Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2025;14(3):765-70

Exploring the anticancer potential of resveratrol through in silico interaction analysis with mitotic regulators Aurora A, Aurora B, and BubR1

Ihsan Nalkiran, Hatice Sevim Nalkiran

Recep Tayyip Erdoğan University, Faculty of Medicine, Department of Medical Biology, Rize, Türkiye

Received 04 May 2025; Accepted 26 June 2025
Available online 27 August 2025 with doi: 10.5455/medscience.2025.05.118

Abstract

Mitotic regulatory proteins such as Aurora A, Aurora B, and BubR1 play critical roles in ensuring accurate chromosome segregation and maintaining genomic stability during cell division. Abnormal expression of these proteins, including the overexpression of Aurora kinases and dysregulation of BubR1, has been associated with tumor development, therapeutic resistance, and unfavorable clinical outcomes in various cancer types. This study aimed to investigate the potential interactions of Resveratrol, a natural polyphenol, with these key mitotic regulators using in silico molecular docking analysis. Additionally, Reversine, a known Aurora B inhibitor, was docked with Aurora B and served as a positive control. Molecular docking analyses were performed with AutoDock Vina, and the resulting interaction patterns were evaluated using Discovery Studio. Resveratrol exhibited favorable binding affinities toward Aurora A, Aurora B, and BubR1, with docking scores of −7.6, −7.3, and −7.1 kcal/mol, respectively. The ligand formed various stabilizing interactions with all target proteins, including hydrophobic contacts, electrostatic forces, and aromatic stacking. These interactions, particularly pi-alkyl and pi-cation bonds, contributed to the stability of the protein-ligand complexes. The Reversine-Aurora B complex demonstrated the strongest binding affinity with a score of −8.6 kcal/mol and was characterized by multiple hydrogen bonds and hydrophobic interactions, supporting its known inhibitory effect. Overall, the results indicate that Resveratrol can form stable and specific interactions with mitotic regulators, suggesting its potential as an antimitotic and anticancer agent. However, as these findings are based solely on in silico analyses using static protein models, further biological validation is required. Future research should focus on cell-based and animal model studies to confirm the functional relevance of these interactions and evaluate the therapeutic potential of Resveratrol in targeting mitotic kinases.

Keywords: Resveratrol, molecular docking, aurora kinase, BubR1, antimitotic activity

Introduction

Mitosis represents a crucial stage of the cell cycle, essential for safeguarding genomic stability. During this phase, the proper attachment of chromosomes to spindle microtubules and their precise distribution are coordinated by the kinetochore, a complex structure composed of multiple proteins [1]. The kinetochore–microtubule network (KMN), situated at the kinetochore, plays a dual role by mediating the attachment of microtubules and sensing attachment defects to trigger the spindle assembly checkpoint (SAC). Activation of this checkpoint temporarily suspends cell cycle progression until chromosome alignment is correctly achieved. Once alignment is ensured, the APC/C becomes active, promoting sister chromatid separation and the completion of mitosis [2]. BubR1 is one of the core components involved in this regulation. By facilitating kinetochore–microtubule attachment, ensuring proper chromosome alignment, and delaying anaphase onset, BubR1 plays a critical role in maintaining chromosomal stability [3].

CITATION
Nalkiran I, Nalkiran HS. Exploring the anticancer potential of resveratrol through in silico interaction analysis with mitotic regulators Aurora A, Aurora B, and BubR1. Med Science. 2025;14(3):765-70.

Corresponding Author: Hatice Sevim Nalkiran, Recep Tayyip Erdoğan University, Faculty of Medicine, Department of Medical Biology, Rize, Türkiye
Email: hatice.sevim@erdogan.edu.tr

DOI: 10.5455/medscience.2025.05.118

The Aurora family of serine/threonine kinases, comprising Aurora A, B, and C in mammals, represents another key group of proteins regulating the cell cycle. Notably, Aurora A and B are active across various stages, from the G2 phase through cytokinesis [4]. Aurora A plays key roles in centrosome maturation, separation, and mitotic spindle formation during mitosis [5]. Therefore, Aurora A overexpression has been observed in several cancer types and is associated with poor clinical outcomes [6]. Meanwhile, Aurora B encodes a passenger protein involved in mitotic checkpoint activity, chromosome segregation, and cytokinesis during cell division [7-9]. Elevated Aurora B expression has been linked to drug resistance and increased metastatic potential in malignancies such as non-small cell lung cancer (NSCLC), colorectal cancer, and renal cell carcinoma [10,11].

The therapeutic targeting of key molecular regulators using natural or synthetic compounds is becoming increasingly important in cancer treatment strategies. Resveratrol, a naturally occurring phenolic compound present in several plant-based foods, has attracted attention due to its antioxidant, anti-inflammatory, immunomodulatory, antihypertensive, and lipid-lowering properties [12,13]. In addition, it has been shown to possess anti-aging effects through suppression of oxidative stress, inhibition of inflammatory responses, improvement of mitochondrial function, and regulation of apoptosis [14,15]. On the other hand, Reversine, a small molecule considered as a positive control in our study, is a purine analog [16] and has been reported to facilitate the differentiation of human fibroblasts into skeletal muscle cells [17]. It has been shown to target Aurora kinases, particularly Aurora B, in both in vitro and in vivo models, and its anticancer potential has been highlighted [18,19]. Moreover, Reversine is a purine derivative that competitively inhibits ATP binding and functions as an Aurora B inhibitor [19].

In this context, the present study aimed to investigate the potential binding interactions of Resveratrol with mitotic regulatory proteins BubR1, Aurora A, and Aurora B through molecular docking analysis. In addition, the binding of Reversine to Aurora B was evaluated as a positive control to validate the reliability of the docking approach. The findings aim to reveal the interactions of Resveratrol with key regulators of the cell cycle and offer a novel perspective on its potential antimitotic and anticancer effects.

Material and Methods

Molecular Docking Analysis

In this study, molecular docking analyses were conducted to predict the potential interactions between Resveratrol, a natural polyphenolic compound, and three key mitotic regulatory proteins: Aurora A, Aurora B, and BubR1. Additionally, Reversine, a synthetic purine analogue identified in the literature as an Aurora B inhibitor, was docked with Aurora B and served as a positive control. The three-dimensional (3D) chemical structures of the ligand molecules used in the study are shown in Figure 1.

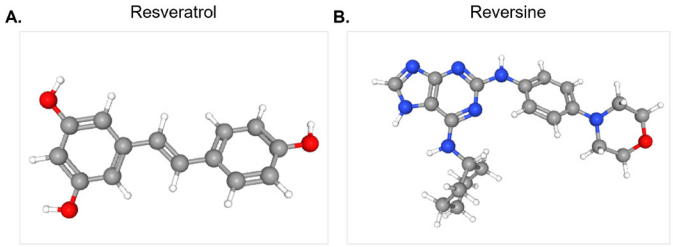

Figure 1. Three-dimensional (3D) structures of the ligand molecules used in the molecular docking study; (**A**) Resveratrol (PubChem CID: 445154), a natural polyphenolic compound; (**B**) Reversine (PubChem CID: 210332), a synthetic purine analogue known to inhibit Aurora B kinase; Atom colors: carbon (gray), hydrogen (white), oxygen (red), and nitrogen (blue)

Resveratrol (PubChem CID: 445154) and Reversine (PubChem CID: 210332) were retrieved from the PubChem database in .sdf file format and then converted to .pdb format using Open Babel software (version 3.1.1) [20]. Before docking preparation, both ligands were subjected to energy minimization using UCSF Chimera (version 1.18) to obtain energetically favorable and stable conformations. Ligand preparation for docking was performed using AutoDock Tools (version 1.5.7) [21]. The 3D models of the target proteins Aurora A, Aurora B, and BubR1 were obtained from the AlphaFold Protein Structure Database [22]. The models were first optimized via energy minimization using UCSF Chimera (version 1.18) [23], followed by structural cleaning with Discovery Studio 2024 Client (version 24.1.0.23298). This included removal of water molecules, co-crystallized ligands, and alternate conformations, along with correction of missing atoms. Subsequently, target proteins were prepared for docking using AutoDock Tools by adding polar hydrogens and assigning Gasteiger charges. Detailed structural information for the proteins is provided in Table 1. The grid box center coordinates were determined based on the predicted binding pockets identified by the PrankWeb server (https://prankweb.cz), which employs deep learning algorithms to predict potential ligand-binding sites on the protein surface. Docking simulations were performed targeting the binding pocket with the highest score predicted for each protein.

Table 1. AlphaFold IDs, UniProt accession numbers, and pLDDT confidence scores for the selected target proteins

AlphaFold ID	Protein	UniProt	Average pLDDT
AF-O14965-F1	Aurora A	O14965	74.86 (High)
AF-Q96GD4-F1	Aurora B	Q96GD4	78.96 (High)
AF-O60566-F1	BubR1	O60566	63.75 (Low)

AF: AlphaFold, pLDDT: predicted local distance difference test, BubR1: budding uninhibited by benzimidazoles-related 1

Molecular docking studies were performed using AutoDock Vina (version 1.1.2) [24]. The grid box centers were positioned according to the predicted binding pockets for each target protein: Aurora A (X: –1.723, Y: 1.034, Z: 3.866), Aurora B (X: 2.705, Y: –1.748, Z: –1.723), and BubR1 (X: –0.896, Y: 13.844, Z: 14.5). A cubic grid box with dimensions of 40 Å × 40 Å × 40 Å was applied to all simulations, and the exhaustiveness parameter

DOI: 10.5455/medscience.2025.05.118

was set to 8. Docking results were analyzed using Discovery Studio Visualizer. Binding affinities (in kcal/mol) were recorded, and protein–ligand interactions were visualized through 3D interaction diagrams.

Ethical Statement

This study did not require ethical committee approval as it was conducted solely through molecular docking analysis using molecular structures obtained from publicly available databases and did not involve human participants or animal experiments.

Results

In this study, the potential binding affinities and interaction profiles of Resveratrol, a natural polyphenolic compound, were evaluated with three key mitosis-regulating target proteins: Aurora A, Aurora B, and BubR1. Additionally, Reversine, a compound previously described in the literature as an Aurora B inhibitor, was docked with Aurora B and used as a positive control. The docking score obtained for the Aurora B–Reversine complex was –8.6 kcal/mol, representing the strongest binding affinity among all tested complexes. This finding is consistent with prior reports on the inhibitory activity of Reversine against Aurora B and validates the reliability of the docking methodology used in this study. Docking scores of –7.0 kcal/mol or lower are typically considered to reflect a high binding affinity. Accordingly, Resveratrol exhibited strong and meaningful interactions with all three target proteins. The obtained docking scores were –7.6, –7.3, and –7.1 kcal/mol for Aurora A, Aurora B, and BubR1, respectively (Table 2).

In the Aurora A–Resveratrol complex, binding was primarily mediated by hydrophobic interactions. Specifically, π-alkyl interactions were observed with residues such as VAL147, LYS162, LEU210, ALA273, LEU139, and LEU263 (Figure 2A). This interaction pattern suggests stable placement of the ligand within the binding pocket, although no hydrogen bonds or electrostatic interactions were detected. Similarly, the Aurora B–Resveratrol complex was dominated by hydrophobic contacts, including π-alkyl and π-sigma interactions with LEU83, LEU207, VAL91, ALA104, and ALA157. A notable π-cation interaction with ARG81 was also identified, which may contribute to the stability of the complex (Figure 2B). The overall binding affinity was comparable to that of Aurora A. In the BubR1–Resveratrol complex, both hydrophobic and aromatic interactions were prominent. Noteworthy π-alkyl and π-π stacking interactions were detected with LEU1047, TRP782, LYS769, ARG770, and LEU1048 (Figure 2C). In particular, π-π stacking involving TRP782 is significant, as such interactions are known to enhance ligand stability within protein binding sites. The Aurora B–Reversine complex, used as the positive control, displayed a diverse interaction profile, including both hydrophobic interactions (e.g., with VAL91, ALA104, LEU207) and hydrogen bonds (notably with ASP218, ALA157, and LEU83) (Figure 2D). The high binding affinity and variety of interaction types support the established role of Reversine as a potent Aurora B inhibitor. Overall, these findings demonstrate that Resveratrol can form strong and significant interactions with both Aurora kinases (A and B) and BubR1. The high binding affinity and stable hydrophobic interactions observed with Aurora A, the π-cation contact with Aurora B, and the aromatic stacking with BubR1 shows versatile binding profile of Resveratrol. Collectively, the results suggest that the interactions of Resveratrol with mitotic regulatory proteins may provide a valuable basis for further biological investigations into its antimitotic or antitumor potential.

Table 2. Docking scores and interaction types between Resveratrol and mitotic regulators (Aurora A, Aurora B, BubR1), with Aurora B–Reversine as a positive control

Protein-ligand	Docking score (kcal/mol)	Protein-ligand interaction	Distance	Types
Aurora A-Resveratrol	-7.6	VAL147	5.21	Pi-Alkyl
		LYS162	4.91	
		LEU210	5.44	
		ALA273	4.51	
		LEU139	4.06	
		LEU263	5.04	
		ARG81	4.59	
Aurora B-Resveratrol	-7.3	LEU207	3.66	Pi-Cation
		LEU83	4.90	Pi-Sigma
		LEU83	5.03	Pi-Alkyl
		VAL91	4.72	
		ALA104	4.09	
		ALA157	5.11	
		LEU1047	3.78	
		TRP782	4.06	
BubR1-Resveratrol	-7.1	TRP782	4.53	Pi-Sigma
		LYS769	4.37	Pi-Pi stacked
		ARG770	5.05	
		LEU791	5.47	Pi-Alkyl
		LEU1048	5.02	
		ASP218	2.60	
		ALA157	3.38	
		LEU83	3.67	
Aurora B-Reversine	-8.6	LEU83	3.96	Conventional hydrogen bond
		LEU207	3.93	
		LEU83	4.68	
		VAL91	4.82	Pi-Sigma
		ALA217	4.66	
		LYS106	5.20	Alkyl
		ALA217	4.11	Pi-Alkyl
		VAL91	5.44	
		ALA104	5.45	
		LEU207	5.12	
		VAL91	5.44	
		ALA104	5.45	
		LEU207	5.12	

DOI: 10.5455/medscience.2025.05.118

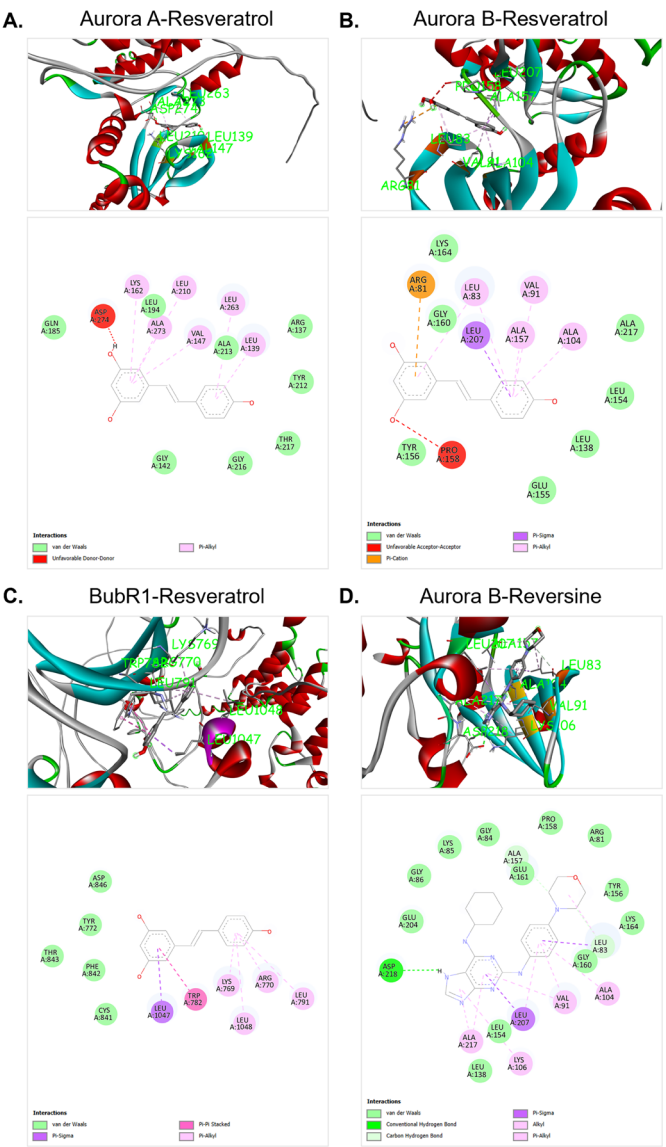

Figure 2. 3D binding conformations (top) and two-dimensional interaction diagrams (bottom) of the ligand–protein complexes; Resveratrol showed predominantly hydrophobic interactions with Aurora A (**A**), hydrophobic and electrostatic interactions with Aurora B (**B**), and both hydrophobic and aromatic π-π stacking interactions with BubR1 (**C**); The Aurora B–Reversine complex (**D**), used as a positive control, exhibited a broader range of interactions including hydrogen bonding and extensive hydrophobic contacts

Discussion

Mitosis is one of the most critical phases of the cell cycle, playing a central role in the preservation of genomic integrity. During this process, the attachment of chromosomes to spindle fibers and their accurate segregation are mediated by the kinetochore, a large multiprotein complex [1]. The KMN network, located on the kinetochore, plays a dual role by enabling microtubule attachment and detecting attachment errors to activate the SAC. This checkpoint halts cell cycle progression until all chromosomes are properly aligned. Subsequently, the APC/C is activated, initiating sister chromatid separation and mitotic exit [2]. Among the key components of this regulatory mechanism, BubR1 acts as a critical SAC protein that inhibits APC/C, thereby preventing premature anaphase onset [25]. This function of BubR1 is vital for maintaining chromosomal stability, as chromosomal instability is a hallmark of cancer, observed in approximately 90% of solid tumors [26]. Changes in BubR1 expression levels thus provide valuable insights into cancer biology. Downregulation of BubR1 has been observed in various studies focusing on colorectal [27] and prostate cancers [28]. Conversely, overexpression of BubR1 has been reported in bladder [29], lung adenocarcinoma [30], breast [31] and pancreatic adenocarcinoma [32].

Another important group in mitotic regulation is the Aurora kinase family, particularly Aurora A and Aurora B, which function at different stages of mitosis and are of growing interest in cancer research [4,7,8]. Aurora A kinase localizes at spindle poles and plays key roles in centrosome duplication, maturation, and separation [4]. Due to these functions, amplification and overexpression of Aurora A have been observed in various cancers and are often associated with poor prognosis [6]. Dysregulation of Aurora A contributes to tumor progression via mechanisms such as enhanced cell cycle progression, survival signaling, activation of anti-apoptotic pathways, maintenance of genomic instability, induction of epithelial-to-mesenchymal transition, and preservation of the cancer stem cell phenotype [33,34]. Therefore, Aurora A has emerged as a promising therapeutic target in oncology, with approaches targeting this kinase demonstrating significant antitumor effects in various cancer models, including thyroid cancer [35,36]. Aurora B kinase, on the other hand, ensures accurate chromosome alignment during early mitosis by monitoring microtubule–kinetochore attachments, and also plays a critical role in cytokinesis [37]. Overexpression of Aurora B has been associated with drug resistance, increased metastatic potential, and aggressive tumor phenotypes in cancers such as NSCLC, colorectal cancer, and renal cell carcinoma [10,11].

Resveratrol, a naturally occurring polyphenol, exhibits a broad range of biological activities due to its structural properties. It has been reported to exert antioxidant, anti-inflammatory, immunomodulatory, hypotensive, and hypolipidemic effects, with therapeutic potential in cancer, cardiovascular diseases, and neurodegenerative disorders [12,13]. By suppressing oxidative stress, inhibiting inflammatory pathways, improving mitochondrial function, and regulating apoptosis, resveratrol has emerged as a promising candidate molecule [14,15]. Its antitumor activity has been demonstrated in various cancers, including liver, pancreas, breast, prostate, colorectal [38]. Reversine, an ATP-competitive purine analog, has been shown to specifically target Aurora kinases. Particularly as an Aurora B inhibitor, Reversine has been reported as a promising anticancer agent [16,18,19].

DOI: 10.5455/medscience.2025.05.118

In this study, molecular docking analyses revealed that Resveratrol exhibited strong binding affinities with the mitotic regulators Aurora A, Aurora B, and BubR1. The docking scores were calculated as –7.6 kcal/mol for Aurora A, –7.3 kcal/mol for Aurora B, and –7.1 kcal/mol for BubR1. Interaction profiling showed a combination of hydrophobic, electrostatic, π-alkyl, and bidirectional π–π stacking interactions. These multi-modal interactions facilitate the ligand's proper accommodation within the binding pocket and enhance the stability of the protein–ligand complexes. In particular, aromatic stacking and electrostatic attractions significantly contribute to the stabilization of the ligand conformation within the binding site. In the Aurora B–Reversine interaction, evaluated as the positive control, a docking score of –8.6 kcal/mol was observed. This high affinity was supported by the presence of conventional hydrogen bonds and extensive hydrophobic contacts, consistent with previously described inhibitory effects of Reversine on Aurora B. These findings suggest that Resveratrol can form specific and multifaceted interactions with key mitotic proteins, providing molecular-level support for its potential antimitotic and antitumor effects.

However, a major limitation of this study is that all data are based solely on in silico molecular docking analyses. These analyses utilize static 3D protein structures, and the calculated binding scores merely reflect geometric and chemical complementarity to the binding site. While these results suggest potential biologically relevant interactions, experimental validation is essential to confirm functional relevance. Importantly, relying exclusively on computational approaches without supporting experimental data may limit the biological validity and translational relevance of these findings. Therefore, the interpretation of these results should be approached with caution until further experimental confirmation is provided. In addition, regarding BubR1 structure selection, it should be noted that the AlphaFold database provides only a single model along with its predicted local distance difference test (pLDDT) score for each protein. Although the overall pLDDT score of BubR1 was moderate, the local scores at the predicted binding pocket regions were considered acceptable for docking analysis. In the absence of an alternative high-resolution structure, the available AlphaFold model was utilized. This limitation has also been addressed within the discussion. Additionally, the absence of molecular dynamics (MD) simulations constitutes another limitation of the present study. Since molecular docking provides only a static snapshot of protein-ligand interactions, the lack of MD analysis prevents assessment of the dynamic stability and persistence of key interactions, particularly electrostatic contacts, under physiological conditions. Incorporating MD simulations in future studies would allow a more comprehensive understanding of the temporal stability, conformational flexibility, and binding stability of these complexes. To draw clinical conclusions and therapeutic implications, these findings must be supported by in vitro and in vivo studies. Therefore, future studies should investigate Resveratrol's interactions with Aurora A, Aurora B, and BubR1 through kinase inhibition assays, cell-based phosphorylation analyses, or mitotic index assessments. Additionally, the compound's dose-dependent inhibition profile, its impact on cell cycle regulation, and roles in modulating apoptotic mechanisms should be explored in detail.

These findings demonstrate that Resveratrol establishes meaningful and multifaceted interactions with mitotic regulatory proteins, supporting its antimitotic and potential antitumor activities at the molecular level. As such, Resveratrol emerges as a promising natural compound for consideration in targeted cancer therapy. However, this therapeutic potential requires validation through comprehensive biochemical, cellular, and preclinical studies.

Conclusion

This study highlights the potential of Resveratrol as a multitarget compound capable of interacting with key mitotic regulators such as Aurora A, Aurora B, and BubR1. The in-silico findings suggest that Resveratrol may exert antimitotic and antitumor effects through stable and specific protein–ligand interactions. While these results provide valuable molecular insights, experimental validation is necessary to confirm their biological relevance. Thus, Resveratrol warrants further investigation as a candidate for targeted cancer therapy.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
This study did not require ethical committee approval as it was conducted solely through molecular docking analysis using molecular structures obtained from publicly available databases and did not involve human participants or animal experiments.

References

1. Santaguida S, Amon A. Short- and long-term effects of chromosome mis-segregation and aneuploidy. Nature Rev Mol Cell Biol. 2015;16:473-85. Erratum in: Nat Rev Mol Cell Biol. 2015;16:576.
2. Musacchio A, Desai A. A molecular view of kinetochore assembly and function. Biology (Basel). 2017;6:5.
3. Kim T , Moyle MW , Lara-Gonzalez P, et al. Kinetochore-localized BUB-1/BUB-3 complex promotes anaphase onset in C. elegans. J Cell Biol. 2015;209:507-17. Erratum in: J Cell Biol. 2016;212:737.
4. Marumoto T , Zhang D, Saya H. Aurora-A - a guardian of poles. Nat Rev Cancer. 2005;5:42-50.
5. Barr AR, Gergely F. Aurora-A: the maker and breaker of spindle poles. J Cell Sci. 2007;120:2987-96.
6. Liewer S, Huddleston A. Alisertib: a review of pharmacokinetics, efficacy and toxicity in patients with hematologic malignancies and solid tumors. Expert Opin Investig Drugs. 2018;27:105-12.
7. Tang A, Gao K, Chu L, et al. Aurora kinases: novel therapy targets in cancers. Oncotarget. 2017;8:23937-23954.

DOI: 10.5455/medscience.2025.05.118

8. Willems E , Dedobbeleer M , Digregorio M, et al. The functional diversity of Aurora kinases: a comprehensive review. Cell Div. 2018;13:7.
9. Krenn V, Musacchio A. The Aurora B kinase in chromosome bi-orientation and spindle checkpoint signaling. Front Oncol. 2015;5:225.
10. Wan B, Huang Y, Liu B, et al. AURKB: a promising biomarker in clear cell renal cell carcinoma. Peer J. 2019;7:e7718.
11. Borah NA, Reddy MM. Aurora Kinase B inhibition: a potential therapeutic strategy for cancer. Molecules. 2021;26:1981.
12. Meng X, Zhou J, Zhao CN, et al. Health benefits and molecular mechanisms of resveratrol: a narrative review. Foods. 2020;9:340.
13. Harikumar KB, Aggarwal BB. Resveratrol: a multitargeted agent for age-associated chronic diseases. Cell Cycle. 2008;7:1020-35.
14. Ginés C, Cuesta S, Kireev R, et al. Protective effect of resveratrol against inflammation, oxidative stress and apoptosis in pancreas of aged SAMP8 mice. Exp Gerontol. 2017;90:61-70.
15. Wang N, Luo Z, Jin M, et al. Exploration of age-related mitochondrial dysfunction and the anti-aging effects of resveratrol in zebrafish retina. Aging (Albany NY). 2019;11:3117-37.
16. Chen S, Zhang Q, Wu X, et al. Dedifferentiation of lineage-committed cells by a small molecule. J Am Chem Soc. 2004;126:410-1.
17. Anastasia L, Sampaolesi M, Papini N, et al. Reversine-treated fibroblasts acquire myogenic competence in vitro and in regenerating skeletal muscle. Cell Death Differ. 2006;13:2042-51.
18. Amabile G, D'Alise AM, Iovino M, et al. The Aurora B kinase activity is required for the maintenance of the differentiated state of murine myoblasts. Cell Death Differ. 2009;16:321-30.
19. D'Alise AM, Amabile G, Iovino M, et al. Reversine, a novel Aurora kinases inhibitor, inhibits colony formation of human acute myeloid leukemia cells. Mol Cancer Ther. 2008;7:1140-9.
20. O'Boyle NM, Banck M, James CA, et al. Open Babel: an open chemical toolbox. J Cheminform. 2011;3:33.
21. Morris GM , Huey R , Lindstrom W, et al. AutoDock4 and AutoDockTools4: automated docking with selective receptor flexibility. J Comput Chem. 2009;30:2785-91.
22. Jumper J, Evans R, Pritzel A, et al. Highly accurate protein structure prediction with AlphaFold. Nature. 2021;596:583-9.
23. Pettersen EF, Goddard TD, Huang CC, et al. UCSF Chimera--a visualization system for exploratory research and analysis. J Comput Chem. 2004;25:1605-12.
24. Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. J Comput Chem. 2010;31:455-61.
25. Bloom CR, North BJ. Physiological relevance of post-translational regulation of the spindle assembly checkpoint protein BubR1. Cell Biosci. 2021;11:76.
26. Hosea R, Hillary S, Naqvi S, et al. The two sides of chromosomal instability: drivers and brakes in cancer. Signal Transduct Target Ther. 2024;9:75.
27. Shichiri M, Yoshinaga K, Hisatomi H, et al. Genetic and epigenetic inactivation of mitotic checkpoint genes hBUB1 and hBUBR1 and their relationship to survival. Cancer Res. 2002;62:13-7.
28. Silva MP, Ferreira LT, Brás NF, et al. BUB1B monoallelic germline variants contribute to prostate cancer predisposition by triggering chromosomal instability. J Biomed Sci. 2024;31:74.
29. Yamamoto Y, Matsuyama H, Chochi Y, et al. Overexpression of BUBR1 is associated with chromosomal instability in bladder cancer. Cancer Genet Cytogenet. 2007;174:42-7.
30. Chen H, Lee J, Kljavin NM, et al. Requirement for BUB1B/BUBR1 in tumor progression of lung adenocarcinoma. Genes Cancer. 2015;6:106-18.
31. Du J, Du Q, Zhang Y, et al. Expression of cell-cycle regulatory proteins BUBR1, MAD2, Aurora A, cyclin A and cyclin E in invasive ductal breast carcinomas. Histol Histopathol. 2011;26:761-8.
32. Gladhaug IP, Westgaard A, Schjølberg AR, et al. Spindle proteins in resected pancreatic head adenocarcinomas: BubR1 is an independent prognostic factor in pancreatobiliary-type tumours. Histopathology. 2010;56:345-55.
33. Lin X, Xiang X, Hao L, et al. The role of Aurora-A in human cancers and future therapeutics. Am J Cancer Res. 2020;10:2705-29.
34. Yan M, Wang C, He B, et al. Aurora-A kinase: a potent oncogene and target for cancer therapy. Med Res Rev. 2016;36:1036-79.
35. Jing XL, Chen SW. Aurora kinase inhibitors: a patent review (2014-2020). Expert Opin Ther Pat. 2021;31:625-44.
36. Li Y, Li X, Pu J, et al. c-Myc Is a Major determinant for antitumor activity of aurora a kinase inhibitor MLN8237 in thyroid cancer. Thyroid. 2018;28:1642-54.
37. Keen N, Taylor S. Aurora-kinase inhibitors as anticancer agents. Nat Rev Cancer. 2004;4:927-36.
38. Carter LG, D'Orazio JA, Pearson KJ. Resveratrol and cancer: focus on in vivo evidence. Endocr Relat Cancer. 2014;21:R209-25.