



## Checkpoint kinase 1 as a promising target in colorectal cancer management

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**Specialty type:** Oncology

**Provenance and peer review:**

Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's classification**

**Scientific Quality:** Grade A, Grade B, Grade C

**Novelty:** Grade A, Grade B, Grade B

**Creativity or Innovation:** Grade A, Grade A, Grade B

**Scientific Significance:** Grade A, Grade B, Grade C

**P-Reviewer:** Bi X; Gugulothu D; Huang Z

**Received:** December 16, 2024

**Revised:** January 14, 2025

**Accepted:** January 15, 2025

**Published online:** April 24, 2025

**Processing time:** 103 Days and 6.2 Hours



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### Abstract

This editorial provides insights into the pivotal role of checkpoint kinase 1 (CHEK1) as both a biomarker and therapeutic target in colorectal cancer (CRC), based on findings from a recent study by Pang *et al.* Using single-cell RNA sequencing and immunohistochemistry, the study demonstrates significant CHEK1 overexpression in CRC tissues and identifies nitidine chloride as a potent CHEK1 inhibitor that disrupts DNA damage repair pathways. These findings underscore the therapeutic potential of CHEK1 inhibition and highlight the need for further research to address gaps in CRC treatment.

**Key Words:** Colorectal cancer; Checkpoint kinase 1; Biomarker; Therapeutic target; Single-cell RNA sequencing; Nitidine chloride

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**Core Tip:** This editorial highlights checkpoint kinase 1 (CHEK1) as a novel biomarker and therapeutic target in colorectal cancer (CRC). Pang *et al* demonstrate significant CHEK1 overexpression in CRC tissues using single-cell RNA sequencing, immunohistochemistry, and tissue microarray analyses. They identify nitidine chloride as a potent CHEK1 inhibitor that disrupts DNA damage repair, impairing tumor progression. These findings emphasize CHEK1's potential for improving CRC diagnosis and treatment while addressing research needs for clinical validation and tumor microenvironment exploration.

**Citation:** Ma W, Baran N. Checkpoint kinase 1 as a promising target in colorectal cancer management. *World J Clin Oncol* 2025; 16(4): 104213

**URL:** <https://www.wjgnet.com/2218-4333/full/v16/i4/104213.htm>

**DOI:** <https://dx.doi.org/10.5306/wjco.v16.i4.104213>

## INTRODUCTION

Colorectal cancer (CRC) represents a significant global health challenge, marked by high mortality rates and limited therapeutic options, particularly in its metastatic stages[1,2]. Despite advances in immunotherapy and targeted therapies, the response rates remain suboptimal, necessitating novel diagnostic and therapeutic approaches[3-5].

The study by Pang *et al*[6] published in this issue of the *World Journal of Clinical Oncology*, addresses these challenges by exploring the role of checkpoint kinase 1 (CHEK1) in CRC. This editorial critically evaluates their findings, emphasizing CHEK1's potential as a biomarker and therapeutic target.

## CHEK1 AS A BIOMARKER IN CRC

The study highlights the biomarker potential of CHEK1 in CRC using cutting-edge techniques and global data analyses. Integrating single-cell RNA sequencing, immunohistochemistry, and tissue microarray analyses, the study reveals significant overexpression of CHEK1 in CRC tissues compared to adjacent non-cancerous tissues. The integration of global datasets further supports the consistent upregulation of CHEK1, positioning it as a promising diagnostic biomarker.

CHEK1's elevated levels align with its established role in cell cycle regulation and DNA damage response, critical pathways in CRC progression[6-8]. These findings highlight CHEK1's potential for improving early detection and prognosis in CRC. Furthermore, comparisons with other biomarkers, such as immune checkpoint pathways and cell-cycle regulators, underscore CHEK1's unique role in CRC biology.

## THERAPEUTIC IMPLICATIONS OF CHEK1 INHIBITION

In addition to its diagnostic value, CHEK1 holds significant promise as a therapeutic target. Pang *et al*[6] identify nitidine chloride (NC) as a potent CHEK1 inhibitor through molecular docking studies, demonstrating its strong binding affinity[9, 10].

By inhibiting CHEK1 activity, NC disrupts DNA damage repair pathways, sensitizing tumor cells to genotoxic stress and impairing their survival. CRISPR knockout experiments further confirm CHEK1's role in promoting CRC cell proliferation[11,12]. These findings underscore the potential of integrating CHEK1 inhibitors into precision oncology frameworks, complementing existing therapeutic strategies. Additionally, this article discusses the potential synergistic effects of CHEK1 inhibition with current CRC treatments, including immunotherapies, to enhance treatment outcomes.

## ADDRESSING GAPS IN CRC RESEARCH

While the study by Pang *et al*[6], provides compelling evidence supporting CHEK1's role as a biomarker and therapeutic target, it also highlights key limitations, including the reliance on specific dataset and the absence of *in vivo* validation. Addressing these gaps requires further exploration of CHEK1's mechanistic role in CRC progression, particularly within the tumor microenvironment (TME)[13-15].

Future research should explore CHEK1's interactions with immune cells, stromal components, and angiogenesis within the TME. Additionally, the potential combinatory effects of CHEK1 inhibition with immunotherapies or chemotherapies warrant investigation. The critical next step is initiating clinical trials to evaluate CHEK1 inhibitor's efficacy and safety in CRC treatment[16,17]. Furthermore, adherence to ethical standards in acquiring and using human and animal tissue samples in the studies cited must be explicitly acknowledged to ensure rigor and transparency.

## CONCLUSION

Pang *et al*[6] have significantly contributed to CRC research, positioning CHEK1 as both a biomarker and therapeutic target. Their findings lay the groundwork for innovative diagnostic tools and targeted therapies. As CRC treatment evolves, studies like this advance precision oncology, offering hope for improved patient outcomes and survival rates.

## FOOTNOTES

**Author contributions:** Ma W reviewed the relevant literature, designed the concept and outline of this editorial, wrote, edited, and finalized the manuscript for publication; Baran N reviewed and provided critical review and edits to enhance the content.

**Conflict-of-interest statement:** The authors report no relevant conflicts of interest for this article.

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**S-Editor:** Lin C

**L-Editor:** A

**P-Editor:** Zheng XM

## REFERENCES

- 1 Pathak PS, Chan G, Deming DA, Chee CE. State-of-the-Art Management of Colorectal Cancer: Treatment Advances and Innovation. *Am Soc Clin Oncol Educ Book* 2024; **44**: e438466 [PMID: 38768405 DOI: 10.1200/EDBK\_438466]
- 2 Li Q, Geng S, Luo H, Wang W, Mo YQ, Luo Q, Wang L, Song GB, Sheng JP, Xu B. Signaling pathways involved in colorectal cancer: pathogenesis and targeted therapy. *Signal Transduct Target Ther* 2024; **9**: 266 [PMID: 39370455 DOI: 10.1038/s41392-024-01953-7]
- 3 González-Montero J, Rojas CI, Burotto M. Predictors of response to immunotherapy in colorectal cancer. *Oncologist* 2024; **29**: 824-832 [PMID: 38920285 DOI: 10.1093/oncolo/oyae152]
- 4 Yan H, Liu J, Zhang Y, Chen S, Xu J, Gao D, Li H, Fang X, Wang Y, Wang H, Wang H. Efficacy and safety of regorafenib in the treatment of metastatic colorectal cancer: a retrospective cohort study. *J Gastrointest Oncol* 2024; **15**: 987-1001 [PMID: 38989408 DOI: 10.21037/jgo-24-180]
- 5 Clerick J, Van Oosterwyck A, Carton S. Transforming the landscape of colorectal cancer treatment with immunotherapy: Evolution and future horizons. *Cancer Treat Res Commun* 2024; **39**: 100807 [PMID: 38461691 DOI: 10.1016/j.ctarc.2024.100807]
- 6 Pang YY, Chen ZY, Zeng DT, Li DM, Li Q, Huang WY, Li B, Luo JY, Chi BT, Huang Q, Feng ZB, He RQ. Checkpoint kinase 1 in colorectal cancer: Upregulation of expression and promotion of cell proliferation. *World J Clin Oncol* 2025; **16**: 101725 [DOI: 10.5306/wjco.v16.i3.101725]
- 7 Li J, Shang L, Zhou F, Wang S, Liu N, Zhou M, Lin Q, Zhang M, Cai Y, Chen G, Yang S. Herba Patriniae and its component Isoviteixin show anti-colorectal cancer effects by inducing apoptosis and cell-cycle arrest via p53 activation. *Biomed Pharmacother* 2023; **168**: 115690 [PMID: 37939611 DOI: 10.1016/j.biopha.2023.115690]
- 8 Weng W, Meng T, Pu J, Ma L, Shen Y, Wang Z, Pan R, Wang M, Chen C, Wang L, Zhang J, Zhou B, Shao S, Qian Y, Liu S, Hu W, Meng X. AMT-562, a Novel HER3-targeting Antibody-Drug Conjugate, Demonstrates a Potential to Broaden Therapeutic Opportunities for HER3-expressing Tumors. *Mol Cancer Ther* 2023; **22**: 1013-1027 [PMID: 37302522 DOI: 10.1158/1535-7163.MCT-23-0198]
- 9 Hrudka J, Kalinová M, Fišerová H, Jelínková K, Nikov A, Waldauf P, Matěj R. Molecular genetic analysis of colorectal carcinoma with an aggressive extraintestinal immunohistochemical phenotype. *Sci Rep* 2024; **14**: 22241 [PMID: 39333321 DOI: 10.1038/s41598-024-72687-3]
- 10 Gong H, Wang L, Zhao J, Wang L, Yu Q, Wan Y. Nitidine chloride inhibits the appearance of cancer stem-like properties and regulates potential the mitochondrial membrane alterations of colon cancer cells. *Ann Transl Med* 2020; **8**: 591 [PMID: 32566618 DOI: 10.21037/atm-20-3432]
- 11 Zhang J, Wu L, Lian C, Lian S, Bao S, Zhang J, Wang P, Ma J, Li Y. Nitidine chloride possesses anticancer property in lung cancer cells through activating Hippo signaling pathway. *Cell Death Discov* 2020; **6**: 91 [PMID: 33024576 DOI: 10.1038/s41420-020-00326-7]
- 12 Yang X, Liu J, Wang S, Al-Ameer WHA, Ji J, Cao J, Dhaen HMS, Lin Y, Zhou Y, Zheng C. Genome wide-scale CRISPR-Cas9 knockout screens identify a fitness score for optimized risk stratification in colorectal cancer. *J Transl Med* 2024; **22**: 554 [PMID: 38858785 DOI: 10.1186/s12967-024-05323-3]
- 13 Meng H, Nan M, Li Y, Ding Y, Yin Y, Zhang M. Application of CRISPR-Cas9 gene editing technology in basic research, diagnosis and treatment of colon cancer. *Front Endocrinol (Lausanne)* 2023; **14**: 1148412 [PMID: 37020597 DOI: 10.3389/fendo.2023.1148412]
- 14 Chen X, Ma Z, Yi Z, Wu E, Shang Z, Tuo B, Li T, Liu X. The effects of metabolism on the immune microenvironment in colorectal cancer. *Cell Death Discov* 2024; **10**: 118 [PMID: 38453888 DOI: 10.1038/s41420-024-01865-z]
- 15 Yu B, Shao S, Ma W. Frontiers in pancreatic cancer on biomarkers, microenvironment, and immunotherapy. *Cancer Lett* 2025; **610**: 217350 [PMID: 39581219 DOI: 10.1016/j.canlet.2024.217350]
- 16 Zhang X, Ma H, Gao Y, Liang Y, Du Y, Hao S, Ni T. The Tumor Microenvironment: Signal Transduction. *Biomolecules* 2024; **14** [PMID: 38672455 DOI: 10.3390/biom14040438]
- 17 Chu X, Tian W, Ning J, Xiao G, Zhou Y, Wang Z, Zhai Z, Tanzhu G, Yang J, Zhou R. Cancer stem cells: advances in knowledge and implications for cancer therapy. *Signal Transduct Target Ther* 2024; **9**: 170 [PMID: 38965243 DOI: 10.1038/s41392-024-01851-y]