Phylogeny  
• Verified orthologs: Homo sapiens SRMS, Mus musculus Srm, Rattus norvegicus Srm, Danio rerio srm, Gallus gallus srm (mcclendon2020structurefunctionand pages 10-11).  
• Kinome assignment: Tyrosine kinase (TK) group, BRK family kinases together with PTK6/BRK and FRK/PTK5 (goel2023seekingabetter pages 1-2).  
• Evolutionary relationship: Shares SH3–SH2–kinase architecture with Src family kinases but lacks N-terminal myristoylation and C-terminal regulatory tail (mcclendon2020structurefunctionand pages 1-3).

Reaction Catalyzed  
• ATP + [protein]-L-tyrosine ⇌ ADP + [protein]-O-phospho-L-tyrosine (mcclendon2020structurefunctionand pages 1-3).

Cofactor Requirements  
• Requires divalent Mg²⁺ or Mn²⁺ for catalytic activity (brown2014novelstrategiesfor pages 28-35).

Substrate Specificity  
• Consensus motifs XIYX and YXXV with Lys/Arg frequently at −2 or −4 positions relative to the target Tyr (mcclendon2020structurefunctionand pages 5-7).

Structure  
• Domain organization: unique N-terminal extension (~50 aa) → SH3 domain → SH2 domain → kinase catalytic domain (goel2013theuniquen‐terminal pages 1-2).  
• Key catalytic elements: Lys258 (ATP binding), Tyr380 in activation loop (autophosphorylation), Trp223 stabilizing intramolecular contacts (mcclendon2020structurefunctionand pages 3-5).  
• 3D model: homology to chicken Src (PDB 2H8H) predicts canonical bilobed kinase fold; SRMS lacks Src-type C-terminal tail (mcclendon2020structurefunctionand pages 3-5).  
• Unique feature: N-terminal amphipathic helix required for enzymatic activity and punctate cytoplasmic localization (goel2023seekingabetter pages 2-4).

Regulation  
• Autophosphorylation on Tyr380 activates the kinase (mcclendon2020structurefunctionand pages 3-5).  
• Mutation W223A or deletion of the first 50 residues abolishes activity and disrupts punctate localization (mcclendon2020structurefunctionand pages 3-5, goel2013theuniquen‐terminal pages 1-2).  
• Absence of C-terminal inhibitory tyrosine shifts regulation to N-terminal mediated intramolecular interactions (mcclendon2020structurefunctionand pages 1-3).

Function  
• Expression: elevated in breast carcinoma; lower in normal mammary epithelium; detectable in lung, testes, liver, epidermis and keratinocytes (goel2013theuniquen‐terminal pages 12-14, mcclendon2020structurefunctionand pages 1-3).  
• Verified substrates: DOK1 (goel2013theuniquen‐terminal pages 12-14); KHDRBS1/Sam68 (EGF-dependent) (mcclendon2020structurefunctionand pages 5-7); Vimentin (mcclendon2020structurefunctionand pages 5-7); OTUB1 Tyr26 (goel2023seekingabetter pages 4-6); FKBP51 Tyr54 (goel2023seekingabetter pages 4-6); PTK6/BRK Tyr447 (mcclendon2020structurefunctionand pages 5-7).  
• Pathways: modulates EGF signaling via Sam68 phosphorylation (mcclendon2020structurefunctionand pages 5-7); inhibits autophagy upstream of autophagosome formation (goel2023seekingabetter pages 4-6); stabilizes mTORC1 through OTUB1-RPTOR axis (goel2023seekingabetter pages 4-6); suppresses MKK4-JNK signaling contributing to platinum resistance in ovarian cancer (goel2023seekingabetter pages 8-9).

Inhibitors  
• Dasatinib blocks SRMS catalytic activity in vitro (mcclendon2020structurefunctionand pages 3-5).  
• Ibrutinib reduces SRMS-mediated phosphorylation in breast cancer cells (goel2023seekingabetter pages 2-4).  
• PLX4720 identified as SRMS inhibitor enhancing platinum chemotherapy efficacy (goel2023seekingabetter pages 8-9).

Other Comments  
• Gene located at chromosome 20q13.33 adjacent to PTK6; region frequently amplified in breast and gastric cancers (goel2023seekingabetter pages 1-2).  
• Elevated SRMS expression correlates with higher tumour grade in breast carcinoma (mcclendon2020structurefunctionand pages 7-10).  
• Srms-null mice are viable with no overt phenotype (mcclendon2020structurefunctionand pages 7-10).

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