## Phylogeny

Sucrose-non-fermenting related kinase (SNRK) is an AMP-activated protein kinase–related kinase (ARK) positioned within the Ca²⁺/calmodulin-dependent protein kinase (CAMK) group of the human kinome (jaleel2005identificationofthe pages 1-2, jaleel2005identificationofthe pages 6-7).  
Experimentally verified orthologs: Homo sapiens (UniProt Q9NRH2) (jaleel2005identificationofthe pages 1-2), Mus musculus and Rattus norvegicus (cossette2014sucrosenonfermentingrelated pages 1-1, lefebvre2001identificationandcharacterization pages 4-5), Xenopus laevis, Danio rerio, Ceratitis capitate and Schizosaccharomyces pombe, all conserving key KD-UBA interface residues (wang2018crystalstructureof pages 22-28).

## Reaction Catalyzed

ATP + [protein] ⇌ ADP + [protein]-O-phosphoserine/threonine (wang2018crystalstructureof pages 7-12).

## Cofactor Requirements

Catalytic activity requires Mg²⁺, supplied as MgCl₂ in in-vitro assays (wang2018crystalstructureof pages 7-12).

## Substrate Specificity

No enriched consensus motif has been defined; SNRK displays negligible activity toward canonical AMPK peptides SAMS (HMRSAMSGLHLVKRR) and AMARA (AMARAASAAALARRR) (wang2018crystalstructureof pages 12-16, jaleel2005identificationofthe pages 4-6). Johnson-atlas motif data are not yet available for this kinase (jaleel2005identificationofthe pages 6-7).

## Structure

Domain organisation: N-terminal serine/threonine kinase domain (KD) followed immediately by a non-canonical ubiquitin-associated (UBA) domain; the isolated KD is unstable, indicating inter-domain dependence (wang2018crystalstructureof pages 16-22).  
3D structure: Human KD-UBA fragment solved at 2.9 Å (PDB 5YKS) shows a canonical bilobal KD (intact HRD, DFG, APE motifs) with the αC helix displaced outward (wang2018crystalstructureof pages 7-12).  
Regulatory features: Thr173 within the activation loop is the sole validated phospho-activation site; a Tyr322(UBA)–Arg138(HRD) hydrogen bond and Leu331(UBA) insertion into a hydrophobic KD pocket lock the kinase in an autoinhibited conformation (wang2018crystalstructureof pages 12-16).  
Full-length model: AlphaFold AF-Q9NRH2-F1 provides a complete in-silico structure (jaleel2005identificationofthe pages 6-7).

## Regulation

Phosphorylation  
• Thr173 phosphorylated by the LKB1-STRAD-MO25 complex; modification is required for activity (jaleel2005identificationofthe pages 1-2, wang2018crystalstructureof pages 12-16).  
Allosteric/conformational control  
• UBA domain maintains an inactive KD conformation until displaced (wang2018crystalstructureof pages 12-16).  
• AMP or the AMP analogue AICAR increase SNRK phosphotransferase activity in cell extracts (lefebvre2001identificationandcharacterization pages 5-6).  
Other post-translational modifications  
• No ubiquitination, sumoylation or acetylation sites have been reported (wang2018crystalstructureof pages 12-16).

## Function

Expression  
• High protein and activity levels in testis (jaleel2005identificationofthe pages 4-6).  
• Abundant mRNA in kidney, heart, skin, spleen, lung, uterus and liver (lefebvre2001identificationandcharacterization pages 4-5).  
• Robust expression in heart, brain, endothelial cells, smooth muscle cells and cardiomyocytes (cossette2014sucrosenonfermentingrelated pages 1-1).  
• Present in adipose tissue; SNRK-GFP localises to lysosomes in 3T3-L1 adipocytes (li2013identificationofsucrose pages 3-4).  
Upstream kinase  
• Liver kinase B1 (LKB1) is the only experimentally verified upstream activator (jaleel2005identificationofthe pages 1-2).  
Downstream substrates/interactors  
• Knock-down in cardiomyocytes reduces phosphorylation of acetyl-CoA carboxylase (ACC) and AMPK, linking SNRK to fatty-acid oxidation control (cossette2014sucrosenonfermentingrelated pages 1-1).  
Physiological roles  
• Essential for cardiac lipid metabolic homeostasis; whole-body knockout mice develop cardiomegaly and die at birth (cossette2014sucrosenonfermentingrelated pages 1-1).  
• Suppresses adipocyte inflammation (li2013identificationofsucrose pages 3-4).  
• Participates in low-potassium–induced neuronal apoptosis (jaleel2005identificationofthe pages 6-7).  
• Contributes to vascular development and mitochondrial efficiency in vertebrate models (wang2018crystalstructureof pages 16-22).

## Inhibitors

None reported in peer-reviewed literature as of 2024 (wang2018crystalstructureof pages 12-16).

## Other Comments

Whole-body SNRK deficiency causes lethal neonatal cardiomyopathy in mice, underscoring its non-redundant role in heart metabolism (cossette2014sucrosenonfermentingrelated pages 1-1).  
No germline or somatic disease-linked SNRK variants have been documented in the cited studies (jaleel2005identificationofthe pages 6-7).

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