## Phylogeny

Assigned to the NKF1 subgroup within the “Other” clade of the human kinome (Manning et al., 2002). The paralogue cluster contains SBK1, SBK2 and SBK3, indicating a close evolutionary relationship inside NKF1 (Hanks, 2003). Comparative kinome surveys report SBK2 orthologues in mouse, rat, zebrafish and Drosophila, although specific gene identifiers were not detailed (Manning et al., 2002).

## Reaction Catalyzed

ATP + [protein]-L-Ser/Thr ⇌ ADP + [protein]-O-phospho-L-Ser/Thr (Hanks, 2003).

## Cofactor Requirements

Divalent-metal dependence has not been experimentally determined (Essegian et al., 2020).

## Substrate Specificity

A global consensus motif has not yet been defined (Johnson et al., 2023). In peptide-array profiling, SBK2 ranked 8th for phosphorylation of PDHA1 Ser293 within RYHGHSMSDP (98.48 percentile), suggesting possible recognition of a basic sequence context (Johnson et al., 2023).

## Structure

The protein comprises a single bilobal serine/threonine kinase domain (~250 aa) with canonical Lys in subdomain II, HRD in subdomain VIB and DFG at the activation-loop N-terminus (Unknown Authors, 2014). No experimental structures are available; an AlphaFold model provides full-length coordinates with pLDDT > 70 across the catalytic core (Tunyasuvunakool et al., 2021). Regulatory elements such as activation-loop phosphorylation status, hydrophobic-spine integrity and C-helix orientation remain unverified (Unknown Authors, 2022).

## Regulation

No post-translational modifications, allosteric regulators or conformational control mechanisms have been reported (Essegian et al., 2020; Johnson et al., 2023; Unknown Authors, 2022).

## Function

SBK2 is categorised as a “Tdark” kinase with limited expression information; GTEx or Human Protein Atlas data were not cited (Essegian et al., 2020). Protein–protein interactors and pathway assignments are currently undocumented (Unknown Authors, 2022). Genomic analyses show focal copy-number amplification in ~3 % of breast-cancer cases, and increased SBK2 dosage correlates with reduced overall and progression-free survival in TCGA datasets (Unknown Authors, 2022). The Clinical Kinase Index identifies SBK2 as prognostic in multiple tumour types (Essegian et al., 2020).

## Other Comments

SBK2 has not been included in large-scale biochemical inhibitor panels; inhibitor sensitivity therefore remains unknown (Gehringer, 2021). The scarcity of structural, biochemical and regulatory data positions SBK2 as a high-priority target for foundational kinase research (Essegian et al., 2020).

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