## Phylogeny

PRKY is a Y-chromosome-encoded serine/threonine kinase that belongs to the AGC kinase group and clusters most closely with the cAMP-dependent protein kinase (PKA) family (Huang et al., 2016; Johnson et al., 2023). It arose from a gene-duplication event followed by primate chromosome rearrangements and is a paralogue of the X-linked kinase PRKX, sharing ~94 % amino-acid identity (Huang et al., 2016; Li et al., 2011; Schiebel et al., 1997).

## Reaction Catalyzed

ATP + L-seryl/threonyl-[protein] ⇌ ADP + H⁺ + O-phospho-L-seryl/threonyl-[protein] (Johnson et al., 2023).

## Cofactor Requirements

Mg²⁺ is required for catalytic activity (Johnson et al., 2023; UnknownAuthors, 2021).

## Substrate Specificity

A kinome-wide peptide library study generated position-specific scoring matrices that define PRKY (annotated as “PRPK” in the dataset) substrate preferences (Johnson et al., 2023). Prior to this, substrates were unknown, but homology with PRKX and other PKA-family members suggested a preference for basic motifs such as R-R-X-S/T (Huang et al., 2016; Li et al., 2011).

## Structure

The gene encodes an intact open reading frame with conserved ATP-binding and catalytic motifs, although the protein is 81 amino acids shorter than PRKX because one exon is missing (Huang et al., 2016; Schiebel et al., 1997). An AlphaFold model was reported in 2025 (Ekhator et al., 2025), whereas earlier sources stated that no experimental or predicted 3-D structure was available (Huang et al., 2016; Li et al., 2011).

## Regulation

Activity and substrate selection are modulated by post-translational modifications, notably phosphorylation, in line with common kinase regulatory mechanisms (Johnson et al., 2023; UnknownAuthors, 2021).

## Function

PRKY transcripts are detected predominantly in testis, indicating a role in male germ-cell development and reproduction (Huang et al., 2016; Li et al., 2011). Lower-level expression has been reported in fetal brain and bone-marrow cDNA libraries (Schiebel et al., 1997). Specific signalling partners have not been detailed in the cited studies (Johnson et al., 2023).

## Other Comments

Several reports classify PRKY as a pseudogene owing to rearrangements or loss of canonical kinase activity (Ekhator et al., 2025; Huang et al., 2016; Li et al., 2011). In contrast, the original cloning study showed an intact coding sequence and distinguished PRKY from the true pseudogene PRKXP1 (Schiebel et al., 1997). Recombination between PRKY and PRKX underlies ~33 % of sex-reversal cases, producing (Y⁺)XX males and (Y⁻)XY females (Schiebel et al., 1997; Ekhator et al., 2025; Huang et al., 2016).

## 9. References

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