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Yong Wu and Jaydutt Vadgama \*

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**Commentary Article** 

# Commentary on Article: The Role of PPM1D in Cancer and Advances in Studies of its Inhibitors

Yong Wu \* and Jaydutt Vadgama \*

Division of Cancer Research and Training, Department of Internal Medicine, Charles Drew University of Medicine and Science, David Geffen UCLA School of Medicine and UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA.

Corresponding Authors: Yong Wu and Jaydutt Vadgama, Charles R. Drew University of Medicine and Science, 1748 E. 118th Street, Los Angeles, CA 90059. USA.

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## **Abstract**

The review article entitled "The role of PPM1D in cancer and advances in studies of its inhibitors" provides a comprehensive overview of the current understanding of the function of PPM1D in cancer and the progress that has been made in the development of inhibitors to target this protein.

PPM1D, also known as WIP1, is a serine/threonine phosphatase that plays a key role in regulating several cellular processes including DNA damage response, cell cycle progression, and apoptosis. Dysregulation of PPM1D has been implicated in various types of cancer, and this article delves into the molecular mechanisms by which PPM1D overexpression can promote tumorigenesis.

**Key words:** role of PPM1D; cancer; inhibitors; WIP1; dysregulation; cancer biology and therapy

# **Summary**

The review article entitled "The role of PPM1D in cancer and advances in studies of its inhibitors" [1] provides a comprehensive overview of the current understanding of the function of PPM1D in cancer and the progress that has been made in the development of inhibitors to target this protein.

PPM1D, also known as WIP1, is a serine/threonine phosphatase that plays a key role in regulating several cellular processes including DNA damage response, cell cycle progression, and apoptosis. Dysregulation of PPM1D has been implicated in various types of cancer [2-5], and this article delves into the molecular mechanisms by which PPM1D overexpression can promote tumorigenesis.

The authors highlight the significance of PPM1D as a potential therapeutic target for cancer treatment. In particular, they discuss the promising preclinical results of various inhibitors that have been developed to target PPM1D, including small molecules, peptides, and monoclonal antibodies. The authors also emphasize the challenges of developing PPM1D inhibitors, including achieving sufficient specificity and minimizing off-target effects.

The review article provides a comprehensive analysis of the current understanding of PPM1D in cancer and the advances made in developing inhibitors to target this protein. However, further research is needed to fully elucidate the role of PPM1D in cancer and to develop more effective

and specific inhibitors for clinical use. One potential avenue for further investigation is the identification of specific subpopulations of cancer cells that are particularly dependent on PPM1D for survival. It is likely that not all cancer cells are equally reliant on PPM1D, and identifying subpopulations that are most susceptible to PPM1D inhibition could lead to more effective and targeted therapies. Additionally, while significant progress has been made in the development of PPM1D inhibitors, there is still room for improvement in terms of specificity and selectivity. Further research could focus on identifying novel compounds that more specifically target PPM1D and have fewer off-target effects. Another area for exploration is the potential for combination therapies that target both PPM1D and other key signaling pathways in cancer cells. For example, combining PPM1D inhibitors with inhibitors of the PI3K/Akt/mTOR pathway, which is frequently dysregulated in cancer [6-10], could lead to synergistic effects and improved therapeutic outcomes. Furthermore, it will be important to explore the potential of PPM1D as a biomarker for cancer diagnosis and prognosis. Dysregulation of PPM1D has been associated with poor outcomes in several types of cancer, and further investigation could lead to the development of new diagnostic and prognostic tools [3, 11, 12].

Overall, this review article provides valuable insights into the role of PPM1D in cancer and the potential of PPM1D inhibitors as a new class of cancer therapeutics. It serves as an informative resource for researchers and clinicians in the field of cancer biology and therapy.

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#### References

- Deng W, Li J, Dorrah K, Jimenez-Tapia D, Arriaga B, Hao Q, Cao W, Gao Z, Vadgama J, Wu Y, (2020), The role of PPM1D in cancer and advances in studies of its inhibitors. Biomed Pharmacother 2020, 125:109956.
- Martinikova AS, Burocziova M, Stoyanov M, Macurek L, (2020), Truncated PPM1D Prevents Apoptosis in the Murine Thymus and Promotes Ionizing Radiation-Induced Lymphoma. Cells 2020, 9(9).
- Khadka P, Reitman ZJ, Lu S, Buchan G, Gionet G, Dubois F, Carvalho DM, Shih J, Zhang S, Greenwald NF et al. (2022), PPM1D mutations are oncogenic drivers of de novo diffuse midline glioma formation. Nat Commun 2022, 13(1):604.
- 4. Al Hinai ASA, Grob T, Rijken M, Kavelaars FG, Zeilemaker A, Erpelinck-Verschueren CAJ, Sanders MA, Lowenberg B, Jongen-Lavrencic M, Valk PJM, (2021), PPM1D mutations appear in complete remission after exposure to chemotherapy without predicting emerging AML relapse. Leukemia 2021, 35(9):2693-2697.
- Lu ZW, Wen D, Wei WJ, Han LT, Xiang J, Wang YL, Wang Y, Liao T, Ji QH, (2020), Silencing of PPM1D inhibits cell proliferation and invasion through the p38 MAPK and p53

- **signaling pathway in papillary thyroid carcinoma**. Oncol Rep 2020, 43(3):783-794.
- Yu L, Wei J, Liu P, (2022), Attacking the PI3K/Akt/mTOR signaling pathway for targeted therapeutic treatment in human cancer. Semin Cancer Biol 2022, 85:69-94.
- Stanciu S, Ionita-Radu F, Stefani C, Miricescu D, Stanescu S, II, Greabu M, Ripszky Totan A, Jinga M, (2022), Targeting PI3K/AKT/mTOR Signaling Pathway in Pancreatic Cancer: From Molecular to Clinical Aspects. Int J Mol Sci 2022, 23(17).
- Miricescu D, Balan DG, Tulin A, Stiru O, Vacaroiu IA, Mihai DA, Popa CC, Papacocea RI, Enyedi M, Sorin NA et al. (2021), PI3K/AKT/mTOR signalling pathway involvement in renal cell carcinoma pathogenesis (Review). Exp Ther Med 2021, 21(5):540.
- Braglia L, Zavatti M, Vinceti M, Martelli AM, Marmiroli S, (2020), Deregulated PTEN/PI3K/AKT/mTOR signaling in prostate cancer: Still a potential druggable target? Biochim Biophys Acta Mol Cell Res 2020, 1867(9):118731.
- Bahrami A, Khazaei M, Shahidsales S, Hassanian SM, Hasanzadeh M, Maftouh M, Ferns GA, Avan A, (2018), The Therapeutic Potential of PI3K/Akt/mTOR Inhibitors in Breast Cancer: Rational and Progress. J Cell Bio-chem 2018, 119(1):213-222.
- Zhang L, Hsu JI, Goodell MA, (2022), PPM1D in Solid and Hematologic Malignancies: Friend and Foe? Mol Cancer Res 2022, 20(9):1365-1378.
- Kojima K, Maeda A, Yoshimura M, Nishida Y, Kimura S, (2016), The pathophysiological significance of PPM1D and therapeutic targeting of PPM1D-mediated signaling by GSK2830371 in mantle cell lymphoma. Oncotarget 2016, 7(43):69625-69637.



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