1. Phylogeny  
   Aurora kinase B (AURKB) is a member of the highly conserved Aurora kinase family, which also includes Aurora A and Aurora C. Phylogenetic analyses have demonstrated that the Aurora kinases evolved from an ancestral kinase—represented in yeast by Ipl1—and that the vertebrate family is composed of at least three paralogs with divergent N‐terminal and regulatory regions yet very similar catalytic domains. In mammals, orthologs of AURKB are found in all dividing cells, and the protein shares significant amino acid sequence conservation in its central kinase domain with both Aurora A and Aurora C, although its N-terminal and C-terminal regions are more variable. This conservation across species from yeast to humans underscores the central role of AURKB in cell division. Comparative studies have placed AURKB in a distinct clade relative to Aurora A, with Aurora B and C being more closely related to each other; this relationship is supported by observations of structural motifs and regulatory domains that are unique to the B‐type auroras (carmena2003thecellulargeography pages 1-2, kollareddy2008aurorakinasesstructure pages 1-2, willems2018thefunctionaldiversity pages 2-4).
2. Reaction Catalyzed  
   Aurora kinase B catalyzes the ATP‐dependent phosphorylation of serine and threonine residues on substrate proteins. The chemical reaction can be represented as follows:  
     ATP + [protein]-(L-serine or L-threonine) → ADP + [protein]-(L-serine/threonine)-phosphate + H⁺.  
   This reaction is fundamental to the role of AURKB in cellular signaling, as the addition of phosphate groups modulates the activity, localization, and interactions of its substrates during mitosis (ashraf2021explorationofthe pages 1-2).
3. Cofactor Requirements  
   Aurora kinase B requires divalent metal ions, most commonly Mg²⁺, as an essential cofactor for its catalytic activity. Mg²⁺ functions to coordinate ATP binding within the active site, thereby facilitating the transfer of the phosphate group to the substrate protein. This requirement for Mg²⁺ is typical of serine/threonine kinases and is critical for optimal catalytic efficiency (ashraf2021explorationofthe pages 1-2, kovacs2023aurorabinhibitors pages 2-4).
4. Substrate Specificity  
   The substrate specificity of Aurora kinase B is determined by its ability to recognize and phosphorylate serine/threonine residues in a defined sequence context. AURKB is well known for phosphorylating Histone H3 at serine 10, a modification that is critical for chromatin condensation during mitosis. In addition, it phosphorylates other substrates involved in chromosome segregation and cytokinesis, including components of the chromosomal passenger complex and proteins that regulate kinetochore–microtubule interactions. Although a single consensus motif has not been unequivocally defined for AURKB, available evidence indicates that its substrates tend to contain proximal basic residues that favor recognition by the kinase. The specificity is further refined by the dynamic association with regulatory proteins within the chromosomal passenger complex, which contributes to the spatial and temporal control of its substrate selection (ashraf2021explorationofthe pages 1-2, borah2021aurorakinaseb pages 22-23, kitzen2010aurorakinaseinhibitors pages 2-3).
5. Structure  
   Aurora kinase B is organized into three primary domains. The N-terminal region is relatively variable and contains sequences that contribute to subcellular localization and interactions with regulatory partners. This is followed by a highly conserved central catalytic kinase domain that is typical of serine/threonine kinases. The kinase domain is composed of a β-stranded N-terminal lobe and an α-helical C-terminal lobe, which are connected by a flexible hinge region forming the ATP-binding pocket. Within this catalytic domain, critical structural features include the activation loop (or T-loop) that contains a key threonine residue (Thr232) whose autophosphorylation is necessary and sufficient to induce the conformational rearrangements required for full kinase activity. In addition, the kinase domain encompasses the hydrophobic spine and the regulatory C-helix that together contribute to the precise orientation of catalytic residues. At the C-terminal end, Aurora B possesses a short segment implicated in protein stability and the incorporation of degradation motifs such as the D-box and KEN box, which signal proteasomal turnover in a cell cycle-dependent manner. High-resolution structural studies and computational models have provided insights into the arrangement of these domains, confirming that inhibitor binding occurs primarily within the deep ATP-binding cleft located between the β-sheet and α-helical lobes (ashraf2021explorationofthe pages 1-2, kollareddy2008aurorakinasesstructure pages 2-4, kovacs2023aurorabinhibitors pages 14-15, carmena2003thecellulargeography pages 10-11, hochegger2013auroraatthe pages 3-4).
6. Regulation  
   The activity of Aurora kinase B is stringently controlled by a variety of post-translational modifications and protein–protein interactions that ensure its function is restricted to mitosis. A primary regulatory mechanism is the autophosphorylation of the activation loop, particularly at Thr232, which induces a conformation that is competent for substrate binding and phosphorylation. Binding to the chromosomal passenger complex (CPC), composed of INCENP, Survivin, and Borealin, further stimulates the kinase activity and directs its precise localization to centromeres during early mitosis and to the spindle midzone and midbody as cells progress through anaphase and cytokinesis. In addition to autophosphorylation, Aurora B is regulated by reversible phosphorylation events mediated by other kinases and counteracted by protein phosphatases such as PP1 and PP2A. These opposing activities modulate not only the catalytic activity but also the spatial distribution of AURKB in dividing cells. Regulatory motifs contained within the N-terminal region, including degradation signals such as the KEN motif and D-box, ensure that Aurora B is appropriately degraded after its function has been fulfilled during mitosis, preventing unscheduled or residual kinase activity that might compromise genomic stability (ashraf2021explorationofthe pages 1-2, borah2021aurorakinaseb pages 1-3, carmena2003thecellulargeography pages 7-8, kollareddy2008aurorakinasesstructure pages 4-5, kovacs2023aurorabinhibitors pages 26-28).
7. Function  
   Aurora kinase B plays a central role in the regulation of mitosis due to its participation as the catalytic core of the chromosomal passenger complex (CPC). During early stages of mitosis, AURKB localizes predominantly to centromeres, where it phosphorylates substrates, such as Histone H3 at Ser10, to promote chromatin condensation and facilitate proper kinetochore–microtubule attachments. As mitosis continues, Aurora B translocates to the central spindle and ultimately the midbody where it functions in the stabilization of the central spindle, regulation of cleavage furrow formation, and coordination of cytokinesis. These activities are critical to ensuring accurate chromosome segregation and the fidelity of cell division. By monitoring and correcting aberrant kinetochore–microtubule interactions via its phosphorylation of kinetochore constituents, AURKB is essential in the activation and maintenance of the spindle assembly checkpoint. In addition, Aurora B has been implicated in regulating key signaling pathways involving cell cycle progression and apoptosis, partly through its interactions with other mitotic regulators and tumor suppressor proteins. Aberrant expression or dysregulation of Aurora B is frequently associated with aneuploidy and chromosomal instability, factors that contribute to the initiation and progression of a broad range of cancers, including those of the lung, thyroid, ovarian, colorectal, and prostate, as well as glioblastomas. The pivotal role of Aurora B in correcting errors in chromosome alignment and ensuring timely cytokinesis underscores its function in maintaining genome integrity in dividing cells (ashraf2021explorationofthe pages 1-2, carmena2003thecellulargeography pages 7-8, borah2021aurorakinaseb pages 22-23, borah2021aurorakinaseb pages 24-26, hochegger2013auroraatthe pages 1-2, kollareddy2008aurorakinasesstructure pages 2-4).
8. Other Comments  
   Numerous small-molecule inhibitors have been developed to target Aurora kinase B with the goal of disrupting its essential mitotic functions for therapeutic benefit. Several ATP-competitive inhibitors—such as barasertib, hesperadin, and GSK1070916—have been designed to engage the ATP-binding pocket of the kinase with high affinity and selectivity, thereby blocking substrate phosphorylation and inducing mitotic arrest and apoptosis in cancer cells. Structural studies have revealed that inhibitor binding involves key residues lining the catalytic cleft, such as Lys122, Glu141, and Ala173, which are critical for ligand recognition and specificity. In clinical contexts, overexpression and hyperactivation of Aurora B have been correlated with aggressive tumor phenotypes and poor prognosis in multiple malignancies. Furthermore, screening data and functional studies have implicated AURKB in other disease processes, including certain neurodegenerative conditions, as evidenced by its association with lysosomal pathways identified in CRISPR screens (OpenTargets Search: -AURKB). The development of inhibitors that are selective for Aurora B over Aurora A is of paramount importance due to the distinct cellular functions and localization patterns of these kinases, despite the high degree of similarity in their catalytic domains. In addition to pharmacological inhibitors, RNA interference and mutagenesis studies have further underscored the essential nature of Aurora B in maintaining genomic stability. These compilations of structural, biochemical, and functional data continue to guide efforts in the design of more potent and selective inhibitors that may eventually translate into effective anticancer therapies (kovacs2023aurorabinhibitors pages 20-21, kitzen2010aurorakinaseinhibitors pages 2-3, cheung2014aurorakinaseinhibitor pages 1-2, groot2015acellbiologist’s pages 1-2, shuda2009aurorakinaseb pages 2-4).
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