1. Phylogeny  
   TEX14 is a testis‐expressed gene with orthologs identified in humans, mice, pigs, and other mammals, indicating its conservation across species that form intercellular bridges during germ cell development (bellil2021humantestisexpressed(tex) pages 12-13). TEX14 is classified among serine/threonine kinases; however, due to key mutations in its active site, it belongs to the subgroup of pseudokinases, which have evolved to serve primarily scaffold or structural roles rather than catalyzing phosphate transfer reactions (greenbaum2006tex14isessential pages 1-2). The evolutionary conservation of TEX14 in species known to require stable intercellular bridges emphasizes its functional importance in male fertility and cell division (sironen2011anexonicinsertion pages 1-2).
2. Reaction Catalyzed  
   Although canonical serine/threonine kinases catalyze the transfer of a phosphate group from ATP to serine or threonine residues on substrate proteins, TEX14 does not catalyze this reaction because its kinase domain is rendered inactive by mutations in critical catalytic residues (bellil2021humantestisexpressed(tex) pages 15-15). No phosphoryl transfer reaction in the form ATP + [protein]-(L-serine/threonine) → ADP + [protein]-(L-serine/threonine)-phosphate + H⁺ has been detected for TEX14 (greenbaum2006tex14isessential pages 3-4).
3. Cofactor Requirements  
   Unlike active serine/threonine kinases that typically require Mg²⁺ as a cofactor for ATP binding and catalysis, TEX14 does not exhibit any such cofactor requirements because no catalytic activity is observed in vitro (bellil2021humantestisexpressed(tex) pages 15-15). Thus, the usual dependence on divalent metal ions such as Mg²⁺ is not applicable for TEX14 (iwamori2010tex14interactswith pages 1-2).
4. Substrate Specificity  
   In active kinases, substrate specificity is defined by consensus motifs that direct phosphorylation on serine or threonine residues; however, TEX14 does not display substrate specificity for phosphorylation because its kinase domain is inactive (greenbaum2006tex14isessential pages 3-4). Instead, TEX14 mediates its function through specific protein–protein interactions, notably binding to CEP55, rather than selecting a peptide motif for catalysis (iwamori2010tex14interactswith pages 2-4).
5. Structure  
   TEX14 is a large protein of approximately 1450 amino acids with a predicted molecular mass of around 162.5 kDa, featuring a multi-domain architecture that includes three N-terminal ankyrin repeat motifs, a central kinase-like domain, and a C-terminal region with limited homology to characterized proteins (greenbaum2006tex14isessential pages 3-4, bellil2021humantestisexpressed(tex) pages 7-9). The central kinase-like domain retains a typical serine/threonine-protein kinase fold, including structural elements such as an activation loop, hydrophobic spines, and a conserved C-helix; however, mutations in key catalytic residues render this domain catalytically inactive (pombar2022novelmissensetex15 pages 37-40). This structural organization suggests that rather than functioning as an enzyme, the kinase-like domain of TEX14 operates as a scaffold to facilitate interactions among proteins critical for intercellular bridge formation (bellil2021humantestisexpressed(tex) pages 5-7).
6. Regulation  
   TEX14 expression is tightly regulated in a testis-specific manner, with its transcription correlating with stages of spermatogenesis, and it is predominantly expressed in male germ cells (bellil2021humantestisexpressed(tex) pages 5-7). During mitosis, TEX14 is recruited to the kinetochores by the serine/threonine kinase PLK1, where it participates in the maturation of outer kinetochores and the establishment of stable microtubule attachments (greenbaum2006tex14isessential pages 2-3). In meiosis, regulatory control is achieved via its interaction with CEP55 at the midbody, where TEX14 inhibits the binding of CEP55 to PDCD6IP/ALIX and TSG101, thereby blocking cell abscission and enabling the transformation of midbodies into stable intercellular bridges (iwamori2010tex14interactswith pages 1-2, bellil2021humantestisexpressed(tex) pages 14-15). These regulatory mechanisms rely on specific protein–protein interactions rather than post‐translational modifications known to modulate catalytic activity (greenbaum2006tex14isessential pages 2-3).
7. Function  
   TEX14 plays an essential structural role in spermatogenesis through its involvement in the formation and maintenance of intercellular bridges between differentiating germ cells (bellil2021humantestisexpressed(tex) pages 12-13). In the context of meiosis, TEX14 is required for the conversion of midbodies—remnants of cytokinesis—into stable intercellular bridges by interacting with CEP55, thereby preventing cell abscission (iwamori2010tex14interactswith pages 1-2). Furthermore, during mitosis, TEX14 is recruited to kinetochores by PLK1 where it is implicated in the maturation of outer kinetochores and the stabilization of kinetochore–microtubule attachments, a process essential for accurate chromosome segregation (greenbaum2006tex14isessential pages 2-3). The disruption of TEX14 function, as observed in knockout models, leads to spermatogenic failure and male infertility due to loss of intercellular bridge integrity (pombar2022novelmissensetex15 pages 16-21).
8. Other Comments  
   Mutations in TEX14 have been linked to male infertility phenotypes such as azoospermia and spermatogenic arrest, underscoring its critical role in germ cell development (pombar2022novelmissensetex15 pages 40-41, sironen2011anexonicinsertion pages 10-10). Despite extensive studies characterizing its functional importance, no specific inhibitors have been reported for TEX14, likely because its function is mediated through scaffolding interactions rather than kinase catalysis (bellil2021humantestisexpressed(tex) pages 15-15, pombar2022novelmissensetex15 pages 16-21). The absence of catalytic activity shifts the focus of potential therapeutic interventions toward modulating its protein–protein interactions rather than inhibiting enzymatic function.
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