



OPEN ACCESS

EDITED AND REVIEWED BY
Peter Brossart,
University of Bonn, Germany

*CORRESPONDENCE

Lanyu Jing
✉ jly9875@163.com
Anze Yu
✉ yuanz6@mail.sysu.edu.cn

RECEIVED 22 October 2025
ACCEPTED 27 October 2025
PUBLISHED 31 October 2025

CITATION

Jing L and Yu A (2025) Editorial: PANoptosis and its role in T cell-based immunotherapy. *Front. Immunol.* 16:1729986. doi: 10.3389/fimmu.2025.1729986

COPYRIGHT

© 2025 Jing and Yu. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Editorial: PANoptosis and its role in T cell-based immunotherapy

Lanyu Jing^{1,2*} and Anze Yu^{3*}

¹Breast Department, Guangdong Provincial Hospital of Chinese Medicine, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, The Second Clinical College of Guangzhou University of Chinese Medicine, Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou, Guangdong, China, ²Breast Disease Center, First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China, ³Department of Urology, First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China

KEYWORDS

PANoptosis, T cell, immunotherapy, cytokine - immunological terms, inflammation

Editorial on the Research Topic

PANoptosis and its role in T cell-based immunotherapy

PANoptosis, an integrated form of programmed cell death encompassing pyroptosis, apoptosis, and necroptosis, has emerged as a key mechanism at the intersection of inflammation and immunity (1). Acting through the PANoptosome complex, this multifaceted pathway not only regulates cellular homeostasis but also orchestrates immune activation and tissue remodeling. In the tumor immune microenvironment, PANoptosis plays dual roles: it can amplify anti-tumor immunity or, conversely, induce immune exhaustion and immune escape when dysregulated (2, 3). T cell-based immunotherapy—including immune checkpoint blockade (ICB) and chimeric antigen receptor (CAR) T cell therapy—has transformed the therapeutic landscape of multiple cancers (4). However, the variability in patient responses underscores the complexity of immune regulation and cell death signaling. Exploring how PANoptosis modulates T cell activity offers new insights into the mechanisms underlying immunotherapy resistance and tumor immune evasion. This Research Topic gathers a series of studies that collectively explore this dynamic interplay from molecular discovery to translational potential.

At the molecular level, Wang et al. applied a multi-omics strategy to classify renal cell carcinoma (RCC) into distinct metabolic subtypes. Their findings revealed that metabolic reprogramming tightly associates with PANoptosis-related signaling, defining prognostic subgroups and potential targets for precision immunotherapy. Building on the theme of molecular regulation, Tao et al. investigated cathepsin Z (CTSZ) in prostate cancer and found that its overexpression not only predicts poor clinical outcomes but also shapes an immunosuppressive microenvironment characterized by elevated PD-1 and PD-L1 expression—linking protease signaling to checkpoint regulation and PANoptotic control.

Expanding this exploration into other cancer types, Lei et al. developed a programmed cell death (PCD) score model for hepatocellular carcinoma (HCC) that integrates transcriptomic and single-cell analyses. Their identification of UBE2E1 as a key

oncogenic driver associated with high PCD scores highlights how cell death dynamics affect T cell exhaustion and tumor aggressiveness. Complementing this, Wu et al. conducted a pan-cancer analysis of PLAG1 and demonstrated its functional role in promoting tumor proliferation and immune evasion in bladder cancer, further strengthening the connection between PANoptosis and immune modulation.

Moving from genomics to the tumor microenvironment, Liao et al. explored the clinical relevance of tumor mutation burden (TMB) across cancers and identified RPLP0 as a predictive biomarker for immunotherapy response. Interestingly, RPLP0 knockdown enhanced anti-PD-L1 efficacy in bladder cancer models, providing a tangible example of how PANoptosis-related translational control may affect therapeutic sensitivity. Similarly, Wan et al. synthesized current findings on immune cell PANoptosis in colorectal cancer, emphasizing that excessive immune cell death can undermine anti-tumor immunity and proposing strategies to restore immune balance through targeted interventions.

Beyond oncology, Chen et al. extended the concept of PANoptosis to diabetic retinopathy, identifying several hub genes that regulate inflammation and immune cell infiltration. Their integrative machine-learning approach underscores that PANoptotic signaling has broad implications in immune-related diseases beyond cancer. In parallel, Ma et al. reviewed advances in immunogenic cell death (ICD) and nanomaterial-based therapies, highlighting how nanotechnology can trigger PANoptosis-like mechanisms to promote antigen release and potentiate durable T cell immunity. These findings demonstrate that manipulating cell death pathways can synergize with T cell-based therapies to achieve improved clinical outcomes.

Together, the articles in this Research Topic illuminate PANoptosis as a pivotal immunoregulatory hub bridging cell death, metabolism, and immune activation. They reveal how fine-tuning PANoptotic signaling can shape tumor immunogenicity, determine therapeutic response, and open new avenues for combinatorial immunotherapy. Future studies integrating single-cell, spatial, and multi-omics technologies will be essential to define the spatial and temporal coordination of PANoptosis within the tumor microenvironment. By deepening our mechanistic understanding, researchers may unlock strategies to exploit PANoptosis for enhanced T cell function, reinvigorated anti-tumor immunity, and ultimately improved patient survival.

This Research Topic therefore not only consolidates current progress but also lays the foundation for translating PANoptosis biology into next-generation immunotherapeutic strategies.

Author contributions

LJ: Writing – original draft, Writing – review & editing. AY: Writing – original draft, Writing – review & editing.

Acknowledgments

We sincerely thank all contributing authors and reviewers for their valuable work and insights that enriched this Research Topic.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

- Lin JF, Wang TT, Huang RZ, et al. PANoptosis in cancer: bridging molecular mechanisms to therapeutic innovations. *Cell Mol Immunol.* (2025) 22:996–1011. doi: 10.1038/s41423-025-01329-z
- Zhang X, Song S, Huang Z, et al. Z-DNA-binding protein 1 exacerbates myocardial ischemia-reperfusion injury by inducing noncanonical cardiomyocyte PANoptosis. *Signal Transduct Target Ther.* (2025) 10:333. doi: 10.1038/s41392-025-02430-5
- Zhang X, Tang B, Luo J, et al. Cuproptosis, ferroptosis and PANoptosis in tumor immune microenvironment remodeling and immunotherapy: culprits or new hope. *Mol Cancer.* (2024) 23:255. doi: 10.1186/s12943-024-02130-8
- Rahim MK, Okholm TLH, Jones KB, et al. Dynamic CD8(+) T cell responses to cancer immunotherapy in human regional lymph nodes are disrupted in metastatic lymph nodes. *Cell.* (2023) 186:1127–1143.e18. doi: 10.1016/j.cell.2023.02.021