several other AGC kinases, GRK2 does not require activation loop phosphorylation for activity; rather, its conformational changes upon receptor engagement are sufficient to trigger full kinase activation (belmonte2011gproteincoupled pages 2-4, cato2019structuralandbiochemical pages 21-25).  
   The carboxy‐terminal portion of GRK2 harbors a pleckstrin homology (PH) domain, which is indispensable for its membrane localization. This domain binds to G protein βγ (Gβγ) subunits as well as to phospholipids such as phosphatidylinositol 4,5‐bisphosphate (PIP₂), thereby recruiting GRK2 to the plasma membrane where its substrates reside (belmonte2011gproteincoupled pages 2-4, penela2019gproteincoupledreceptor pages 5-6). Collectively, the spatial arrangement of these domains—namely, the flexible N-terminal αN helix, the RH domain, the catalytic kinase domain, and the PH domain—enables GRK2 to integrate multiple regulatory signals and to efficiently catalyze receptor phosphorylation only when the receptor is in its active state (homan2014structuralinsightsinto pages 6-9, belmonte2011gproteincoupled pages 1-2).
6. Regulation  
   The activity of GRK2 is subject to multifaceted regulation that ensures that receptor phosphorylation occurs with high spatial and temporal precision. A primary regulatory mechanism involves the binding of Gβγ subunits released upon GPCR activation; the interaction of these subunits with the PH domain of GRK2 induces its translocation to the plasma membrane, thereby positioning it in close proximity to activated receptors (belmonte2011gproteincoupled pages 2-4, hullmann2016theexpandinggrk pages 16-18). In addition to this membrane recruitment, GRK2 activity is modulated by post-translational modifications such as phosphorylation. Kinases like protein kinase A (PKA), protein kinase C (PKC), and c-Src can phosphorylate GRK2 at specific sites, which in turn either potentiate or attenuate its kinase activity; for instance, phosphorylation events have been linked to enhanced Gβγ binding or to alterations in GRK2 stability (homan2014structuralinsightsinto pages 5-6, murga2019gproteincoupledreceptor pages 15-16).  
   Furthermore, GRK2 undergoes allosteric regulation through conformational changes upon receptor binding. The engagement of the N-terminal αN helix with the cytosolic pocket of an activated receptor helps stabilize a fully active conformation of the kinase domain without the need for activation loop phosphorylation (belmonte2011gproteincoupled pages 2-4, cato2019structuralandbiochemical pages 21-25). In addition to these intrinsic regulatory features, exogenous inhibitors such as the βARKct peptide have been developed, which act by sequestering Gβγ subunits to prevent GRK2 membrane recruitment and thereby block receptor phosphorylation (pfleger2019gproteincoupledreceptor pages 10-10, cannavo2013targetingcardiacβadrenergic pages 1-2). These combined regulatory mechanisms—protein–protein interactions, post‐translational modifications, and conformational rearrangements—allow GRK2 to function as a finely tuned regulator of receptor desensitization, ensuring that its activity is appropriately matched to the level and duration of receptor stimulation (cato2019structuralandbiochemical pages 25-29, sato2015theevolvingimpact pages 21-22).
7. Function  
   The primary function of GRK2 is to modulate cellular responsiveness to extracellular stimuli by regulating the signaling of G protein–coupled receptors (GPCRs). GRK2 specifically recognizes and phosphorylates the agonist-occupied forms of receptors, most notably beta‐adrenergic receptors, which leads to the recruitment of beta‐arrestins. This in turn results in receptor desensitization, internalization, and the subsequent attenuation of G protein–mediated signaling (belmonte2011gproteincoupled pages 1-2, belmonte2011gproteincoupled pages 4-5). In cardiac tissue, GRK2 is particularly significant because its overexpression or hyperactivity is associated with reduced beta‐adrenergic receptor signaling responsiveness, a phenomenon that contributes to the progression of heart failure (pfleger2019gproteincoupledreceptor pages 8-9, sato2015theevolvingimpact pages 28-29).  
   Beyond its canonical role in GPCR desensitization, GRK2 also influences alternative signaling pathways. For example, it plays a regulatory role in the modulation of lysophosphatidic acid receptor (LPAR1) signaling by competing with RALA for receptor binding, thereby affecting downstream signaling properties; in the case of LPAR2, GRK2 can desensitize the receptor by phosphorylation-independent mechanisms (belmonte2011gproteincoupled pages 4-5). In addition, GRK2 is reported to positively regulate the ciliary smoothened (SMO)–dependent Hedgehog signaling pathway by facilitating the trafficking of SMO into the cilium, which in turn promotes pathway activity (Information provided). By orchestrating these processes, GRK2 serves as a central hub in receptor signaling modulation, integrating inputs from both G protein–dependent and –independent pathways to regulate cellular responses (ciccarelli2011gprotein–coupledreceptor pages 6-7, murga2019gproteincoupledreceptor pages 1-2).  
   In tissues such as the heart, the proper balance of GRK2 activity is critical for maintaining appropriate beta‐adrenergic receptor responsiveness and, by extension, normal cardiac contractility and output. Dysregulation of GRK2, including its increased expression, has been associated with maladaptive changes such as receptor hyperphosphorylation and desensitization, ultimately contributing to pathophysiological states like heart failure and hypertrophy (pfleger2019gproteincoupledreceptor pages 11-11, sato2015theevolvingimpact pages 28-29). Moreover, the ubiquitous expression of GRK2 and its participation in non‐canonical substrate phosphorylation underscore its broader roles in modulating intracellular signaling networks, including pathways that regulate cell motility, cytoskeletal dynamics, and metabolic signaling (gurevich2012gproteincoupledreceptor pages 62-63, murga2019gproteincoupledreceptor pages 17-17).
8. Other Comments  
   In addition to its central role in receptor desensitization, GRK2 has emerged as an important therapeutic target, particularly for cardiovascular diseases such as heart failure. Experimental inhibitors of GRK2, including the βARKct peptide and small molecules like paroxetine, have been shown to directly inhibit its kinase activity and restore receptor sensitivity, thereby improving myocardial contractility and overall cardiac function in preclinical models (thal2012paroxetineisa pages 8-9, pfleger2019gproteincoupledreceptor pages 10-10). GRK2’s function extends beyond GPCR phosphorylation; it contributes to regulating LPAR1 signaling and the trafficking of ciliary SMO, processes that have implications for diverse physiological responses and potentially for the treatment of conditions beyond heart disease (Information provided, belmonte2011gproteincoupled pages 4-5). Ongoing research in structure‐based drug design has identified several classes of compounds—from peptide inhibitors to small molecules—that selectively target the kinase domain or disrupt the GRK2–Gβγ interaction, further validating GRK2 as a multifaceted therapeutic target (cato2019structuralandbiochemical pages 25-29, mangmool2018therapeutictargetsfor pages 1-2). Such targeted inhibition of GRK2 holds promise not only in the context of heart failure but may also be beneficial in correcting receptor signaling abnormalities observed in metabolic disorders and conditions linked to dysregulated G protein–coupled receptor function (pfleger2019gproteincoupledreceptor pages 11-11, sato2015theevolvingimpact pages 28-29).
9. References  
   Belmonte, S. L. & Blaxall, B. C. “G protein coupled receptor kinases as therapeutic targets in cardiovascular disease.” Circulation Research, 109:309-319, Jul 2011 (belmonte2011gproteincoupled pages 1-2; belmonte2011gproteincoupled pages 4-5; belmonte2011gproteincoupled pages 11-13; belmonte2011gproteincoupled pages 2-4).  
   Cannavo, A., Liccardo, D. & Koch, W. J. “Targeting cardiac β-adrenergic signaling via GRK2 inhibition for heart failure therapy.” Frontiers in Physiology, Aug 2013 (cannavo2013targetingcardiacβadrenergic pages 1-2).  
   Cato, M. “Structural and biochemical analysis of G protein-coupled receptor kinase activation and small molecule inhibitor selectivity.” 2019 (cato2019structuralandbiochemical pages 133-136; cato2019structuralandbiochemical pages 17-21; cato2019structuralandbiochemical pages 21-25; cato2019structuralandbiochemical pages 25-29; cato2019structuralandbiochemical pages 63-67; cato2019structuralandbiochemical pages 8-12).  
   Ciccarelli, M. et al. “G protein–coupled receptor kinase 2 activity impairs cardiac glucose uptake and promotes insulin resistance after myocardial ischemia.” Circulation, 123:1953-1962, May 2011 (ciccarelli2011gprotein–coupledreceptor pages 6-7).  
   Gurevich, E. V., Tesmer, J. J. G., Mushegian, A. & Gurevich, V. V. “G protein-coupled receptor kinases: more than just kinases and not only for GPCRs.” Pharmacology & Therapeutics, 133:40-69, Jan 2012 (gurevich2012gproteincoupledreceptor pages 1-2; gurevich2012gproteincoupledreceptor pages 12-13; gurevich2012gproteincoupledreceptor pages 13-15; gurevich2012gproteincoupledreceptor pages 2-4; gurevich2012gproteincoupledreceptor pages 23-24; gurevich2012gproteincoupledreceptor pages 50-51; gurevich2012gproteincoupledreceptor pages 59-62; gurevich2012gproteincoupledreceptor pages 62-63; gurevich2012gproteincoupledreceptor pages 63-64).  
   Homan, K. T. & Tesmer, J. J. G. “Structural insights into G protein-coupled receptor kinase function.” Current Opinion in Cell Biology, 27:25-31, Apr 2014 (homan2014structuralinsightsinto pages 1-2; homan2014structuralinsightsinto pages 2-4; homan2014structuralinsightsinto pages 5-6; homan2014structuralinsightsinto pages 6-9).  
   Homan, K. T. et al. “Crystal structure of G protein-coupled receptor kinase 5 in complex with a rationally designed inhibitor.” Journal of Biological Chemistry, 290:20649-20659, Aug 2015 (homan2015crystalstructureof pages 11-11).  
   Hullmann, J. et al. “The expanding GRK interactome: implications in cardiovascular disease and potential for therapeutic development.” Pharmacological Research, 110:52-64, Aug 2016 (hullmann2016theexpandinggrk pages 1-3; hullmann2016theexpandinggrk pages 3-5; hullmann2016theexpandinggrk pages 16-18).  
   Murga, C. et al. “G protein-coupled receptor kinase 2 (GRK2) as a potential therapeutic target in cardiovascular and metabolic diseases.” Frontiers in Pharmacology, Feb 2019 (murga2019gproteincoupledreceptor pages 1-2; murga2019gproteincoupledreceptor pages 15-16; murga2019gproteincoupledreceptor pages 17-17).  
   Penela, P. et al. “G protein-coupled receptor kinase 2 (GRK2) as a multifunctional signaling hub.” Cellular and Molecular Life Sciences, 76:4423-4446, Aug 2019 (penela2019gproteincoupledreceptor pages 18-19; penela2019gproteincoupledreceptor pages 2-3; penela2019gproteincoupledreceptor pages 5-6).  
   Pfleger, J., Gresham, K. & Koch, W. J. “G protein-coupled receptor kinases as therapeutic targets in the heart.” Nature Reviews Cardiology, 16:612-622, Jun 2019 (pfleger2019gproteincoupledreceptor pages 8-9; pfleger2019gproteincoupledreceptor pages 10-10; pfleger2019gproteincoupledreceptor pages 11-11).  
   Sato, P. Y. et al. “The evolving impact of G protein-coupled receptor kinases in cardiac health and disease.” Physiological Reviews, 95:377-404, Apr 2015 (sato2015theevolvingimpact pages 1-2; sato2015theevolvingimpact pages 20-21; sato2015theevolvingimpact pages 21-22; sato2015theevolvingimpact pages 28-29).  
   Seo, M. J. & Yu, W. “Uncovering conserved networks and global conformational changes in G protein-coupled receptor kinases.” Computational and Structural Biotechnology Journal, 23:3445-3453, Dec 2024 (seo2024uncoveringconservednetworks pages 8-9).  
   Thal, D. M. et al. “Paroxetine is a direct inhibitor of G protein-coupled receptor kinase 2 and increases myocardial contractility.” ACS Chemical Biology, 7:1830-1839, Aug 2012 (thal2012paroxetineisa pages 8-9).  
   Watari, K., Nakaya, M. & Kurose, H. “Multiple functions of G protein-coupled receptor kinases.” Journal of Molecular Signaling, 9:1, Mar 2014 (watari2014multiplefunctionsof pages 1-2; watari2014multiplefunctionsof pages 9-9).  
   Apostolakou, A. E. et al. “Extended human G-protein coupled receptor network: cell-type-specific analysis of G-protein coupled receptor signaling pathways.” Journal of Proteome Research, 19:511-524, Nov 2019 (apostolakou2019extendedhumangprotein pages 14-14).  
   Mangmool, S., Parichatikanond, W. & Kurose, H. “Therapeutic targets for treatment of heart failure: focus on GRKs and β-arrestins affecting βAR signaling.” Frontiers in Pharmacology, Nov 2018 (mangmool2018therapeutictargetsfor pages 1-2).

References

1. (belmonte2011gproteincoupled pages 1-2): Stephen L. Belmonte and Burns C. Blaxall. G protein coupled receptor kinases as therapeutic targets in cardiovascular disease. Circulation Research, 109:309-319, Jul 2011. URL: https://doi.org/10.1161/circresaha.110.231233, doi:10.1161/circresaha.110.231233. This article has 151 citations and is from a highest quality peer-reviewed journal.
2. (belmonte2011gproteincoupled pages 11-13): Stephen L. Belmonte and Burns C. Blaxall. G protein coupled receptor kinases as therapeutic targets in cardiovascular disease. Circulation Research, 109:309-319, Jul 2011. URL: https://doi.org/10.1161/circresaha.110.231233, doi:10.1161/circresaha.110.231233. This article has 151 citations and is from a highest quality peer-reviewed journal.
3. (belmonte2011gproteincoupled pages 2-4): Stephen L. Belmonte and Burns C. Blaxall. G protein coupled receptor kinases as therapeutic targets in cardiovascular disease. Circulation Research, 109:309-319, Jul 2011. URL: https://doi.org/10.1161/circresaha.110.231233, doi:10.1161/circresaha.110.231233. This article has 151 citations and is from a highest quality peer-reviewed journal.
4. (belmonte2011gproteincoupled pages 4-5): Stephen L. Belmonte and Burns C. Blaxall. G protein coupled receptor kinases as therapeutic targets in cardiovascular disease. Circulation Research, 109:309-319, Jul 2011. URL: https://doi.org/10.1161/circresaha.110.231233, doi:10.1161/circresaha.110.231233. This article has 151 citations and is from a highest quality peer-reviewed journal.
5. (cannavo2013targetingcardiacβadrenergic pages 1-2): Alessandro Cannavo, Daniela Liccardo, and Walter J. Koch. Targeting cardiac β-adrenergic signaling via grk2 inhibition for heart failure therapy. Frontiers in Physiology, Aug 2013. URL: https://doi.org/10.3389/fphys.2013.00264, doi:10.3389/fphys.2013.00264. This article has 138 citations and is from a peer-reviewed journal.
6. (cato2019structuralandbiochemical pages 133-136): M Cato. Structural and biochemical analysis of g protein-coupled receptor kinase activation and small molecule inhibitor selectivity. Unknown journal, 2019.
7. (cato2019structuralandbiochemical pages 17-21): M Cato. Structural and biochemical analysis of g protein-coupled receptor kinase activation and small molecule inhibitor selectivity. Unknown journal, 2019.
8. (cato2019structuralandbiochemical pages 25-29): M Cato. Structural and biochemical analysis of g protein-coupled receptor kinase activation and small molecule inhibitor selectivity. Unknown journal, 2019.
9. (cato2019structuralandbiochemical pages 63-67): M Cato. Structural and biochemical analysis of g protein-coupled receptor kinase activation and small molecule inhibitor selectivity. Unknown journal, 2019.
10. (cato2019structuralandbiochemical pages 8-12): M Cato. Structural and biochemical analysis of g protein-coupled receptor kinase activation and small molecule inhibitor selectivity. Unknown journal, 2019.
11. (ciccarelli2011gprotein–coupledreceptor pages 6-7): Michele Ciccarelli, J. Kurt Chuprun, Giuseppe Rengo, Erhe Gao, Zhengyu Wei, Raymond J. Peroutka, Jessica I. Gold, Anna Gumpert, Mai Chen, Nicholas J. Otis, Gerald W. Dorn, Bruno Trimarco, Guido Iaccarino, and Walter J. Koch. G protein–coupled receptor kinase 2 activity impairs cardiac glucose uptake and promotes insulin resistance after myocardial ischemia. Circulation, 123:1953-1962, May 2011. URL: https://doi.org/10.1161/circulationaha.110.988642, doi:10.1161/circulationaha.110.988642. This article has 173 citations and is from a highest quality peer-reviewed journal.
12. (gurevich2012gproteincoupledreceptor pages 1-2): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
13. (gurevich2012gproteincoupledreceptor pages 12-13): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
14. (gurevich2012gproteincoupledreceptor pages 13-15): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
15. (gurevich2012gproteincoupledreceptor pages 2-4): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
16. (gurevich2012gproteincoupledreceptor pages 23-24): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
17. (gurevich2012gproteincoupledreceptor pages 50-51): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
18. (homan2014structuralinsightsinto pages 1-2): KT Homan and JJG Tesmer. Structural insights into g protein-coupled receptor kinase function. Current opinion in cell biology, 27:25-31, Apr 2014. URL: https://doi.org/10.1016/j.ceb.2013.10.009, doi:10.1016/j.ceb.2013.10.009. This article has 85 citations and is from a peer-reviewed journal.
19. (homan2014structuralinsightsinto pages 2-4): KT Homan and JJG Tesmer. Structural insights into g protein-coupled receptor kinase function. Current opinion in cell biology, 27:25-31, Apr 2014. URL: https://doi.org/10.1016/j.ceb.2013.10.009, doi:10.1016/j.ceb.2013.10.009. This article has 85 citations and is from a peer-reviewed journal.
20. (homan2014structuralinsightsinto pages 5-6): KT Homan and JJG Tesmer. Structural insights into g protein-coupled receptor kinase function. Current opinion in cell biology, 27:25-31, Apr 2014. URL: https://doi.org/10.1016/j.ceb.2013.10.009, doi:10.1016/j.ceb.2013.10.009. This article has 85 citations and is from a peer-reviewed journal.
21. (homan2014structuralinsightsinto pages 6-9): KT Homan and JJG Tesmer. Structural insights into g protein-coupled receptor kinase function. Current opinion in cell biology, 27:25-31, Apr 2014. URL: https://doi.org/10.1016/j.ceb.2013.10.009, doi:10.1016/j.ceb.2013.10.009. This article has 85 citations and is from a peer-reviewed journal.
22. (homan2015crystalstructureof pages 11-11): Kristoff T. Homan, Helen V. Waldschmidt, Alisa Glukhova, Alessandro Cannavo, Jianliang Song, Joseph Y. Cheung, Walter J. Koch, Scott D. Larsen, and John J.G. Tesmer. Crystal structure of g protein-coupled receptor kinase 5 in complex with a rationally designed inhibitor. Journal of Biological Chemistry, 290:20649-20659, Aug 2015. URL: https://doi.org/10.1074/jbc.m115.647370, doi:10.1074/jbc.m115.647370. This article has 59 citations and is from a domain leading peer-reviewed journal.
23. (hullmann2016theexpandinggrk pages 1-3): Jonathan Hullmann, Christopher J. Traynham, Ryan C. Coleman, and Walter J. Koch. The expanding grk interactome: implications in cardiovascular disease and potential for therapeutic development. Pharmacological Research, 110:52-64, Aug 2016. URL: https://doi.org/10.1016/j.phrs.2016.05.008, doi:10.1016/j.phrs.2016.05.008. This article has 78 citations and is from a highest quality peer-reviewed journal.
24. (hullmann2016theexpandinggrk pages 16-18): Jonathan Hullmann, Christopher J. Traynham, Ryan C. Coleman, and Walter J. Koch. The expanding grk interactome: implications in cardiovascular disease and potential for therapeutic development. Pharmacological Research, 110:52-64, Aug 2016. URL: https://doi.org/10.1016/j.phrs.2016.05.008, doi:10.1016/j.phrs.2016.05.008. This article has 78 citations and is from a highest quality peer-reviewed journal.
25. (hullmann2016theexpandinggrk pages 3-5): Jonathan Hullmann, Christopher J. Traynham, Ryan C. Coleman, and Walter J. Koch. The expanding grk interactome: implications in cardiovascular disease and potential for therapeutic development. Pharmacological Research, 110:52-64, Aug 2016. URL: https://doi.org/10.1016/j.phrs.2016.05.008, doi:10.1016/j.phrs.2016.05.008. This article has 78 citations and is from a highest quality peer-reviewed journal.
26. (murga2019gproteincoupledreceptor pages 1-2): Cristina Murga, Alba C. Arcones, Marta Cruces-Sande, Ana M. Briones, Mercedes Salaices, and Federico Mayor Jr. G protein-coupled receptor kinase 2 (grk2) as a potential therapeutic target in cardiovascular and metabolic diseases. Frontiers in Pharmacology, Feb 2019. URL: https://doi.org/10.3389/fphar.2019.00112, doi:10.3389/fphar.2019.00112. This article has 115 citations and is from a peer-reviewed journal.
27. (murga2019gproteincoupledreceptor pages 15-16): Cristina Murga, Alba C. Arcones, Marta Cruces-Sande, Ana M. Briones, Mercedes Salaices, and Federico Mayor Jr. G protein-coupled receptor kinase 2 (grk2) as a potential therapeutic target in cardiovascular and metabolic diseases. Frontiers in Pharmacology, Feb 2019. URL: https://doi.org/10.3389/fphar.2019.00112, doi:10.3389/fphar.2019.00112. This article has 115 citations and is from a peer-reviewed journal.
28. (murga2019gproteincoupledreceptor pages 17-17): Cristina Murga, Alba C. Arcones, Marta Cruces-Sande, Ana M. Briones, Mercedes Salaices, and Federico Mayor Jr. G protein-coupled receptor kinase 2 (grk2) as a potential therapeutic target in cardiovascular and metabolic diseases. Frontiers in Pharmacology, Feb 2019. URL: https://doi.org/10.3389/fphar.2019.00112, doi:10.3389/fphar.2019.00112. This article has 115 citations and is from a peer-reviewed journal.
29. (penela2019gproteincoupledreceptor pages 18-19): Petronila Penela, Catalina Ribas, Francisco Sánchez-Madrid, and Federico Mayor. G protein-coupled receptor kinase 2 (grk2) as a multifunctional signaling hub. Cellular and Molecular Life Sciences, 76:4423-4446, Aug 2019. URL: https://doi.org/10.1007/s00018-019-03274-3, doi:10.1007/s00018-019-03274-3. This article has 99 citations and is from a domain leading peer-reviewed journal.
30. (penela2019gproteincoupledreceptor pages 2-3): Petronila Penela, Catalina Ribas, Francisco Sánchez-Madrid, and Federico Mayor. G protein-coupled receptor kinase 2 (grk2) as a multifunctional signaling hub. Cellular and Molecular Life Sciences, 76:4423-4446, Aug 2019. URL: https://doi.org/10.1007/s00018-019-03274-3, doi:10.1007/s00018-019-03274-3. This article has 99 citations and is from a domain leading peer-reviewed journal.
31. (penela2019gproteincoupledreceptor pages 5-6): Petronila Penela, Catalina Ribas, Francisco Sánchez-Madrid, and Federico Mayor. G protein-coupled receptor kinase 2 (grk2) as a multifunctional signaling hub. Cellular and Molecular Life Sciences, 76:4423-4446, Aug 2019. URL: https://doi.org/10.1007/s00018-019-03274-3, doi:10.1007/s00018-019-03274-3. This article has 99 citations and is from a domain leading peer-reviewed journal.
32. (pfleger2019gproteincoupledreceptor pages 10-10): Jessica Pfleger, Kenneth Gresham, and Walter J. Koch. G protein-coupled receptor kinases as therapeutic targets in the heart. Nature Reviews Cardiology, 16:612-622, Jun 2019. URL: https://doi.org/10.1038/s41569-019-0220-3, doi:10.1038/s41569-019-0220-3. This article has 155 citations and is from a domain leading peer-reviewed journal.
33. (pfleger2019gproteincoupledreceptor pages 11-11): Jessica Pfleger, Kenneth Gresham, and Walter J. Koch. G protein-coupled receptor kinases as therapeutic targets in the heart. Nature Reviews Cardiology, 16:612-622, Jun 2019. URL: https://doi.org/10.1038/s41569-019-0220-3, doi:10.1038/s41569-019-0220-3. This article has 155 citations and is from a domain leading peer-reviewed journal.
34. (pfleger2019gproteincoupledreceptor pages 8-9): Jessica Pfleger, Kenneth Gresham, and Walter J. Koch. G protein-coupled receptor kinases as therapeutic targets in the heart. Nature Reviews Cardiology, 16:612-622, Jun 2019. URL: https://doi.org/10.1038/s41569-019-0220-3, doi:10.1038/s41569-019-0220-3. This article has 155 citations and is from a domain leading peer-reviewed journal.
35. (sato2015theevolvingimpact pages 1-2): Priscila Y. Sato, J. Kurt Chuprun, Mathew Schwartz, and Walter J. Koch. The evolving impact of g protein-coupled receptor kinases in cardiac health and disease. Physiological Reviews, 95:377-404, Apr 2015. URL: https://doi.org/10.1152/physrev.00015.2014, doi:10.1152/physrev.00015.2014. This article has 184 citations and is from a highest quality peer-reviewed journal.
36. (sato2015theevolvingimpact pages 20-21): Priscila Y. Sato, J. Kurt Chuprun, Mathew Schwartz, and Walter J. Koch. The evolving impact of g protein-coupled receptor kinases in cardiac health and disease. Physiological Reviews, 95:377-404, Apr 2015. URL: https://doi.org/10.1152/physrev.00015.2014, doi:10.1152/physrev.00015.2014. This article has 184 citations and is from a highest quality peer-reviewed journal.
37. (sato2015theevolvingimpact pages 21-22): Priscila Y. Sato, J. Kurt Chuprun, Mathew Schwartz, and Walter J. Koch. The evolving impact of g protein-coupled receptor kinases in cardiac health and disease. Physiological Reviews, 95:377-404, Apr 2015. URL: https://doi.org/10.1152/physrev.00015.2014, doi:10.1152/physrev.00015.2014. This article has 184 citations and is from a highest quality peer-reviewed journal.
38. (sato2015theevolvingimpact pages 28-29): Priscila Y. Sato, J. Kurt Chuprun, Mathew Schwartz, and Walter J. Koch. The evolving impact of g protein-coupled receptor kinases in cardiac health and disease. Physiological Reviews, 95:377-404, Apr 2015. URL: https://doi.org/10.1152/physrev.00015.2014, doi:10.1152/physrev.00015.2014. This article has 184 citations and is from a highest quality peer-reviewed journal.
39. (seo2024uncoveringconservednetworks pages 8-9): Min Jae Seo and Wookyung Yu. Uncovering conserved networks and global conformational changes in g protein-coupled receptor kinases. Computational and Structural Biotechnology Journal, 23:3445-3453, Dec 2024. URL: https://doi.org/10.1016/j.csbj.2024.09.014, doi:10.1016/j.csbj.2024.09.014. This article has 0 citations and is from a peer-reviewed journal.
40. (thal2012paroxetineisa pages 8-9): David M. Thal, Kristoff T. Homan, Jun Chen, Emily K. Wu, Patricia M. Hinkle, Z. Maggie Huang, J. Kurt Chuprun, Jianliang Song, Erhe Gao, Joseph Y. Cheung, Larry A. Sklar, Walter J. Koch, and John J.G. Tesmer. Paroxetine is a direct inhibitor of g protein-coupled receptor kinase 2 and increases myocardial contractility. ACS Chemical Biology, 7:1830-1839, Aug 2012. URL: https://doi.org/10.1021/cb3003013, doi:10.1021/cb3003013. This article has 234 citations and is from a domain leading peer-reviewed journal.
41. (watari2014multiplefunctionsof pages 1-2): Kenji Watari, Michio Nakaya, and Hitoshi Kurose. Multiple functions of g protein-coupled receptor kinases. Journal of Molecular Signaling, 9:1, Mar 2014. URL: https://doi.org/10.1186/1750-2187-9-1, doi:10.1186/1750-2187-9-1. This article has 132 citations.
42. (watari2014multiplefunctionsof pages 9-9): Kenji Watari, Michio Nakaya, and Hitoshi Kurose. Multiple functions of g protein-coupled receptor kinases. Journal of Molecular Signaling, 9:1, Mar 2014. URL: https://doi.org/10.1186/1750-2187-9-1, doi:10.1186/1750-2187-9-1. This article has 132 citations.
43. (apostolakou2019extendedhumangprotein pages 14-14): Avgi E. Apostolakou, Fotis A. Baltoumas, Dimitrios J. Stravopodis, and Vassiliki A. Iconomidou. Extended human g-protein coupled receptor network: cell-type-specific analysis of g-protein coupled receptor signaling pathways. Journal of Proteome Research, 19:511-524, Nov 2019. URL: https://doi.org/10.1021/acs.jproteome.9b00754, doi:10.1021/acs.jproteome.9b00754. This article has 18 citations and is from a peer-reviewed journal.
44. (cato2019structuralandbiochemical pages 21-25): M Cato. Structural and biochemical analysis of g protein-coupled receptor kinase activation and small molecule inhibitor selectivity. Unknown journal, 2019.
45. (gurevich2012gproteincoupledreceptor pages 59-62): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
46. (gurevich2012gproteincoupledreceptor pages 62-63): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
47. (gurevich2012gproteincoupledreceptor pages 63-64): Eugenia V. Gurevich, John J.G. Tesmer, Arcady Mushegian, and Vsevolod V. Gurevich. G protein-coupled receptor kinases: more than just kinases and not only for gpcrs. Pharmacology & Therapeutics, 133:40-69, Jan 2012. URL: https://doi.org/10.1016/j.pharmthera.2011.08.001, doi:10.1016/j.pharmthera.2011.08.001. This article has 544 citations.
48. (mangmool2018therapeutictargetsfor pages 1-2): Supachoke Mangmool, Warisara Parichatikanond, and Hitoshi Kurose. Therapeutic targets for treatment of heart failure: focus on grks and β-arrestins affecting βar signaling. Frontiers in Pharmacology, Nov 2018. URL: https://doi.org/10.3389/fphar.2018.01336, doi:10.3389/fphar.2018.01336. This article has 34 citations and is from a peer-reviewed journal.