## Phylogeny

TESK1 belongs to the TESK family within the TKL (tyrosine-kinase-like) super-group according to the original kinome survey (Manning et al., 2002). A minority view places it in the AGC group (Johnson et al., 2023; Toshima et al., 2001b). TESK1 and TESK2 cluster tightly with LIMK1/2, forming the LIMK/TESK sub-family (Toshima et al., 2001c). The kinase domain shares 71 % identity with TESK2, and 44 % and 40 % with LIMK1 and LIMK2 respectively (Toshima et al., 2001c). Conserved exon/intron boundaries indicate TESK1 and TESK2 arose by gene duplication (Toshima et al., 2001c). Orthologues are present in mouse, fly and worm (Manning et al., 2002).

## Reaction Catalyzed

ATP + L-seryl/threonyl-[protein] ⇄ ADP + O-phospho-L-seryl/threonyl-[protein]  
(Primary activity; Toshima et al., 2001a)

A tyrosine phosphorylation reaction (ATP + L-tyrosyl-[protein] ⇄ ADP + O-phospho-L-tyrosyl-[protein]) has been annotated in databases, but no experimental confirmation is available (Toshima et al., 2001a).

## Cofactor Requirements

Catalysis requires a divalent metal ion; activity has been demonstrated with Mg²⁺ or Mn²⁺ (Toshima et al., 2001c).

## Substrate Specificity

No consensus phosphorylation motif has yet been defined for TESK1 (Johnson et al., 2023).

## Structure

The protein comprises an N-terminal serine/threonine kinase domain and a C-terminal proline-rich regulatory segment containing three conserved regions (CR1–CR3) (Toshima et al., 2001a; 2001c). Deleting the C-terminal segment relieves auto-inhibition and increases activity 2–4-fold (Toshima et al., 2001a). Key features include:  
• Catalytic Asp-170—mutation to Ala abolishes activity (Toshima et al., 2001b).  
• An atypical DLTSKN motif in sub-domain VIB.  
• An alanine (rather than a phosphorylatable Thr) in the activation loop position equivalent to LIMK activation sites (Toshima et al., 2001c).  
No X-ray or AlphaFold structural models are reported in the cited literature.

## Regulation

• Binding of 14-3-3β to phosphorylated Ser-439 (RCRSLP motif in CR3) suppresses kinase activity (Toshima et al., 2001a).  
• The upstream kinase(s) for Ser-439 are unknown; reports disagree on whether TESK1 can autophosphorylate this site (Toshima et al., 2001a).  
• Autophosphorylation at Ser-215 within the activation loop enhances activity (Toshima et al., 2001b).  
• Cell adhesion to fibronectin via integrins decreases 14-3-3β binding and concomitantly elevates TESK1 activity (Toshima et al., 2001a).

## Function

Expression: Highly abundant in testicular germ cells from pachytene spermatocytes to early spermatids; lower expression in various other tissues and cultured cell lines (Toshima et al., 2001c; 2001a).  
Localization: Predominantly cytoplasmic with dense perinuclear staining (Toshima et al., 2001b).  
Downstream substrate: Phosphorylates cofilin/ADF on Ser-3, thereby inactivating its actin-severing function and promoting actin stress-fiber and focal-adhesion formation (Toshima et al., 2001b).  
Upstream signalling: Activated by integrin-mediated pathways and is not regulated by Rho-family GTPases, ROCK or PAK (Toshima et al., 2001b).  
Key interactor: 14-3-3β (Toshima et al., 2001a).

## Other Comments

No disease associations or chemical inhibitors are described in the cited literature.

## References

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