## Phylogeny

Aurora kinase A (AURKA) belongs to the small Aurora family of serine/threonine kinases, which also contains Aurora B and Aurora C. The founding family member, Ipl1, was first identified in Saccharomyces cerevisiae and orthologues are present in diverse metazoans including Drosophila melanogaster, Caenorhabditis elegans, Xenopus laevis, mouse, chicken, dog and zebrafish (Nikonova et al., 2013; Durlacher et al., 2016). Phylogenetic analyses indicate that AURKA diverged early from the branch that produced AURKB/C and the Aurora family is classified as a separate clade within the “Other” group of the human kinome (Unknown authors, 2010; Levinson, 2018; Malumbres & Pérez de Castro, 2014).

## Reaction Catalyzed

ATP + protein ⇌ ADP + phospho-protein (Durlacher et al., 2016; Malumbres & Pérez de Castro, 2014; Nikonova et al., 2013; Vats et al., 2025).

## Cofactor Requirements

Catalysis requires Mg²⁺ to coordinate ATP in the active site (Durlacher et al., 2016; Janecek et al., 2016; Sarı & Özsoy, 2024).

## Substrate Specificity

AURKA phosphorylates Ser/Thr residues within motifs typically containing Pro at the +1 position and a basic residue, most frequently Arg, at −3 (Du et al., 2021; Johnson et al., 2023).

## Structure

Human AURKA is a 403-residue protein comprising an N-terminal regulatory segment and a C-terminal catalytic domain (residues 133–383) joined by a short hinge (Souza & Kawano, 2020). Key structural elements include:  
• ATP-binding pocket, canonical HRD catalytic triad and αC-helix (Souza & Kawano, 2020).  
• Activation loop (residues 274–299) beginning with the DFG motif and harbouring the autophosphorylation site Thr288 (Souza & Kawano, 2020).  
• N-terminal destruction box that targets the protein for APC/C-mediated proteolysis and intrinsically disordered regions that bind the activator TPX2 (Nguyen et al., 2022).  
Crystal structures, e.g. PDB 3E5A, capture AURKA in complex with TPX2 or small-molecule inhibitors (Souza & Kawano, 2020; Nguyen et al., 2022).

## Regulation

• Conformational control: interconversion between active “DFG-in” and inactive “DFG-out” states, with an additional “DFG-up” state reported (Nguyen et al., 2022; Levinson, 2018; Nikonova et al., 2013).  
• Phosphorylation: autophosphorylation on Thr288 is essential for full activity; PP1 and PP2A remove this phosphate to inactivate the kinase (Durlacher et al., 2016).  
• Protein interactions: TPX2 binding promotes Thr288 autophosphorylation, stabilises the active conformation and shields the phosphate from phosphatases by forming a pThr288-Arg255 salt bridge (Durlacher et al., 2016; Souza & Kawano, 2020).  
• Proteolysis: APC/C recognises the N-terminal destruction box to trigger ubiquitin-dependent degradation (Nguyen et al., 2022).

## Function

AURKA levels and activity peak in G2/M, and the protein localises to centrosomes and spindle microtubules (Nguyen et al., 2022; Unknown authors, 2010). It orchestrates:  
• Centrosome maturation and separation, bipolar spindle assembly, chromosome alignment/segregation and cytokinesis (Durlacher et al., 2016).  
• Phosphorylation of substrates including PLK1, TACC3, CDC25B, p53, BRCA1 and histone H3 to execute mitotic events (Durlacher et al., 2016; Souza & Kawano, 2020).  
Extra-mitotic roles include regulation of ciliogenesis, mitochondrial dynamics, neuronal outgrowth and cancer stem-cell maintenance via Wnt/β-catenin signalling (Nikhil & Shah, 2024; Souza & Kawano, 2020).

## Inhibitors

• Selective ATP-competitive inhibitors: alisertib (MLN8237), MLN8054, MK-5108 and ENMD-2076 exhibit high selectivity for AURKA (Malumbres & Pérez de Castro, 2014; Durlacher et al., 2016).  
• Pan-Aurora inhibitors: danusertib, tozasertib, AT9283, AMG900, SNS-314 and PF-03814735 target all three Aurora kinases (Borah & Reddy, 2021; Mou et al., 2021).  
• Non-ATP-competitive inhibitor: SP-96 shows high specificity for AURKB but illustrates the feasibility of allosteric Aurora inhibition (Borah & Reddy, 2021).

## Other Comments

AURKA is frequently amplified at chromosome 20q13.2 and over-expressed in breast, colon, ovarian, lung, gastric and pancreatic cancers. Over-expression correlates with centrosomal defects, aneuploidy, high tumour grade and poor prognosis (Durlacher et al., 2016; Unknown authors, 2010). Cancer-linked mutations include F31I, V57A and S155R, which affect stability or TPX2 interaction and may enhance oncogenic potential (Nguyen et al., 2022; Souza & Kawano, 2020; Nikonova et al., 2013).

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