## Phylogeny

• Tyrosine-protein kinase Tec is classified in the TK group, Tec family, which comprises Tec, Btk, Itk, Txk/Rlk and Bmx; this clade is distinguished from Src kinases by an N-terminal PH–TH module and absence of a C-terminal regulatory phosphotyrosine (unknownauthors2009conformationalsnapshotsof pages 1-2).  
• Paralogous duplication on human chromosome 4p12 produced the adjacent TEC and TXK loci (mano1999tecfamilyof pages 2-3).  
• Experimentally verified vertebrate orthologs include murine Tec (prototype cloned from mouse liver) and additional fish homologs detected in phylogenetic surveys (mano1999tecfamilyof pages 2-3, unknownauthors2025dimerizationofthe pages 26-28).  
• An invertebrate ortholog is the Drosophila Bruton’s tyrosine kinase–like protein, required for fly viability, indicating conservation back to pre-metazoan ancestry (unknownauthors2025dimerizationofthe pages 26-28).  
• Catalytic domain architecture and regulatory logic more closely resemble Csk than Src because activation depends on positive input from regulatory domains rather than de-repression of a C-terminal tail (bradshaw2010thesrcsyk pages 6-6).

## Reaction Catalyzed

protein-L-tyrosine + ATP → protein-L-tyrosine-phosphate + ADP + H⁺ (unknownauthors2009conformationalsnapshotsof pages 1-2).

## Cofactor Requirements

• Requires divalent Mg²⁺ for nucleotide binding and catalysis; Mn²⁺ can substitute in vitro (unknownauthors2009conformationalsnapshotsof pages 15-16).

## Substrate Specificity

• No stringent linear consensus has been defined; catalytic efficiency relies on substrate docking via basic surfaces on substrate SH2 domains that engage an acidic patch on the kinase N-lobe (unknownauthors2009conformationalsnapshotsof pages 9-11).  
• Representative sites: autophosphorylation of Y180 within the Tec SH3 domain and phosphorylation of PLC-γ1 Y783, both requiring adjacent SH2 domains for productive orientation (unknownauthors2009conformationalsnapshotsof pages 9-11).

## Structure

• Domain organization: PH (lipid binding) – TH (Btk zinc-binding motif + dual PRRs) – SH3 – SH2 – kinase (SH1) (unknownauthors2009conformationalsnapshotsof pages 2-4).  
• High-resolution structures exist for:  
– PH-TH region (Btk, PDB 1b55) showing zinc-stabilized fold (unknownauthors2009conformationalsnapshotsof pages 20-23).  
– Tec SH3 domain (PDB 1gl5) with canonical hydrophobic groove (unknownauthors2009conformationalsnapshotsof pages 20-23).  
– Tec-family SH2 domains homologous to Itk SH2 (PDB 2etz) that bind phosphotyrosine peptides (unknownauthors2009conformationalsnapshotsof pages 20-23).  
– Kinase domains of Btk/Itk (PDB 1k2p, 1sm2) displaying conserved catalytic motifs VAIK-HRD-DFG (unknownauthors2009conformationalsnapshotsof pages 20-23, unknownauthors2009conformationalsnapshotsof pages 1-2).  
• Key regulatory features:  
– Activation-loop tyrosine (Tec Y519 numbering) whose phosphorylation increases activity without extensive global rearrangement (berg2005tecfamilykinases pages 17-18).  
– Extended regulatory spine comprising C-helix Met (M410 Itk equivalent) and SH2-kinase linker Trp (W355 Itk equivalent); mutation of either residue collapses the spine and inactivates the enzyme (joseph2010identificationofan pages 9-10, unknownauthors2009conformationalsnapshotsof pages 8-9).  
• No full-length crystal structure is available; NMR and modeling reveal compact packing of SH3–SH2 against the kinase N-lobe, stabilized by intramolecular PRR–SH3 contacts (berg2005tecfamilykinases pages 15-17, bradshaw2010thesrcsyk pages 6-6).

## Regulation

• Membrane recruitment via PH-domain binding to PtdIns(3,4,5)P₃ generated by class I PI3-kinase (schwartzberg2005tecfamilykinasesregulators pages 1-2).  
• Activation-loop tyrosine phosphorylated by Src-family kinases (e.g., Fyn/Lyn) primes Tec for autophosphorylation and full activation (yang2000teckinasesa pages 5-6).  
• Autophosphorylation of the conserved SH3 tyrosine modulates SH3 ligand affinity without altering catalytic turnover (unknownauthors2009conformationalsnapshotsof pages 4-5).  
• Autoinhibition maintained by intramolecular PRR engagement of the SH3 groove and SH3–SH2 packing; lipid binding and phosphorylation relieve these contacts (berg2005tecfamilykinases pages 15-17).  
• Allosteric control via regulatory spine assembly; activation-loop phosphorylation disrupts an electrostatic E445:R544 lock (Btk numbering) allowing C-helix rotation, whereas gatekeeper mutation (T474M in Btk) pre-assembles the spine independently of phosphorylation (joseph2010identificationofan pages 9-10).  
• Negative regulation by SHP-1 tyrosine phosphatase downstream of antigen receptors (yang2000teckinasesa pages 5-6).

## Function

• Expression: low in resting T cells (~100-fold less than Itk) but markedly up-regulated 2-3 days post-activation, especially in Th2 cells; present in B cells, mast cells and myeloid lineages (berg2005tecfamilykinases pages 3-6).  
• Upstream inputs: TCR, CD28, BCR, heterodimeric cytokine receptors (gp130), and CSF3R activate Tec via PI3K-derived lipids and Src-family phosphorylation (yang2000teckinasesa pages 2-4, mano1999tecfamilyof pages 9-11).  
• Downstream targets and partners: phosphorylates PLC-γ, CD28, Dok1, STAP1 and its own SH3 domain; interacts with LAT, SLP-76, Vav and Src-family SH3 domains (berg2005tecfamilykinases pages 3-6, mano1999tecfamilyof pages 5-6, berg2005tecfamilykinases pages 15-17).  
• Pathway roles: drives Ca²⁺ mobilization, MAPK activation, actin cytoskeleton remodeling, IL-2 transcription and Th2 differentiation; functionally redundant with Itk in T cells and with Btk in B cells (schwartzberg2005tecfamilykinasesregulators pages 1-2, berg2005tecfamilykinases pages 17-18).

## Inhibitors

• Broad-spectrum ATP-competitive staurosporine binds the Tec-family kinase domain and blocks catalytic activity in crystallographic assays (unknownauthors2009conformationalsnapshotsof pages 20-23).  
• The covalent BTK inhibitor ibrutinib engages the active site cysteine in Btk and shows cross-reactivity toward other Tec-family kinases, including Tec, in biochemical studies (unknownauthors2025dimerizationofthe pages 26-28).

## Other Comments

• No human immunodeficiency has been attributed to TEC; however, an R28C PH-domain mutation in mice disrupts phospholipid binding and impairs activation, contributing to the Xid phenotype (mano1999tecfamilyof pages 5-6).  
• Tec expression is elevated in inflammatory skin lesions such as atopic dermatitis (schwartzberg2005tecfamilykinasesregulators pages 1-2).  
• Tec family members lack the C-terminal inhibitory phosphotyrosine typical of Src kinases, enforcing reliance on alternative intramolecular restraints (unknownauthors2009conformationalsnapshotsof pages 1-2).

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