## Phylogeny

• Kinome assignment: STE group → Germinal Center Kinase subfamily 6 (GCK-VI) within the Ste20-like serine/threonine kinases (serafim2021discoveryofa pages 1-6, thiriet2013cytoplasmicproteinserinethreonine pages 11-14).  
• Closest human paralog: SLK, sharing 76–84 % identity in the kinase domain and 61–70 % in the coiled-coil region (unknownauthors2020investigationofresistance pages 26-31, serafim2021discoveryofa pages 1-6).  
• Verified vertebrate orthologs: mouse LOK (98 % identity in the kinase domain), rat Stk10, zebrafish Stk10 (unknownauthors2020investigationofresistance pages 26-31, serafim2021discoveryofa pages 43-46).  
• Invertebrate orthologs: Drosophila Slik and Caenorhabditis elegans GCK-3, demonstrating conservation across metazoa (serafim2021discoveryofa pages 43-46, leroy2016caspasecleavagesof pages 14-14).

## Reaction Catalyzed

ATP + [protein]-L-Ser/Thr ⇌ ADP + [protein]-O-phospho-L-Ser/Thr (serafim2021discoveryofa pages 22-25).

## Cofactor Requirements

Mg²⁺ is required for catalytic activity as used in in-vitro kinase assays (serafim2021discoveryofa pages 22-25).

## Substrate Specificity

• Cellular substrates: ezrin, radixin and moesin (phosphorylation of moesin Thr558 is a standard read-out) (leroy2016caspasecleavagesof pages 1-2, serafim2021discoveryofa pages 22-25).  
• Additional substrates: vimentin Ser56 and PLK1 in vitro (serafim2021discoveryofa pages 43-46, unknownauthors2020investigationofresistance pages 26-31).  
• Motif profiling: STK10 was included in the 2023 kinome atlas; a distinct consensus motif was reported but exact sequence information is not present in the excerpt (serafim2021discoveryofa pages 46-48).

## Structure

• Domain organisation: N-terminal kinase domain (≈ residues 1–300), a proline-rich segment, and a long C-terminal coiled-coil lacking a CRIB motif (thiriet2013cytoplasmicproteinserinethreonine pages 11-14, unknownauthors2020investigationofresistance pages 26-31).  
• Crystal structure: isolated kinase domain (PDB 2J7T) shows activation-segment exchange dimerisation that drives trans-autophosphorylation (goldsmith2007substrateanddocking pages 5-6).  
• Catalytic motifs: VAIK Lys49, HRD Asp158, DFG Asp176; autophosphorylation site Thr183 resides in the activation loop (goldsmith2007substrateanddocking pages 5-6).  
• Regulatory cleavage: Asp332 marks a caspase-3 site separating kinase and coiled-coil regions (goldsmith2007substrateanddocking pages 5-6).  
• Inhibitor complex: co-crystal with a 3-anilino-4-arylmaleimide (compound 56) reveals bifurcated hinge hydrogen bonds (E111/C113) and displacement of the glycine-rich loop (serafim2021discoveryofa pages 11-15).  
• Membrane-targeting feature: basic residues adjacent to αG participate in a PIP₂-dependent wedge that confines activity to the cortical membrane (serafim2021discoveryofa pages 43-46).

## Regulation

• Autophosphorylation on Thr183 enhances catalytic output (goldsmith2007substrateanddocking pages 5-6).  
• Activation-segment exchange homodimer augments activity (goldsmith2007substrateanddocking pages 5-6).  
• Caspase-3 cleavage at Asp332 during apoptosis abolishes ERM phosphorylation (leroy2016caspasecleavagesof pages 1-2).  
• Spatial regulation: PIP₂-anchored wedge restricts kinase action to apical cortex and lymphocyte uropod (serafim2021discoveryofa pages 43-46).  
• Signalling cross-talk: functions as a negative modulator of MAP3K1/MEKK1 (annunziata2020phosphorylationsitesin pages 22-24).

## Function

• Expression: highest in spleen, thymus and bone marrow, predominantly in lymphocytes (leroy2016caspasecleavagesof pages 1-2, thiriet2013cytoplasmicproteinserinethreonine pages 11-14).  
• Cytoskeletal control: ERM phosphorylation maintains cortical rigidity, microvilli structure and drives lymphocyte migration (leroy2016caspasecleavagesof pages 14-14, serafim2021discoveryofa pages 1-6).  
• Cell-cycle interface: associates with and phosphorylates PLK1, linking STK10 to G2/M progression (unknownauthors2020investigationofresistance pages 26-31, thiriet2013cytoplasmicproteinserinethreonine pages 11-14).  
• MAPK pathway modulation: suppresses MAP3K1/MEKK1 signalling (annunziata2020phosphorylationsitesin pages 22-24).  
• Broader interactome: proximity labelling detects KRAS, RHOA, RHOB and adaptor CRKL, situating STK10 in Rho/Ras cytoskeletal networks (unknownauthors2023profilingtheinteractome pages 93-98).

## Inhibitors

• 3-Anilino-4-arylmaleimide series: compound 31, enzymatic IC₅₀ ≈ 12 nM; cellular IC₅₀ ≈ 1.4 µM; co-crystal data confirm ATP-site binding (serafim2021discoveryofa pages 15-18, serafim2021discoveryofa pages 11-15).

## Other Comments

• Cancer-associated missense mutation R634H in the coiled-coil abrogates NF-κB suppression and confers anti-apoptotic activity in peripheral T-cell lymphoma (unknownauthors2020investigationofresistance pages 26-31, leroy2016caspasecleavagesof pages 14-14).  
• Stk10 knockout mice exhibit accelerated tumour growth due to tumour-microenvironment dysregulation (ma2022stk10deficiencyin pages 13-14).  
• STK10 depletion sensitises triple-negative breast-cancer cells to the PI3Kα inhibitor BYL-719 (unknownauthors2020investigationofresistance pages 60-67).

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