Phylogeny  
- Orthologs have been verified in Saccharomyces cerevisiae (Psk1, Psk2), Drosophila melanogaster, Danio rerio, Xenopus laevis, Gallus gallus, Mus musculus and Homo sapiens (unknownauthors2015desireedemilleabryan pages 16-21).  
- No orthologs are detected in Arabidopsis thaliana or Caenorhabditis elegans (unknownauthors2015desireedemilleabryan pages 16-21).  
- The catalytic domain clusters within the Ca²⁺/calmodulin-dependent kinase (CAMK) group, AMPK-related branch (grose2010theroleof pages 3-6).  
- PASK is the sole mammalian kinase that couples a sensory PAS module to a serine/threonine catalytic domain (demille2013paskinasea pages 3-4).  
- The PAS domains show homology to the bacterial oxygen sensor FixL, indicating conservation of PAS-regulated kinase architecture across kingdoms (schlafli2009thepasdomainkinase pages 4-5).

Reaction Catalyzed  
- ATP + protein-Ser/Thr → ADP + protein-Ser/Thr-phosphate (rutter2001paskinasean pages 5-6).

Cofactor Requirements  
- Mg²⁺ is required for catalytic activity and observed in the crystal structure (kikani2010structuralbasesof pages 2-3).  
- Mn²⁺ can substitute for Mg²⁺ in vitro (rutter2001paskinasean pages 5-6).

Substrate Specificity  
- Optimal motif determined as R-X-A/x-S/T\* with invariant Arg at –3 (kikani2010structuralbasesof pages 1-2).  
- Proteomic profiling confirms the same consensus and notes additional preference for basic residues at –5 (unknownauthors2005identificationofsubstrates pages 65-70).

Structure  
- Domain organization: two N-terminal PAS domains, a ~400-residue linker, and a C-terminal kinase domain (grose2010theroleof pages 3-6).  
- PAS-A adopts a canonical PAS α/β fold and directly inhibits the kinase domain (rutter2001paskinasean pages 4-5).  
- Kinase domain crystal structure (2.3 Å) shows an active conformation without activation-loop phosphorylation (kikani2010structuralbasesof pages 2-3).  
- Activation loop contains Thr1161 and Thr1165 that autophosphorylate but are dispensable for basal activity (rutter2001paskinasean pages 4-5).  
- An alanine at the DFG+3 position enables RD-pocket formation in the unphosphorylated state (kikani2010structuralbasesof pages 6-7).  
- A unique β-hairpin replaces part of the αC helix (demille2013paskinasea pages 1-3).  
- PAS FG-loop dynamics transmit ligand-induced signals to the kinase core (grose2010theroleof pages 1-3).

Regulation  
- Intramolecular binding of PAS-A represses catalytic turnover (rutter2001paskinasean pages 6-6).  
- Isolated PAS-A added in trans inhibits the kinase with IC₅₀ ≈ 100 µM (rutter2001paskinasean pages 6-6).  
- Ligand binding to PAS relieves inhibition; physiological ligand remains unidentified (demille2013paskinasea pages 3-4).  
- Monophosphorylated phosphatidylinositols activate, whereas di-/tri-phosphorylated species inhibit PASK (demille2013paskinasea pages 3-4).  
- Autophosphorylation at Thr1161/Thr1165 enhances activity, while Ser1149 has minor effect (rutter2001paskinasean pages 4-5).  
- Yeast Snf1/AMPK signaling activates Psk1 under non-fermentable carbon sources (hao2008theroleof pages 3-4).  
- Yeast cell-integrity stress also stimulates Psk1/Psk2 (demille2013paskinasea pages 3-4).  
- High glucose and GLP-1 rapidly activate mammalian PASK in β-cells (demille2013paskinasea pages 3-4).

Function  
- Highest expression in testis; widespread lower expression elsewhere (grose2010theroleof pages 3-6).  
- Enrichment also noted in brain, liver and prostate (zhang2015perarntsimkinase(pask) pages 1-4).  
- Phosphorylation of glycogen synthase Ser640 inactivates the enzyme and regulates glycogen storage (grose2010theroleof pages 6-9).  
- Phosphorylation of PDX1 Thr152 supports glucose-stimulated insulin gene transcription (grose2010theroleof pages 3-6).  
- PASK suppresses glucagon secretion from α-cells under high glucose (zhang2015perarntsimkinase(pask) pages 4-6).  
- In yeast, phosphorylation of Ugp1 Ser11 diverts UDP-glucose toward cell-wall glucan synthesis (hao2008theroleof pages 3-4).  
- Proteomic screens identify eEF1A1 and ribosomal protein S6 as substrates, linking PASK to translational control (unknownauthors2005identificationofsubstrates pages 74-80).  
- Snf1/AMPK positions PASK within cellular energy-sensing networks (demille2013paskinasea pages 3-4).

Inhibitors  
- A selective inhibitor inhibits human PASK with IC₅₀ ≈ 200 nM and shows minimal activity on PKA, CKIε and CaMKII (unknownauthors2005identificationofsubstrates pages 116-120).

Other Comments  
- Pask-knockout mice are protected from diet-induced obesity, hepatic triglyceride accumulation and insulin resistance (grose2010theroleof pages 3-6).  
- MODY mutation p.G1117E increases autophosphorylation and causes basal insulin hypersecretion (semplici2011humanmutationwithin pages 1-2).

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