## Phylogeny

Human NIM1 kinase (NIM1K) is a serine/threonine kinase that is part of the human kinome (johnson2023anatlasof pages 4-5, johnson2023anatlasof pages 7-7). The phylogenetic classification of NIM1K is contradictory across sources. One classification places NIM1K within the CAMK (Calcium/calmodulin-dependent protein kinase) group and the NIM1 family (ostale2021functionalrequirementsof pages 6-7, johnson2023anatlasof pages 4-5). Another source, referencing the Manning et al. 2002 framework, places NIM1K in the ‘Other’ group of kinases, which is distinct from the major eukaryotic protein kinase (ePK) groups such as CAMK (moret2020aresourcefor pages 51-54).

The ortholog in *Schizosaccharomyces pombe* is Nim1, also known as Cdr1, a serine/threonine kinase that functions as a mitotic inducer (wu1997nif1anovel pages 1-2, wu1997nif1anovel pages 2-3).

## Reaction Catalyzed

The chemical reaction catalyzed by NIM1 kinase is: ATP + a protein = ADP + a phosphoprotein (wu1997rolesofwee1 pages 2-3, moret2020aresourcefor pages 23-26). In *S. pombe*, a specific instance of this reaction involves the phosphorylation of the Wee1 protein: ATP + Wee1 = ADP + phospho-Wee1 (wu1997nif1anovel pages 1-2, wu1997nif1anovel pages 2-3).

## Cofactor Requirements

The catalytic activity of NIM1K requires ATP as the phosphate donor (johnson2023anatlasof pages 4-5, wu1997nif1anovel pages 1-2, moret2020aresourcefor pages 57-57). The phosphotransfer reaction is also dependent on divalent metal ions, specifically Mg²⁺ or Mn²⁺, as cofactors (johnson2023anatlasof pages 7-7, moret2020aresourcefor pages 51-54). One source also reports that its kinase function is activated by calcium/calmodulin (ostale2021functionalrequirementsof pages 6-7).

## Substrate Specificity

An atlas of substrate specificities for 303 human serine/threonine kinases profiled the kinome group to which NIM1K (Q8IY84) belongs (johnson2023anatlasof pages 1-2, johnson2023anatlasof pages 4-5). However, a specific consensus substrate motif and amino acid preferences for NIM1K are not detailed within the provided context (johnson2023anatlasof pages 1-2, johnson2023anatlasof pages 3-4, johnson2023anatlasof pages 6-7).

## Structure

Protein kinases typically possess a conserved eukaryotic protein kinase (ePK) fold, which consists of two lobes that form an ATP-binding catalytic cleft (moret2020aresourcefor pages 4-7, moret2020aresourcefor pages 4-7). For the *S. pombe* ortholog Nim1, the amino acid region 291–354 is necessary for its kinase activity and its interaction with the inhibitor Nif1 (wu1997nif1anovel pages 2-3). No specific information on the 3D structure or domain organization of human NIM1K is available in the provided context.

## Regulation

In *Schizosaccharomyces pombe*, the kinase activity of the ortholog Nim1 is inhibited by the protein Nif1 (wu1997nif1anovel pages 1-2). Nim1 negatively regulates the Wee1 kinase through direct phosphorylation within Wee1’s C-terminal catalytic domain, which inhibits Wee1’s function as a mitotic inhibitor (wu1997nif1anovel pages 1-2, wu1997nif1anovel pages 2-3). The activity of human NIM1K is reported to be activated by the cofactor calcium/calmodulin (ostale2021functionalrequirementsof pages 6-7).

## Function

NIM1K is a protein kinase that phosphorylates substrate proteins and modulates signaling pathways (johnson2023anatlasof pages 4-5). It has a role in regulating the cell cycle (ostale2021functionalrequirementsof pages 6-7). As an understudied kinase, NIM1K is expressed in Cancer Cell Line Encyclopedia (CCLE) cell lines, with expression detected via protein or mRNA measurements, contradicting prior assumptions of no available expression data (moret2020aresourcefor pages 1-4, moret2020aresourcefor pages 13-17, moret2020aresourcefor pages 29-33). In some cancer cell lines, NIM1K shows significant expression with RPKM values above the threshold of 1 (moret2020aresourcefor pages 36-39).

In *S. pombe*, the ortholog Nim1 promotes mitotic entry by phosphorylating and inhibiting the Wee1 kinase, which is an inhibitor of the cyclin-dependent kinase Cdc2 (wu1997nif1anovel pages 1-2). The known interacting partners for the *S. pombe* ortholog are its substrate, Wee1, and its inhibitor, Nif1 (wu1997nif1anovel pages 1-2, wu1997nif1anovel pages 2-3).

## Other Comments

NIM1K is considered an understudied or “dark” kinase that merits further investigation (moret2020aresourcefor pages 4-7, moret2020aresourcefor pages 26-29). The provided context does not contain information on specific disease associations for NIM1K (moret2020aresourcefor pages 4-7).

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