## Phylogeny

ADCK2 (UniProt Q7Z695) belongs to the AarF domain-containing kinase (ADCK/UbiB) family, an ancestral branch of the protein-kinase superfamily that is classified within the atypical kinase (aPK) group (Jacquet & Zhao, 2025, pp. 15–17; Manning et al., 2002, pp. 1912-1914). Five vertebrate paralogues (ADCK1-5) form two subgroups; ADCK2 clusters with ADCK1 and ADCK5 in the first subgroup (Unknown Authors, 2017, pp. 49-51). Orthologues are evolutionarily conserved and include yeast Coq8 and YPL109c, bacterial UbiB proteins, and Drosophila ADCK1 (Jacquet & Zhao, 2025, pp. 15–17; Vazquez-Fonseca et al., 2019, pp. 1374-1376). Human paralogues comprise ADCK1, ADCK3/COQ8A and ADCK4 (Jacquet & Zhao, 2025, pp. 15–17).

## Reaction Catalyzed

The ATP-dependent phosphorylation reaction catalyzed by ADCK2 has not yet been defined; no specific protein or lipid substrate reaction has been reported (Jacquet & Zhao, 2025, pp. 15–17). Members of the ADCK family can phosphorylate lipids such as phosphatidylinositol and phosphoinositides (Unknown Authors, 2017, pp. 49-51).

## Cofactor Requirements

Mg²⁺ is coordinated by two conserved Asp residues within kinase motifs VIB and VII (Unknown Authors, 2017, pp. 49-51).

## Substrate Specificity

No substrate-recognition motif or preferred residue pattern has been identified for ADCK2 (Jacquet & Zhao, 2025, pp. 15–17).

## Structure

The ADCK2 gene maps to chromosome 7q34, spans ~22 kb and comprises eight exons (Jacquet & Zhao, 2025, pp. 5-8). A solved 3-D structure is not available (Jacquet & Zhao, 2025, pp. 3-9). The protein possesses:  
• an N-terminal KxGQ domain with a strictly conserved Lys implicated in coenzyme Q (CoQ) metabolism (Unknown Authors, 2017, pp. 49-51)  
• four “universal core” protein-kinase motifs (I, II, VIB, VII) plus motif III required for ATP binding and phosphotransfer (Unknown Authors, 2017, pp. 49-51).  
Truncating mutations abolish the ability to rescue CoQ biosynthesis, underscoring the functional importance of these structural elements (Vazquez-Fonseca et al., 2019, pp. 1374-1376).

## Regulation

Post-translational regulation of ADCK2 has not been reported; no modification sites or responsible enzymes are described (Jacquet & Zhao, 2025, pp. 3-9; Vazquez-Fonseca et al., 2019, pp. 1374-1376).

## Function

ADCK2 localises to the mitochondrial matrix and is also detected at the inner mitochondrial membrane; it is absent from endoplasmic-reticulum and cytosolic fractions (Jacquet & Zhao, 2025, pp. 5-8; Vazquez-Fonseca et al., 2019, pp. 1374-1376). Reported roles include:  
• Coenzyme Q biosynthesis and mitochondrial oxidative phosphorylation (Jacquet & Zhao, 2025, pp. 3-8)  
• mitochondrial lipid metabolism and fatty-acid β-oxidation (Jacquet & Zhao, 2025, pp. 6-8; Vazquez-Fonseca et al., 2019, pp. 1374-1376)  
• interaction, direct or indirect, with CoQ pathway enzymes COQ2 and COQ3 (Jacquet & Zhao, 2025, pp. 3-5).

Cancer-related signalling activities:  
• activates the Akt-mTOR pathway via phosphorylation of Akt and S6K1 in non-small-cell lung cancer (Jacquet & Zhao, 2025, pp. 6-8)  
• modulates RELB-dependent NF-κB signalling and TNFα-induced HIF-1α accumulation in prostate cancer and osteosarcoma (Jacquet & Zhao, 2025, pp. 6-8)  
• regulates melanoma cell motility through MYL6 and other cytoskeletal proteins (Jacquet & Zhao, 2025, pp. 6-8, 15-17).

## Inhibitors

(No inhibitors reported in the provided literature.)

## Other Comments

ADCK2 haploinsufficiency causes a mitochondrial disorder characterised by reduced CoQ content, impaired lipid oxidation, decreased β-oxidation capacity and myopathy; CoQ supplementation partially rescues mitochondrial dysfunction (Jacquet & Zhao, 2025, pp. 6-8; Vazquez-Fonseca et al., 2019, pp. 1374-1376).

Oncology observations: elevated ADCK2 expression correlates with tumour size in ER-positive luminal A breast cancer; somatic mutations are detected in a subset of breast tumours. High expression predicts poor survival in NSCLC, and gene knockout suppresses tumour growth (Jacquet & Zhao, 2025, pp. 6-8). ADCK2 also promotes hypoxia-driven progression in prostate cancer and osteosarcoma and influences melanoma metastasis (Jacquet & Zhao, 2025, pp. 6-8).

## References

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