Phylogeny  
• Member of the group G branch of the human kinome; classified as a class 1 pseudokinase because the kinase‐like domain lacks the canonical VAIK, HRD and DFG motifs (Kerr & Wilson, 2013; Murphy et al., 2014).  
• Forms a distinct NRBP1/NRBP2 clade within the “other/atypical” sector of the kinome (Yang W. et al., 2024).  
• Orthologue conservation: Homo sapiens vs Mus musculus 98.3 % identity; Caenorhabditis elegans 60.7 %; Drosophila melanogaster 53.8 % (Kerr & Wilson, 2013).

Reaction Catalyzed  
No protein-serine/threonine kinase activity is detected; NRBP1 does not catalyse ATP-dependent phosphoryl transfer (Murphy et al., 2014).

Cofactor Requirements  
No requirement for Mg²⁺, Mn²⁺ or other divalent cations has been observed (Murphy et al., 2014).

Substrate Specificity  
A phosphorylation consensus motif is undefined because NRBP1 is catalytically inactive (Murphy et al., 2014).

Structure  
• Modular organisation: SH2-interaction segment (aa 1–70), NES (aa 121–129), pseudokinase domain (aa 73–327), NLS (aa 163–181), BC-box for Elongin B/C binding (aa 332–341), LisH/Cullin region, MLF1-binding segment (aa 406–479), two LXXLL motifs (aa 462–466; 507–511) and a TSC22-binding module (Kerr & Wilson, 2013; Yang X. et al., 2023).  
• AlphaFold models retain the bilobal kinase scaffold but confirm loss of the β3 catalytic lysine, HRD aspartate and DFG motif, abolishing the regulatory spine and the C-helix salt bridge (Yang X. et al., 2023).  
• Thermal-shift assays show no binding to ATP, ADP or divalent cations, corroborating structural incompetence for catalysis (Murphy et al., 2014).  
• The exposed BC-box provides a docking surface for CRL5 E3 ligase assembly, a feature absent from active kinases (Kerr & Wilson, 2013).

Regulation  
• Phosphorylation: multiple sites reported by phospho-proteomics; individual sites and upstream kinases remain unmapped (Yang X. et al., 2023).  
• Ubiquitination: the BC-box recruits Elongin B/C and CUL5, positioning NRBP1 as a substrate-recognition module of CRL5; CRL2 and CRL4A complexes contribute to NRBP1 turnover (Kerr & Wilson, 2013; Magaña-Ávila et al., 2024).  
• Osmotic stress: binding to WNK kinases modulates CRL5 association during osmotic adaptation (Amnekar et al., 2024).  
• Nucleocytoplasmic shuttling is directed by intrinsic NES and NLS signals (Kerr & Wilson, 2013).

Function  
• Expression: ubiquitous across mammalian tissues (Kerr & Wilson, 2013).  
• Development: Nrbp1-null mice die at embryonic day 7.5, indicating an essential embryonic role (Kerr & Wilson, 2013).  
• Intestine: conditional knockout causes crypt elongation, increased progenitor proliferation and elevated Wnt-responsive gene expression (Kerr & Wilson, 2013).  
• Ubiquitination adaptor: acts as the substrate selector in CRL5 complexes (Kerr & Wilson, 2013).  
• Trafficking: binds activated Rac3 to influence ER-to-Golgi transport (Kerr & Wilson, 2013).  
• Oncogenic signalling: scaffolds P-Rex1 with Rac1/Cdc42, enhancing ROS production, migration and metastasis in triple-negative breast cancer (Yang X. et al., 2023); promotes PI3K/AKT-dependent malignancy in glioblastoma (Zhang et al., 2024).  
• Osmoregulation: associates with WNK kinases to modulate distal convoluted tubule signalling (Amnekar et al., 2024; Magaña-Ávila et al., 2024).  
• Viral replication: interacts with dengue virus NS3, altering intracellular membrane architecture (Yang X. et al., 2023).  
• Transcription: binds JAB1 to repress AP-1 activity (Kerr & Wilson, 2013).

Other Comments  
• Tumour context-dependence: down-regulation correlates with poor survival in lung and colorectal adenocarcinomas and cooperates with oncogenic KRAS, whereas over-expression drives proliferation and invasion in triple-negative breast, bladder and prostate cancers (Kerr & Wilson, 2013; Yang X. et al., 2023).  
• Functional interplay with the paralogue NRBP2 regulates LINE-1 retrotransposition, accounting for tissue-specific phenotypes (Yang W. et al., 2024).

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