## Phylogeny

• Assigned to the NKF1 subgroup within the “Other” clade of the human kinome according to catalytic-domain phylogeny (manning2002theproteinkinase pages 3-3).  
• Paralogue cluster comprises SBK1, SBK2 and SBK3, demonstrating close evolutionary relationship within NKF1 (hanks2003genomicanalysisof pages 5-6).  
• Comparative kinome analyses indicate the presence of SBK2 orthologs in mouse, rat, zebrafish and Drosophila, although specific identifiers were not listed in the primary sources (manning2002theproteinkinase pages 2-3).

## Reaction Catalyzed

ATP + [protein]-L-Ser/Thr ⇌ ADP + [protein]-O-phospho-L-Ser/Thr (hanks2003genomicanalysisof pages 1-2).

## Cofactor Requirements

No experimental data on divalent-metal dependence have been reported for SBK2 (essegian2020theclinicalkinase pages 10-11).

## Substrate Specificity

• Global consensus phosphorylation motif: not determined (johnson2023anatlasof pages 4-4).  
• Johnson et al. report SBK2 as the 8th-ranked kinase for phosphorylation of PDHA1 Ser293 within the sequence RYHGHSMSDP (98.48 percentile), indicating potential recognition of a basic motif context (johnson2023anatlasof pages 21-23).

## Structure

• Architecture: single bilobal serine/threonine kinase domain (~250 aa) with N-terminal β-sheet lobe and C-terminal α-helical lobe connected by the hinge (unknownauthors2022datadrivencomputational pages 83-88).  
• Conserved catalytic features: Lys in subdomain II, HRD motif in subdomain VIB and DFG motif at the N-terminus of the activation loop are present in the UniProt sequence and predicted structure (unknownauthors2014creationandcharacterization pages 14-15).  
• Structural data: no experimental PDB entry; a high-confidence AlphaFold model (pLDDT > 70 for the kinase core) provides full-length coordinates and residue-level confidence (tunyasuvunakool2021highlyaccurateprotein pages 1-2).  
• Model confidence and absence of resolved structures confirmed by the PDB coverage analysis referenced by AlphaFold authors (tunyasuvunakool2021highlyaccurateprotein pages 6-7).  
• Regulatory elements (activation loop phosphorylation sites, hydrophobic spine integrity, C-helix orientation) have not yet been experimentally verified (unknownauthors2022datadrivencomputational pages 83-88).

## Regulation

• Curated post-translational modifications: none reported for SBK2 in PhosphoSitePlus or peer-reviewed literature (johnson2023anatlasof pages 12-18).  
• Enzymes responsible for SBK2 modification, allosteric regulators and conformational control mechanisms remain uncharacterised (essegian2020theclinicalkinase pages 10-11, unknownauthors2022datadrivencomputational pages 30-34).

## Function

• Expression: SBK2 is categorised as a “Tdark” kinase with limited mRNA/protein expression data; GTEx and Human Protein Atlas information were not provided in the cited sources (essegian2020theclinicalkinase pages 10-11).  
• Protein–protein interactors and pathway assignments are currently undocumented in large-scale AP-MS datasets referenced (unknownauthors2022datadrivencomputational pages 30-34).  
• Genetic alteration: focal copy-number amplification (~3 % of breast-cancer cases) and broader TCGA analyses link elevated SBK2 dosage to poorer overall and progression-free survival (unknownauthors2022datadrivencomputational pages 30-34).  
• Clinical Kinase Index ranks SBK2 as prognostic across multiple tumour types, underscoring its potential oncogenic relevance (essegian2020theclinicalkinase pages 10-11).

## Other Comments

• No biochemical inhibitor profiling data (Davis2011, Anastassiadis2011 or subsequent large-scale panels) include SBK2, leaving inhibitor sensitivity unknown (gehringer2021covalentkinaseinhibitors pages 47-49).  
• The paucity of structural, biochemical and regulatory information positions SBK2 as a high-priority target for foundational kinase research (essegian2020theclinicalkinase pages 10-11).

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