## Phylogeny

• Kinome assignment: MATK is classified in the Tyrosine Kinase (TK) group, CSK family, based on catalytic-domain phylogeny of the human kinome (manning2002theproteinkinase pages 3-3).  
• Evolutionary branch: MATK shares ~50 % sequence identity with CSK and forms a distinct sub-branch with CSK within the non-receptor TKs possessing SH3-SH2-kinase topology (unknownauthors2015cskhomologouskinase(chkmatk) pages 12-18).  
• Orthologs: mouse Matk (Chr 8), chicken Matk, and zebrafish matk have been annotated and cluster with human MATK in the CSK lineage (unknownauthors2015cskhomologouskinase(chkmatk) pages 1-5).  
• Nomenclature consolidation: proteins previously termed LSK and HYL derive from the same MATK locus located at 19q13.3 (grgurevich1997thecsklikeproteins pages 1-3).  
• Comparative tools: multiple-sequence alignment resources (KinView) confirm conservation of catalytic HRD and DFG motifs across MATK orthologs (mcskimming2016kinviewavisual pages 3-4).

## Reaction Catalyzed

ATP + Src-family kinase [C-terminal Tyr] ⇌ ADP + Src-family kinase [C-terminal phospho-Tyr] (unknownauthors2015cskhomologouskinase(chkmatk) pages 1-5).

## Cofactor Requirements

Catalysis requires divalent Mg²⁺ coordinated by the conserved DFG-Asp (Asp-370) within the activation loop (unknownauthors2015cskhomologouskinase(chkmatk) pages 22-24).

## Substrate Specificity

• Primary targets: conserved C-terminal regulatory tyrosines of Src-family kinases including Src, Lyn, and Lck (unknownauthors2015cskhomologouskinase(chkmatk) pages 12-18).  
• Additional validated substrate: β-synuclein in neuronal tissue (unknownauthors2015cskhomologouskinase(chkmatk) pages 9-12).  
• Consensus requirement: a C-terminal tail bearing the inhibitory tyrosine preceded by hydrophobic residues typical of SFK autoinhibition; no broader linear motif has been defined in the cited literature (unknownauthors2015cskhomologouskinase(chkmatk) pages 12-18).

## Structure

• Domain architecture: N-terminal SH3 domain (residues 1–60), SH2 domain (≈61–150), flexible linker, and a C-terminal bilobed kinase domain (≈170–510); the p56 isoform contains an additional 41-residue N-terminal extension absent in the p52 neuronal isoform (unknownauthors2015cskhomologouskinase(chkmatk) pages 5-7, grgurevich1997thecsklikeproteins pages 3-4).  
• 3D model: homology modelling using the CSK crystal structure positions the glycine-rich loop (Gly-241–Gly-246), Lys-262–Glu-276 ion pair, catalytic loop HRDLAARN (His-352–Asn-359), DFG motif (Asp-370–Gly-372) and the activation loop (Asp-370–Glu-390) in canonical orientations (unknownauthors2015cskhomologouskinase(chkmatk) pages 22-24).  
• Regulatory surface: a unique non-catalytic interface on the N-lobe and αD/αF-αG regions mediates high-affinity binding to active SFK conformations, a property absent in CSK (unknownauthors2015cskhomologouskinase(chkmatk) pages 12-18).  
• Isoform feature: the 41-residue extension of p56 carries a nuclear localisation signal critical for nuclear accumulation in T-cell lymphoma (unknownauthors2015cskhomologouskinase(chkmatk) pages 5-7).

## Regulation

• Transcriptional: SCF (50-100 ng ml⁻¹) and PMA strongly up-regulate MATK mRNA (peak 6 h) and protein (peak 12 h) in the megakaryoblastic line M07e (grgurevich1997thecsklikeproteins pages 9-11).  
• Epigenetic: CpG-rich promoter undergoes hypermethylation in colorectal cancer, glioma, and acute lymphoblastic leukemia, leading to loss of expression (unknownauthors2015cskhomologouskinase(chkmatk) pages 5-7, unknownauthors2015cskhomologouskinase(chkmatk) pages 18-22).  
• Post-translational: MATK lacks activating autophosphorylation; ATP binding alone is required for adoption of the inhibitory conformation that engages active SFKs (unknownauthors2015cskhomologouskinase(chkmatk) pages 7-9).  
• Subcellular targeting: the SH2 domain binds phosphotyrosine motifs on receptors such as c-Kit and TrkA, recruiting MATK to membrane micro-domains; absence of N-terminal myristoylation keeps the kinase predominantly cytosolic until engagement (unknownauthors2015cskhomologouskinase(chkmatk) pages 5-7, radhakrishnan2011igfistimulatescooperative pages 13-14).

## Function

• Expression: high in neurons and hematopoietic cells; moderate in small intestine, colon, lung, and stomach (unknownauthors2015cskhomologouskinase(chkmatk) pages 1-5).  
• Upstream signalling: SCF/c-Kit in megakaryocytes, IGF-I receptor and TrkA in neuronal or vascular smooth-muscle contexts recruit MATK via SH2 interactions (grgurevich1997thecsklikeproteins pages 9-11, radhakrishnan2011igfistimulatescooperative pages 13-14).  
• Downstream effectors: catalytic phosphorylation plus non-catalytic binding suppress Src, Lyn, and Lck activities, thereby attenuating MAPK and Akt cascades and restraining T-cell proliferation and hematopoietic cell spreading (unknownauthors2015cskhomologouskinase(chkmatk) pages 12-18, radhakrishnan2011igfistimulatescooperative pages 13-14).

## Other Comments

• Cancer biology: MATK is frequently down-regulated or mutated in colorectal, lung, gastric, breast, skin, endometrial, and ovarian cancers; missense mutations in the glycine-rich loop (E243A), αC-helix (T277M), catalytic loop (R356H) and activation loop (D370N, R385Q) abolish kinase activity or disrupt SFK binding (unknownauthors2015cskhomologouskinase(chkmatk) pages 22-24, unknownauthors2015cskhomologouskinase(chkmatk) pages 18-22).  
• Diagnostic use: nuclear localisation of the p52 isoform serves as a marker for type II enteropathy-associated T-cell lymphoma (unknownauthors2015cskhomologouskinase(chkmatk) pages 12-18).

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