## 1. Phylogeny

Extracellular serine/threonine protein kinase FAM20C belongs to the Fam20 family of atypical secretory pathway kinases, a small and evolutionarily divergent group that also comprises Fam20A and Fam20B, each having distinct yet complementary roles in the phosphorylation of secreted substrates (gersongurwitz2018ancestralrolesof pages 15-18, worby2021theabcsof pages 1-2). Unlike classical cytoplasmic kinases that display high sequence conservation within groups like the AGC, CAMK, or CMGC families, Fam20C exhibits a very different primary structure with limited sequence similarity to conventional kinases, although it retains conserved catalytic residues key for phosphoryl transfer (chen2021proteolyticprocessingof pages 1-2, zhang2018structureandevolution pages 1-2). Phylogenetic analyses indicate that the emergence of Fam20 kinases predates the diversification of metazoans and that orthologs of FAM20C can be found from invertebrate species such as Caenorhabditis elegans up to vertebrates, reflecting a fundamental role in extracellular protein regulation that has been maintained throughout evolution (gersongurwitz2018ancestralrolesof pages 1-5, worby2021theabcsof pages 2-3). In many invertebrates, a single Fam20 kinase exists that appears to display substrate specificity mimicking that of vertebrate FAM20C; in vertebrates, gene duplication events have led to the emergence of three paralogues – Fam20A, Fam20B, and Fam20C – which have specialized functions. Fam20B, for instance, has evolved to act as a xylose kinase involved in proteoglycan biosynthesis, whereas Fam20A has lost catalytic activity and instead functions as an allosteric activator of Fam20C, reinforcing the concept that extracellular phosphorylation is a tightly regulated process adapted for the secretory pathway (du2023regulationofsecretory pages 11-11, worby2021theabcsof pages 1-2). The restricted tissue expression of Fam20C, particularly in cells that participate in biomineralization such as osteoblasts and ameloblasts, further emphasizes its evolutionary adaptation for processing a subset of proteins essential for mineralized tissue formation (palmalara2021fam20coverviewclassic pages 1-2, xu2021fam20cinhuman pages 1-2).

Moreover, sequence comparisons and phylogenetic reconstructions show that despite the divergence in overall amino acid sequence, key features such as the catalytic loop, glycine-rich loop, and motifs involved in ATP binding have been conserved in FAM20C to ensure its kinase function is preserved (zhang2018structureandevolution pages 11-11, du2023regulationofsecretory pages 4-5). This evolutionary conservation suggests that FAM20C’s role in phosphorylating secreted proteins was of critical importance to early multicellular organisms, ultimately contributing to the complex regulation of the extracellular matrix and biomineralization observed in higher vertebrates (gersongurwitz2018ancestralrolesof pages 18-22, worby2021theabcsof pages 1-2). Its unique phylogenetic lineage and divergence from canonical kinases underscore a specialized evolutionary strategy that allows FAM20C to function optimally in the oxidizing environments of the Golgi and extracellular space, thereby meeting the biochemical demands of extracellular protein modification (chen2021proteolyticprocessingof pages 1-2, worby2021theabcsof pages 2-3).

## 2. Reaction Catalyzed

FAM20C catalyzes an ATP‐dependent phosphorylation reaction that is central to the post‐translational modification of secretory proteins, ensuring that a large proportion of the extracellular phosphoproteome is correctly processed (chen2021proteolyticprocessingof pages 10-11, johnson2023anatlasof pages 4-5). The chemical reaction involves the transfer of a phosphate group from ATP to the hydroxyl group of serine residues within target proteins, generating ADP and a phosphorylated protein product, along with the release of a proton (H⁺):  
  ATP + protein–(L‑serine/L‑threonine) → ADP + protein–(L‑serine/threonine‑phosphate) + H⁺ (chen2021proteolyticprocessingof pages 10-11).  
This reaction occurs predominantly within the Golgi lumen as secretory proteins traverse through the secretory pathway. FAM20C displays a strong predilection for serine residues that are situated within the canonical consensus sequence Ser–x–Glu, where “x” can be any amino acid but the presence of a glutamate at the +2 position is highly favoured, although substrates with a pre‐phosphorylated serine in that region can experience enhanced phosphorylation efficiency (johnson2023anatlasof pages 4-5, chen2021proteolyticprocessingof pages 10-11).

In addition to phosphorylating classical extracellular matrix proteins involved in biomineralization, FAM20C also targets substrates that play roles in endoplasmic reticulum (ER) function. For instance, the phosphorylation of oxidoreductase ERO1A by FAM20C is a crucial step in maintaining an appropriate redox environment in the ER that is necessary for oxidative protein folding (du2023regulationofsecretory pages 5-7, johnson2023anatlasof pages 6-7). Under conditions of ER stress, FAM20C phosphorylates protein disulfide isomerase (P4HB/PDIA1), triggering a functional switch that converts the enzyme from its oxidoreductase role to that of a chaperone; this modification is instrumental in sustaining ER proteostasis and reducing cell death by attenuating the activation of the unfolded protein response sensor ERN1 (chen2021proteolyticprocessingof pages 10-11, du2023regulationofsecretory pages 5-7). Thus, the reaction catalyzed by FAM20C not only influences extracellular matrix formation but also interconnects the extracellular secretory pathway with intracellular stress response mechanisms.

## 3. Cofactor Requirements

The catalytic activity of FAM20C is highly dependent on the availability of divalent metal ions, a common attribute among protein kinases (fulcher2020functionsandregulation pages 14-15, shrestha2023elucidatingtheunderstudied pages 95-101). Magnesium ions (Mg²⁺) are the principal cofactors required by FAM20C for efficient catalysis. Mg²⁺ facilitates the proper positioning and stabilization of ATP within the active site, neutralizing the negative charges on the phosphate groups and thus promoting efficient phosphoryl transfer to the target serine or threonine residues (du2023regulationofsecretory pages 4-5, fulcher2020functionsandregulation pages 14-15).

Although some reports have suggested that manganese (Mn²⁺) can support the activity of certain secretory pathway kinases, the biochemical evidence predominantly highlights a requirement for Mg²⁺ in the case of FAM20C, aligning it with the general mechanistic paradigm observed for most serine/threonine kinases (du2023regulationofsecretory pages 4-5, shrestha2023elucidatingtheunderstudied pages 95-101). No additional unusual cofactors or small molecular activators have been documented to be necessary for FAM20C activity, thereby underscoring a reliance on conventional divalent metal ions in its catalytic mechanism. This strict cofactor dependency is critical for ensuring the spatial and temporal regulation of extracellular phosphorylation events in the Golgi apparatus, where ion concentrations are favorable for such catalytic activity (fulcher2020functionsandregulation pages 14-15).

## 4. Substrate Specificity

FAM20C is recognized for its broad substrate specificity, with a strong predilection for phosphorylating residues within the canonical consensus motif Ser–x–Glu or a variant thereof that includes a pre-phosphorylated serine at the +2 position (chen2021proteolyticprocessingof pages 10-11, palmalara2021fam20coverviewclassic pages 1-2). This canonical motif serves as a primary signal for substrate recognition by FAM20C; however, proteomic studies have revealed that the kinase modifies a wide array of secreted proteins, indicating that its substrate preference extends beyond strict adherence to this motif (johnson2023anatlasof pages 4-5, du2023regulationofsecretory pages 11-11).

Among the well-established physiological substrates of FAM20C are secreted proteins that play pivotal roles in biomineralization processes. Notably, FAM20C phosphorylates casein, which has historically served as a marker for casein kinase activity, and a suite of enamel matrix proteins including amelogenin (AMELX), amelotin (AMTN), enamelin (ENAM), and osteopontin (SPP1/OPN); these substrates are essential for the mineralization of bone and dental tissues (chen2021proteolyticprocessingof pages 10-11, palmalara2023potentialroleof pages 24-26). In addition, FAM20C targets ER-resident proteins that transit the secretory pathway. For example, phosphorylation of ERO1A by FAM20C enhances its oxidoreductase activity, which is fundamental for proper disulfide bond formation in nascent proteins (johnson2023anatlasof pages 6-7, gersongurwitz2018ancestralrolesof pages 18-22). Furthermore, under stress conditions, FAM20C phosphorylates P4HB/PDIA1, leading to a functional switch that promotes its chaperone activity—a modification that is critical for alleviating ER stress and maintaining proteostasis (du2023regulationofsecretory pages 5-7, chen2021proteolyticprocessingof pages 10-11).

The breadth of FAM20C’s substrate recognition is supported by phosphoproteomic analyses which have identified that it is responsible for the phosphorylation of the majority of proteins found in the extracellular phosphoproteome. This expansive substrate repertoire includes proteins that, while lacking the exact consensus sequence, display a pattern of acidic or polar residues that enable binding and phosphorylation by FAM20C (johnson2023anatlasof pages 6-7, du2023regulationofsecretory pages 11-11). Thus, FAM20C demonstrates a versatile substrate specificity that is finely tuned to regulate diverse processes including biomineralization, extracellular matrix remodeling, and ER redox homeostasis.

## 5. Structure

FAM20C is characterized by a central kinase domain that adopts the typical two-lobe architecture observed in most protein kinases, with a smaller N-terminal lobe involved predominantly in ATP binding and a larger C-terminal lobe that facilitates substrate binding and catalytic activity (fulcher2020functionsandregulation pages 1-2, shrestha2023elucidatingtheunderstudied…I’llunderstudied pages 1-13). Within this kinase domain, several conserved motifs critical for function are maintained: the glycine-rich loop, which stabilizes ATP binding; the catalytic loop, which contains key residues such as aspartate and lysine for phosphotransfer; and the activation loop, which is thought to contribute to substrate recognition (zhang2018structureandevolution pages 1-2, johnson2023anatlasof pages 3-4).

Unique to FAM20C is the presence of structural insertions that distinguish it from canonical kinases. These insertions and additional surface loops are believed to extend the substrate-binding surface, thereby allowing FAM20C to accommodate a broader range of substrates beyond the strict Ser–x–Glu motif (lopez2022elucidatingthesecreteda pages 13-17, park2021anatypicalminimal pages 9-12). Moreover, structural studies—including crystallographic investigations and AlphaFold predictive modeling—have revealed that FAM20C possesses unique features tailored for functioning in the oxidizing environment of the Golgi apparatus, such as stabilization elements that may be involved in disulfide bond formation and subcellular retention (chen2021proteolyticprocessingof pages 1-2, lopez2022elucidatingthesecreteda pages 13-17).

FAM20C is further characterized by signals in its N-terminal region that drive its localization to the Golgi, ensuring that its kinase activity is confined to the secretory pathway where its substrates predominantly reside (chen2021proteolyticprocessingof pages 1-2, govitvattana2021molecularcloningof pages 8-9). One of the most distinguishing structural features of FAM20C is its ability to form oligomeric complexes. In particular, FAM20C forms complexes with Fam20A, a related but catalytically inactive pseudokinase; this association has been demonstrated to allosterically enhance FAM20C’s enzymatic activity by stabilizing its active conformation and potentially facilitating the proper orientation of substrates within its catalytic cleft (worby2021theabcsof pages 11-12, shrestha2023elucidatingtheunderstudieda pages 65-71). Such oligomerization not only contributes to efficient catalysis but also represents a regulatory mechanism by which the kinase’s activity can be modulated in response to changing cellular conditions.

In summary, the structure of FAM20C reflects a fusion of a conserved kinase core with specialized regions that tailor its function to the secretory pathway. The combination of a standard two-lobe kinase domain, unique insertions that expand substrate recognition, and Golgi-targeting signals ensures that FAM20C is optimally configured to phosphorylate a diverse array of extracellular proteins in a tightly regulated fashion (fulcher2020functionsandregulation pages 1-2, lopez2022elucidatingthesecreteda pages 13-17).

## 6. Regulation

The activity of FAM20C is subject to several layers of regulation that together ensure precise control over extracellular phosphorylation. A central regulatory mechanism involves the formation of heterooligomeric complexes with Fam20A, a catalytically inactive pseudokinase that exerts allosteric control over FAM20C. Through direct interaction, Fam20A stabilizes FAM20C and enhances its catalytic efficiency, thus enabling a more robust phosphorylation activity when high throughput modification of secretory proteins is required (worby2021theabcsof pages 11-12, shrestha2023elucidatingtheunderstudieda pages 65-71).

In addition to its allosteric regulation by Fam20A, FAM20C activity is modulated by its spatial confinement within the Golgi apparatus. This subcellular localization is mediated by specific Golgi retention signals embedded within its N-terminal region, which ensure that FAM20C remains in the vicinity of proteins transiting through the secretory pathway. Disruption of this targeting mechanism, whether by mutation or misfolding, can lead to a loss of function and has been implicated in disease conditions characterized by aberrant biomineralization (chen2021proteolyticprocessingof pages 1-2, lopez2022elucidatingthesecreteda pages 13-17).

Furthermore, FAM20C is responsive to cellular stress conditions, particularly endoplasmic reticulum (ER) stress. Under such circumstances, FAM20C phosphorylates key ER-resident proteins such as P4HB/PDIA1. This phosphorylation induces a functional switch in P4HB, converting it from an enzyme that primarily catalyzes disulfide bond formation into a molecular chaperone that assists in the proper folding of proteins under stress conditions. Consequently, this modification facilitates an adaptive response that reduces the burden of misfolded proteins and attenuates the activation of ER stress sensors like ERN1 (chen2021proteolyticprocessingof pages 10-11, du2023regulationofsecretory pages 5-7). Such regulation is critical for maintaining ER proteostasis and ensuring cell survival during periods of elevated stress.

Less extensively characterized but potentially significant are the post‐translational modifications of FAM20C itself. Although the direct evidence for autophosphorylation or other modifications such as ubiquitination is limited, it is conceivable that FAM20C may also be subject to modifications that fine‐tune its activity or turnover (fulcher2020functionsandregulation pages 14-15, shrestha2023elucidatingtheunderstudied pages 95-101). These modifications could represent additional layers of control in response to metabolic cues or changes in cellular state.

In aggregate, the regulatory mechanisms governing FAM20C involve both allosteric interactions—most notably with Fam20A—and spatial regulation dictated by Golgi localization, with further modulation occurring in response to ER stress. This multi-tiered regulation ensures that FAM20C activity is tightly coupled to the functional demands of the secretory pathway and the broader cellular context (du2023regulationofsecretory pages 5-7, worby2021theabcsof pages 12-13).

## 7. Function

FAM20C plays a critical and multifaceted role in cellular physiology through its function as the principal kinase responsible for the phosphorylation of secretory proteins. One of its most well-documented functions is its involvement in biomineralization—a process essential for the proper formation of bones and teeth. By phosphorylating a wide array of mineralization-related substrates such as casein, amelogenin (AMELX), amelotin (AMTN), enamelin (ENAM), and osteopontin (SPP1/OPN), FAM20C directly influences the deposition of calcium and the formation of hydroxyapatite crystals within the extracellular matrix, thereby driving osteoblast differentiation and mineralization (chen2021proteolyticprocessingof pages 10-11, palmalara2021fam20coverviewclassic pages 1-2). The critical role of FAM20C in biomineralization is further underscored by the observation that genetic mutations resulting in its loss-of-function lead to Raine syndrome, a severe osteosclerotic dysplasia characterized by profound skeletal defects and dental anomalies (maan2024analysisofmutations pages 15-20).

In addition to its extracellular functions, FAM20C also exerts control over intracellular processes that are intimately linked with protein folding and redox homeostasis within the endoplasmic reticulum (ER). The kinase phosphorylates ERO1A, thereby increasing the enzyme’s oxidoreductase activity that is crucial for forming correct disulfide bonds in nascent proteins, ensuring efficient oxidative protein folding (johnson2023anatlasof pages 6-7, du2023regulationofsecretory pages 5-7). Under conditions of ER stress, FAM20C targets P4HB/PDIA1 for phosphorylation, triggering a switch in P4HB function from an oxidoreductase to a molecular chaperone. This switch not only aids in the alleviation of ER stress by promoting proper protein folding but also reduces pro-apoptotic signalling which is often associated with prolonged ER stress. In this manner, FAM20C acts as an important modulator of ER proteostasis and cell survival (chen2021proteolyticprocessingof pages 10-11, du2023regulationofsecretory pages 5-7).

The impact of FAM20C extends beyond biomineralization and ER function. It also plays roles in various aspects of cellular homeostasis including lipid metabolism, cell migration, wound healing, and adhesion. The phosphorylation of secreted factors involved in these processes modulates their function and stability, thereby influencing extracellular signaling pathways that are central to tissue repair and cellular communication (johnson2023anatlasof pages 4-5, du2023regulationofsecretory pages 11-11). In tissues characterized by high secretory activity, such as the mammary gland during lactation or dental tissues during enamel formation, FAM20C’s expression is elevated, reflecting its importance in modulating the extracellular environment (chen2021proteolyticprocessingof pages 1-2, govitvattana2021molecularcloningof pages 8-9).

Moreover, by phosphorylating a diverse range of secreted proteins, FAM20C creates a complex network of extracellular signals that regulate the composition, physical properties, and functional activity of the extracellular matrix. This network is not restricted solely to the enhancement of mineralization but also includes the modulation of cell–cell interactions and signaling pathways that govern tissue development and repair. The extensive substrate range of FAM20C, which encompasses both structural matrix proteins and regulatory molecules, positions it as a central hub in the orchestration of extracellular phosphorylation events that underlie a myriad of physiological processes (johnson2023anatlasof pages 10-11, palmalara2023potentialroleof pages 24-26).

Additionally, FAM20C’s role in controlling ER redox balance through the activation of ERO1A and the modulation of chaperone function via P4HB/PDIA1 has implications for systemic protein quality control. This function is particularly vital under stress conditions when the accumulation of misfolded proteins can trigger pathological responses such as the unfolded protein response. Hence, FAM20C serves as an important link between extracellular matrix dynamics and intracellular stress response pathways, ensuring coordinated regulation of protein synthesis, folding, and secretion (du2023regulationofsecretory pages 5-7, johnson2023anatlasof pages 6-7).

Overall, FAM20C’s functions are far-reaching, encompassing the regulation of both extracellular and intracellular environments. Its precise control over the phosphorylation of secretory proteins is essential for the formation and maintenance of mineralized tissues, the management of ER stress, and the coordination of diverse signaling pathways that together sustain cellular and tissue homeostasis (chen2021proteolyticprocessingof pages 10-11, worby2021theabcsof pages 1-2).

## 8. Other Comments

Ongoing research continues to elucidate the multifaceted roles of FAM20C, making it an attractive target for therapeutic intervention in a variety of diseases. Genetic mutations that impair the catalytic activity or proper Golgi localization of FAM20C have been directly linked to Raine syndrome—a congenital disorder characterized by severe osteosclerotic bone dysplasia, craniofacial malformations, and dental defects—emphasizing the critical nature of precise extracellular phosphorylation in skeletal development (palmalara2021fam20coverviewclassic pages 1-2, maan2024analysisofmutations pages 15-20). The pathogenic manifestations of these mutations underscore the enzyme’s indispensable role in biomineralization and suggest that even subtle alterations in FAM20C activity can have profound developmental and systemic consequences.

Beyond congenital skeletal dysplasias, aberrant FAM20C activity has also been implicated in processes such as dysregulated cell migration and altered lipid metabolism, both of which are important factors in cancer progression and metastasis. Although no specific inhibitors of FAM20C have been widely adopted in clinical practice, the development of small molecules that either enhance or mimic its activity—particularly by promoting the formation of the activating Fam20A–FAM20C complex—represents a promising area of pharmacological research (venerando2022editorialcaseinkinases pages 4-5, park2019thinkingoutsideof pages 9-9).

Furthermore, the expansive substrate repertoire of FAM20C, which extends to both extracellular matrix proteins and key regulators of ER homeostasis, positions it as a potential biomarker for diverse pathological states, including metabolic disorders, impaired wound healing, and even neurodegenerative conditions where ER stress is a contributing factor. Changes in the phosphorylation status of FAM20C substrates may serve as early indicators of disease progression, thereby offering a route to early diagnosis and targeted therapy (johnson2023anatlasof pages 10-11, du2023regulationofsecretory pages 11-11).

Research into the regulation of FAM20C is also active, with studies examining both its allosteric activation by Fam20A and the potential for post‐translational modifications that might further modulate its activity. Although comprehensive details of such modifications remain to be fully elucidated, the prospect of developing allosteric activators—compounds that enhance FAM20C function by mimicking the effect of Fam20A—is particularly intriguing given that many disease states associated with FAM20C are thought to arise from a loss-of-function scenario (shrestha2023elucidatingtheunderstudieda pages 65-71, venerando2022editorialcaseinkinases pages 5-6).

The integration of extracellular phosphorylation with intracellular stress responses, as mediated by FAM20C, represents a novel paradigm in cell biology that continues to challenge traditional boundaries between intracellular and extracellular regulatory mechanisms. As our understanding deepens, it is becoming increasingly clear that FAM20C operates at a critical nexus where secretory pathway function, extracellular matrix dynamics, and ER protein quality control converge. Such insights could pave the way for innovative therapeutic approaches targeting FAM20C activity to treat a range of pathological conditions from skeletal disorders to cancer and metabolic disease (worby2021theabcsof pages 1-2, johnson2023anatlasof pages 10-11).

In summary, FAM20C serves as a central hub in the regulation of extracellular phosphorylation, with its activity being crucial for both the formation of healthy biomineralized tissues and the maintenance of ER homeostasis. Its broad substrate specificity, combined with sophisticated regulatory mechanisms involving subcellular localization and allosteric activation, underscore the enzyme’s pivotal role in ensuring systemic cellular homeostasis. The ongoing exploration of its structure–function relationships, regulatory networks, and disease associations continues to present new opportunities for both fundamental biological discovery and the development of novel clinical interventions.

## 9. References

* chen2021proteolyticprocessingof pages 1-2
* chen2021proteolyticprocessingof pages 10-11
* du2023regulationofsecretory pages 11-11
* du2023regulationofsecretory pages 4-5
* du2023regulationofsecretory pages 5-7
* fulcher2020functionsandregulation pages 1-2
* fulcher2020functionsandregulation pages 14-15
* gersongurwitz2018ancestralrolesof pages 1-5
* gersongurwitz2018ancestralrolesof pages 15-18
* gersongurwitz2018ancestralrolesof pages 18-22
* gersongurwitz2018ancestralrolesof pages 40-42
* govitvattana2021molecularcloningof pages 8-9
* johnson2023anatlasof pages 4-5
* johnson2023anatlasof pages 6-7
* lopez2022elucidatingthesecreted pages 13-17
* lopez2022elucidatingthesecreted pages 8-13
* lopez2022elucidatingthesecreteda pages 13-17
* maan2024analysisofmutations pages 15-20
* palmalara2021fam20coverviewclassic pages 1-2
* palmalara2023potentialroleof pages 24-26
* park2019thinkingoutsideof pages 1-2
* park2019thinkingoutsideof pages 9-9
* park2021anatypicalminimal pages 9-12
* shrestha2023elucidatingtheunderstudied pages 13-17
* shrestha2023elucidatingtheunderstudied pages 95-101
* shrestha2023elucidatingtheunderstudieda pages 13-17
* shrestha2023elucidatingtheunderstudieda pages 65-71
* shrestha2023…I’llunderstudied pages 1-13
* shrestha2023…I’llunderstudied pages 121-126
* shrestha2023…I’llunderstudied pages 22-27
* shrestha2023…I’llunderstudied pages 95-101
* shrestha2023…I’llunderstudieda pages 1-13
* shrestha2023…I’llunderstudieda pages 121-126
* shrestha2023…I’llunderstudieda pages 22-27
* shrestha2023…I’llunderstudieda pages 65-71
* shrestha2023…I’llunderstudieda pages 95-101
* venerando2022editorialcaseinkinases pages 4-5
* venerando2022editorialcaseinkinases pages 5-6
* worby2021theabcsof pages 1-2
* worby2021theabcsof pages 11-12
* worby2021theabcsof pages 12-13
* worby2021theabcsof pages 13-14
* worby2021theabcsof pages 2-3
* xu2021fam20cinhuman pages 1-2
* xu2021fam20cinhuman pages 7-9
* zhang2018structureandevolution pages 1-2
* zhang2018structureandevolution pages 11-11
* johnson2023anatlasof pages 1-2
* johnson2023anatlasof pages 3-4
* johnson2023anatlasof pages 10-11
* johnson2023anatlasof pages 9-10
* costa2024gingivalproteomicsreveals pages 20-21

References

1. (chen2021proteolyticprocessingof pages 1-2): Xinxin Chen, Jianchao Zhang, Pulan Liu, Yangyang Wei, Xi’e Wang, Junyu Xiao, Chih‐chen Wang, and Lei Wang. Proteolytic processing of secretory pathway kinase fam20c by site-1 protease promotes biomineralization. Proceedings of the National Academy of Sciences, Aug 2021. URL: https://doi.org/10.1073/pnas.2100133118, doi:10.1073/pnas.2100133118. This article has 24 citations.
2. (chen2021proteolyticprocessingof pages 10-11): Xinxin Chen, Jianchao Zhang, Pulan Liu, Yangyang Wei, Xi’e Wang, Junyu Xiao, Chih‐chen Wang, and Lei Wang. Proteolytic processing of secretory pathway kinase fam20c by site-1 protease promotes biomineralization. Proceedings of the National Academy of Sciences, Aug 2021. URL: https://doi.org/10.1073/pnas.2100133118, doi:10.1073/pnas.2100133118. This article has 24 citations.
3. (du2023regulationofsecretory pages 11-11): Shaonan Du, Chen Zhu, Xiaolin Ren, Xin Chen, Xiaohui Cui, and Shu Guan. Regulation of secretory pathway kinase or kinase-like proteins in human cancers. Frontiers in Immunology, Feb 2023. URL: https://doi.org/10.3389/fimmu.2023.942849, doi:10.3389/fimmu.2023.942849. This article has 3 citations and is from a peer-reviewed journal.
4. (du2023regulationofsecretory pages 4-5): Shaonan Du, Chen Zhu, Xiaolin Ren, Xin Chen, Xiaohui Cui, and Shu Guan. Regulation of secretory pathway kinase or kinase-like proteins in human cancers. Frontiers in Immunology, Feb 2023. URL: https://doi.org/10.3389/fimmu.2023.942849, doi:10.3389/fimmu.2023.942849. This article has 3 citations and is from a peer-reviewed journal.
5. (du2023regulationofsecretory pages 5-7): Shaonan Du, Chen Zhu, Xiaolin Ren, Xin Chen, Xiaohui Cui, and Shu Guan. Regulation of secretory pathway kinase or kinase-like proteins in human cancers. Frontiers in Immunology, Feb 2023. URL: https://doi.org/10.3389/fimmu.2023.942849, doi:10.3389/fimmu.2023.942849. This article has 3 citations and is from a peer-reviewed journal.
6. (fulcher2020functionsandregulation pages 1-2): Luke J. Fulcher and Gopal P. Sapkota. Functions and regulation of the serine/threonine protein kinase ck1 family: moving beyond promiscuity. Biochemical Journal, 477:4603-4621, Dec 2020. URL: https://doi.org/10.1042/bcj20200506, doi:10.1042/bcj20200506. This article has 56 citations and is from a domain leading peer-reviewed journal.
7. (fulcher2020functionsandregulation pages 14-15): Luke J. Fulcher and Gopal P. Sapkota. Functions and regulation of the serine/threonine protein kinase ck1 family: moving beyond promiscuity. Biochemical Journal, 477:4603-4621, Dec 2020. URL: https://doi.org/10.1042/bcj20200506, doi:10.1042/bcj20200506. This article has 56 citations and is from a domain leading peer-reviewed journal.
8. (gersongurwitz2018ancestralrolesof pages 1-5): Adina Gerson-Gurwitz, Carolyn A. Worby, Kian-Yong Lee, Renat Khaliullin, Jeff Bouffard, Dhanya Cheerambathur, Erin J. Cram, Karen Oegema, Jack E. Dixon, and Arshad Desai. Ancestral roles of the fam20c family of secreted protein kinases revealed by functional analysis inc. elegans. bioRxiv, Jul 2018. URL: https://doi.org/10.1101/363440, doi:10.1101/363440. This article has 2 citations.
9. (gersongurwitz2018ancestralrolesof pages 15-18): Adina Gerson-Gurwitz, Carolyn A. Worby, Kian-Yong Lee, Renat Khaliullin, Jeff Bouffard, Dhanya Cheerambathur, Erin J. Cram, Karen Oegema, Jack E. Dixon, and Arshad Desai. Ancestral roles of the fam20c family of secreted protein kinases revealed by functional analysis inc. elegans. bioRxiv, Jul 2018. URL: https://doi.org/10.1101/363440, doi:10.1101/363440. This article has 2 citations.
10. (gersongurwitz2018ancestralrolesof pages 18-22): Adina Gerson-Gurwitz, Carolyn A. Worby, Kian-Yong Lee, Renat Khaliullin, Jeff Bouffard, Dhanya Cheerambathur, Erin J. Cram, Karen Oegema, Jack E. Dixon, and Arshad Desai. Ancestral roles of the fam20c family of secreted protein kinases revealed by functional analysis inc. elegans. bioRxiv, Jul 2018. URL: https://doi.org/10.1101/363440, doi:10.1101/363440. This article has 2 citations.
11. (gersongurwitz2018ancestralrolesof pages 40-42): Adina Gerson-Gurwitz, Carolyn A. Worby, Kian-Yong Lee, Renat Khaliullin, Jeff Bouffard, Dhanya Cheerambathur, Erin J. Cram, Karen Oegema, Jack E. Dixon, and Arshad Desai. Ancestral roles of the fam20c family of secreted protein kinases revealed by functional analysis inc. elegans. bioRxiv, Jul 2018. URL: https://doi.org/10.1101/363440, doi:10.1101/363440. This article has 2 citations.
12. (govitvattana2021molecularcloningof pages 8-9): Nattanan Govitvattana, Masaru Kaku, Yoshio Ohyama, Haytham Jaha, I-Ping Lin, Hanna Mochida, Prasit Pavasant, and Yoshiyuki Mochida. Molecular cloning of mouse homologue of enamel protein c4orf26 and its phosphorylation by fam20c. Calcified Tissue International, 109:445-454, Apr 2021. URL: https://doi.org/10.1007/s00223-021-00847-y, doi:10.1007/s00223-021-00847-y. This article has 3 citations and is from a peer-reviewed journal.
13. (johnson2023anatlasof pages 4-5): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 416 citations and is from a highest quality peer-reviewed journal.
14. (johnson2023anatlasof pages 6-7): Jared L. Johnson, Tomer M. Yaron, Emily M. Huntsman, Alexander Kerelsky, Junho Song, Amit Regev, Ting-Yu Lin, Katarina Liberatore, Daniel M. Cizin, Benjamin M. Cohen, Neil Vasan, Yilun Ma, Konstantin Krismer, Jaylissa Torres Robles, Bert van de Kooij, Anne E. van Vlimmeren, Nicole Andrée-Busch, Norbert F. Käufer, Maxim V. Dorovkov, Alexey G. Ryazanov, Yuichiro Takagi, Edward R. Kastenhuber, Marcus D. Goncalves, Benjamin D. Hopkins, Olivier Elemento, Dylan J. Taatjes, Alexandre Maucuer, Akio Yamashita, Alexei Degterev, Mohamed Uduman, Jingyi Lu, Sean D. Landry, Bin Zhang, Ian Cossentino, Rune Linding, John Blenis, Peter V. Hornbeck, Benjamin E. Turk, Michael B. Yaffe, and Lewis C. Cantley. An atlas of substrate specificities for the human serine/threonine kinome. Nature, 613:759-766, Jan 2023. URL: https://doi.org/10.1038/s41586-022-05575-3, doi:10.1038/s41586-022-05575-3. This article has 416 citations and is from a highest quality peer-reviewed journal.
15. (lopez2022elucidatingthesecreted pages 13-17): VA Lopez. Elucidating the secreted bacterial kinome. Unknown journal, 2022.
16. (lopez2022elucidatingthesecreted pages 8-13): VA Lopez. Elucidating the secreted bacterial kinome. Unknown journal, 2022.
17. (lopez2022elucidatingthesecreteda pages 13-17): VA Lopez. Elucidating the secreted bacterial kinome. Unknown journal, 2022.
18. (maan2024analysisofmutations pages 15-20): Shivani Maan. Analysis of mutations in protein kinase CK2 linked to Okur-Chung’s Neuropathy. PhD thesis, West Virginia University Libraries, 2024. URL: https://doi.org/10.33915/etd.12375, doi:10.33915/etd.12375.
19. (palmalara2021fam20coverviewclassic pages 1-2): Icela Palma-Lara, Monserrat Pérez-Ramírez, Patricia García Alonso-Themann, Ana María Espinosa-García, Ricardo Godinez-Aguilar, José Bonilla-Delgado, Adolfo López-Ornelas, Georgina Victoria-Acosta, María Guadalupe Olguín-García, José Moreno, and Carmen Palacios-Reyes. Fam20c overview: classic and novel targets, pathogenic variants and raine syndrome phenotypes. International Journal of Molecular Sciences, 22:8039, Jul 2021. URL: https://doi.org/10.3390/ijms22158039, doi:10.3390/ijms22158039. This article has 25 citations and is from a peer-reviewed journal.
20. (palmalara2023potentialroleof pages 24-26): Icela Palma-Lara, Patricia García Alonso-Themann, Javier Pérez-Durán, Ricardo Godínez-Aguilar, José Bonilla-Delgado, Damián Gómez-Archila, Ana María Espinosa-García, Manuel Nolasco-Quiroga, Georgina Victoria-Acosta, Adolfo López-Ornelas, Juan Carlos Serrano-Bello, María Guadalupe Olguín-García, and Carmen Palacios-Reyes. Potential role of protein kinase fam20c on the brain in raine syndrome, an in silico analysis. International Journal of Molecular Sciences, 24:8904, May 2023. URL: https://doi.org/10.3390/ijms24108904, doi:10.3390/ijms24108904. This article has 2 citations and is from a peer-reviewed journal.
21. (park2019thinkingoutsideof pages 1-2): Brenden C. Park, Michael Reese, and Vincent S. Tagliabracci. Thinking outside of the cell: secreted protein kinases in bacteria, parasites, and mammals. IUBMB Life, 71:749-759, Apr 2019. URL: https://doi.org/10.1002/iub.2040, doi:10.1002/iub.2040. This article has 16 citations and is from a peer-reviewed journal.
22. (park2019thinkingoutsideof pages 9-9): Brenden C. Park, Michael Reese, and Vincent S. Tagliabracci. Thinking outside of the cell: secreted protein kinases in bacteria, parasites, and mammals. IUBMB Life, 71:749-759, Apr 2019. URL: https://doi.org/10.1002/iub.2040, doi:10.1002/iub.2040. This article has 16 citations and is from a peer-reviewed journal.
23. (park2021anatypicalminimal pages 9-12): BC Park. An atypical minimal kinase inactivates the molecular chaperone hsp90. Unknown journal, 2021.
24. (shrestha2023elucidatingtheunderstudied pages 13-17): S Shrestha. Elucidating the understudied fructosamine-3-kinase (fn3k) family: a combined experimental and computational study on structure, function, evolution, and …. Unknown journal, 2023.
25. (shrestha2023elucidatingtheunderstudied pages 95-101): S Shrestha. Elucidating the understudied fructosamine-3-kinase (fn3k) family: a combined experimental and computational study on structure, function, evolution, and …. Unknown journal, 2023.
26. (shrestha2023elucidatingtheunderstudieda pages 13-17): S Shrestha. Elucidating the understudied fructosamine-3-kinase (fn3k) family: a combined experimental and computational study on structure, function, evolution, and …. Unknown journal, 2023.
27. (shrestha2023elucidatingtheunderstudieda pages 65-71): S Shrestha. Elucidating the understudied fructosamine-3-kinase (fn3k) family: a combined experimental and computational study on structure, function, evolution, and …. Unknown journal, 2023.
28. (venerando2022editorialcaseinkinases pages 4-5): Andrea Venerando, Victor H. Bustos, Lorenzo A. Pinna, and Giorgio Cozza. Editorial: casein kinases in human diseases. Frontiers in Molecular Biosciences, Dec 2022. URL: https://doi.org/10.3389/fmolb.2022.1094922, doi:10.3389/fmolb.2022.1094922. This article has 2 citations and is from a peer-reviewed journal.
29. (venerando2022editorialcaseinkinases pages 5-6): Andrea Venerando, Victor H. Bustos, Lorenzo A. Pinna, and Giorgio Cozza. Editorial: casein kinases in human diseases. Frontiers in Molecular Biosciences, Dec 2022. URL: https://doi.org/10.3389/fmolb.2022.1094922, doi:10.3389/fmolb.2022.1094922. This article has 2 citations and is from a peer-reviewed journal.
30. (worby2021theabcsof pages 1-2): Carolyn A. Worby, Joshua E. Mayfield, Adam J. Pollak, Jack E. Dixon, and Sourav Banerjee. The abcs of the atypical fam20 secretory pathway kinases. Journal of Biological Chemistry, 296:100267, Jan 2021. URL: https://doi.org/10.1016/j.jbc.2021.100267, doi:10.1016/j.jbc.2021.100267. This article has 34 citations and is from a domain leading peer-reviewed journal.
31. (worby2021theabcsof pages 11-12): Carolyn A. Worby, Joshua E. Mayfield, Adam J. Pollak, Jack E. Dixon, and Sourav Banerjee. The abcs of the atypical fam20 secretory pathway kinases. Journal of Biological Chemistry, 296:100267, Jan 2021. URL: https://doi.org/10.1016/j.jbc.2021.100267, doi:10.1016/j.jbc.2021.100267. This article has 34 citations and is from a domain leading peer-reviewed journal.