## Phylogeny

Member of the GRK1 subfamily within the AGC kinase group (Kang et al., 2020). GRK7 and GRK1 constitute the “visual” GRK branch, distinct from the GRK2/3 and GRK4/5/6 lineages (Sato et al., 2015). Orthologs are present in human, macaque, pig, dog, carp, zebrafish and Xenopus, whereas mouse and rat lack GRK7 (Hsu & Chen, 2016; Weiss et al., 2001). GRK7 shares ~85 % sequence identity with GRK1 and ~59 % with fish visual GRKs (Hsu & Chen, 2016). The closest paralog is rhodopsin kinase GRK1 (Gurevich et al., 2012; Hsu & Chen, 2016).

## Reaction Catalyzed

ATP + [photo-activated cone opsin]-Ser/Thr → ADP + [cone opsin]-O-phospho-Ser/Thr (Hsu & Chen, 2016).

## Cofactor Requirements

Requires divalent Mg²⁺ or Mn²⁺ ions (Hsu & Chen, 2016; Sato et al., 2015).

## Substrate Specificity

Efficiently phosphorylates light-activated L, M and S cone opsins as well as rhodopsin cytoplasmic tails (Hsu & Chen, 2016; Gurevich et al., 2012). Shows ~10-fold higher specific activity toward cone opsins than GRK1 (Gurevich et al., 2012). A definitive peptide consensus motif has not yet been reported (Hsu & Chen, 2016). Receptor recognition involves docking of the kinase N-terminal helix onto a hydrophobic patch on transmembrane helix 5 of the opsin (Brunette et al., 2016).

## Structure

Domain architecture: N-terminal α-helix → regulator of G-protein signaling homology (RH) domain → bilobed protein-kinase core → C-terminal regulatory tail ending in a CaaX geranylgeranylation motif (Hsu & Chen, 2016; Weiss et al., 2001). AlphaFold model AF-Q8WTQ7-F1 and comparison with the GRK1 crystal structure (PDB 4PNI) reveal a canonical AGC fold with conserved C-helix, activation segment, and catalytic HRD/DFG motifs (Hsu & Chen, 2016; Gurevich et al., 2012). The C-terminal extension serves as an autoinhibitory latch and membrane anchor for the prenylated cysteine (Hsu & Chen, 2016).

## Regulation

• C-terminal cysteine is geranylgeranylated, promoting membrane association (Weiss et al., 2001).  
• Protein kinase A phosphorylates Ser36 in darkness, reducing activity; phosphorylation declines in light (Unknown authors, 2008; Chrispell et al., 2022). Elevation of cAMP enhances this modification, which is reversed by phosphatases (Chrispell et al., 2022).  
• Ca²⁺-bound visinin binds and inhibits GRK7 (Hsu & Chen, 2016).  
• The kinase autophosphorylates C-terminal serines (Hsu & Chen, 2016).  
• Prenyl-binding protein PrBP/δ transports the lipidated enzyme to cone outer segments (Hsu & Chen, 2016).

## Function

Expressed specifically in cone photoreceptor inner and outer segments of humans, primates, pigs, dogs and fish; absent from rodent cones (Weiss et al., 2001; Hsu & Chen, 2016). Rapid phosphorylation of light-activated cone opsins enables arrestin binding and transducin shut-down, ensuring fast recovery of the photopic response (Hsu & Chen, 2016; Sato et al., 2015). GRK7 can sustain daylight vision in patients lacking cone GRK1 activity (Unknown authors, 2001). Interacts with cone arrestin, opsins, PrBP/δ, visinin and PKA (Hsu & Chen, 2016; Chrispell et al., 2022).

## Other Comments

No pathogenic human GRK7 variants have been reported, whereas GRK1 mutations cause Oguchi disease, underscoring the importance of visual GRKs (Hsu & Chen, 2016; Sato et al., 2015). The superior catalytic efficiency of GRK7 highlights its critical role in bright-light cone adaptation (Gurevich et al., 2012).

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