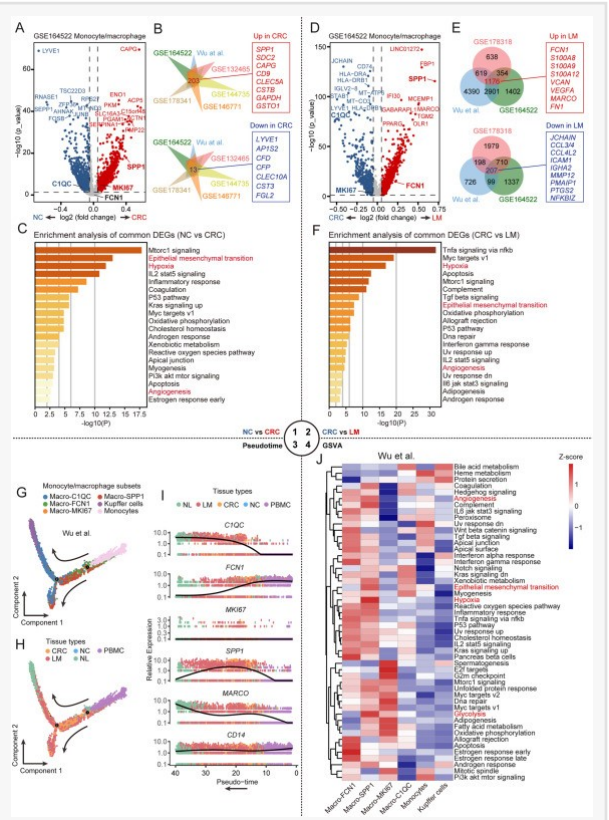
SPP1+ Macrophages Identified as Key Drivers and Therapeutic Targets In Colorectal Cancer Progression

New Study Unveils Critical Role of SPP1+ Macrophages in Colorectal Cancer Progression and Treatment

CHINA, March 17, 2025 /EINPresswire.com/ -- Colorectal cancer (CRC) is the third most common malignancy and the second leading cause of cancer-related deaths worldwide. Despite the success of immune checkpoint blockade therapies in various solid tumors, immunotherapy for CRC remains a challenge. Hence, there is a critical need to understand the complex tumor microenvironment (TME) of CRC and identify potential targets to develop new immunotherapies.



(A) Volcano plot of DEGs in monocytes/macrophages between NC and CRC samples in the GSE164552 dataset. (B) Venn diagrams of common DEGs up- or down-regulated across the six scRNA-seq datasets (NC vs. CRC). (C) Metascape bar graph of functional enrichment

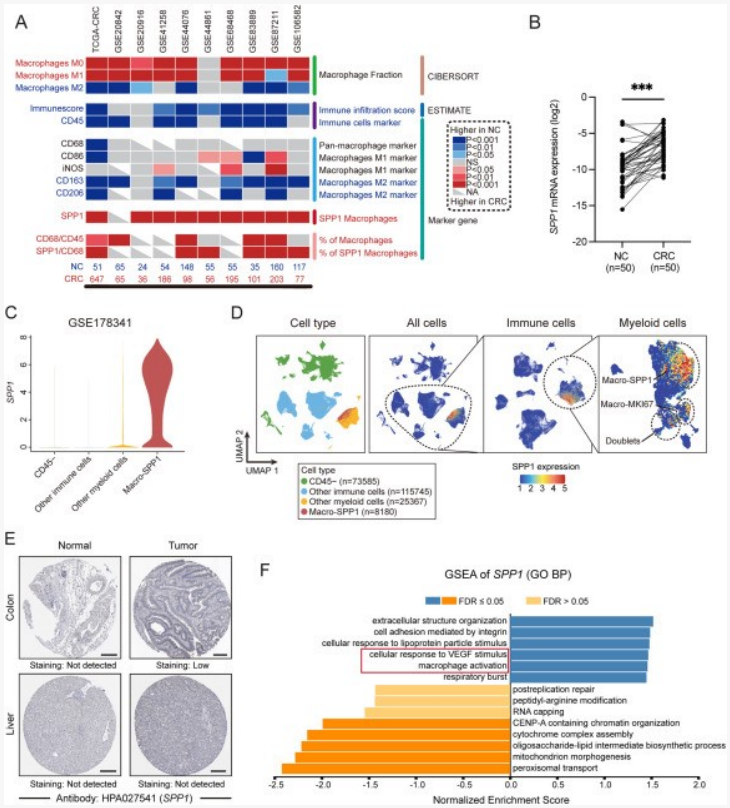
This research, published in the Genes & Diseases journal by a team from Xi'an Medical University, The First Hospital of China Medical University, and Air Force Medical University integrates single-cell and spatial transcriptomics with bulk sequencing to investigate the roles and mechanisms of SPP1+ macrophages in CRC.

The researchers identified four macrophage subsets from CRC tissue, including FCN1+ macrophages, C1QC+ macrophages, SPP1+ macrophages, and MKI67+ macrophages. They found that the number and proportion of SPP1+ macrophages consistently increased during CRC occurrence, progression, and metastasis. This finding suggests that SPP1+ macrophages play an important role in driving CRC development and metastasis.

Interestingly, this study noted an increase in the proportion of M1 macrophages and a decrease in M2 macrophages in CRC, contradicting the M1/M2 polarization theory. Functional analyses

suggests that SPP1+ macrophages may promote CRC through epithelial-mesenchymal transition (EMT), hypoxia, glycolysis, and immunosuppressive pathways. These macrophages interact with other cells through the SPP1-CD44, SPP1-PTGER4, and SPP1 a4b1 complex axes, highlighting potential therapeutic intervention points.

In addition, the research findings suggest that preoperative chemotherapy can significantly reduce SPP1 expression in CRC macrophages, particularly in treatment responders, indicating a potential role in immunotherapy. Inhibition of the CSF1-CSF1R axis, a major research direction of macrophage-targeted immunotherapy, led to the depletion of the protective C1QC+ macrophage subset while sparing malignant SPP1+ macrophages. This drawback contributes to the poor efficacy of anti-CSF1R therapies in clinical studies.



(A) Heatmap of the proportion of M0, M1, and M2 macrophages (CIBERSORT), immune score (ESTIMATE), expression of markers (CD45, CD68, CD86, iNOS, CD163, CD206, and SPP1), CD68/CD45, and SPP1/CD68 in 10 bulk RNA-seq datasets (NC vs. CRC). The color gradient

In summary, this study provides a comprehensive analysis of SPP1+ macrophages in CRC, including their origin, distribution, clinical value, functional pathways, and implications for treatment. Based on the results, the researchers propose the SPP1+ macrophage model theory, which explains the changes in macrophages during CRC liver metastasis (CRLM) and guides clinical diagnosis and treatment. These findings open new avenues for CRC treatment and emphasize the need for more precise macrophage-targeted immunotherapy strategies.

Reference

Title of Original Paper: SPP1+ macrophages in colorectal cancer: Markers of malignancy and promising therapeutic targets

DOI: https://doi.org/10.1016/j.gendis.2024.101340

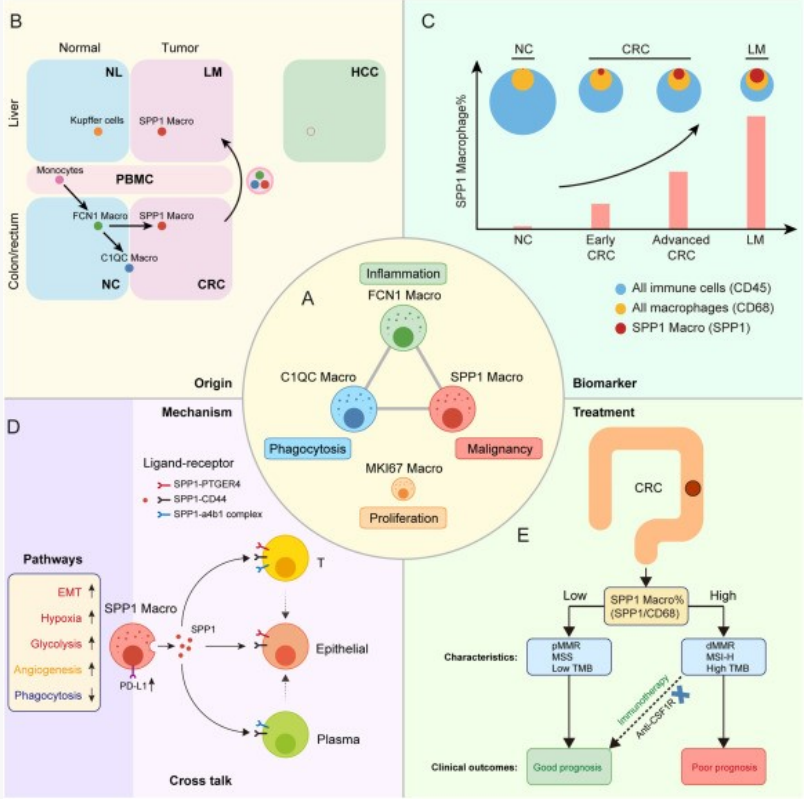
Journal: Genes & Diseases
Genes & Diseases is a journal for molecular and translational medicine. The journal primarily focuses on publishing investigations on the molecular bases and experimental therapeutics of

human diseases. Publication formats include full length research article, review article, short communication, correspondence, perspectives, commentary, views on news, and research watch.

Funding Information:

National Natural Science Foundation of China (No. 82072655)
Scientific and technological innovation team of Shaanxi Innovation Capability Support Plan (China) (No. 2023-CX-TD-67)
Key R&D Plan of Shaanxi Province, China (No. 2022SF-603)

# # # # # #



(A) Classification of macrophage subsets in CRC, including FCN1+, C1QC+, SPP1+, and MKI67+ macrophages, defined by their core features of inflammation, phagocytosis, malignancy, and proliferation, respectively. (B) Model of the developmental trajectory of

Genes & Diseases publishes rigorously peer-reviewed and high quality original articles and authoritative reviews that focus on the molecular bases of human diseases. Emphasis is placed on hypothesis-driven, mechanistic studies relevant to pathogenesis and/or experimental therapeutics of human diseases. The journal has worldwide authorship, and a broad scope in basic and translational biomedical research of molecular biology, molecular genetics, and cell biology, including but not limited to cell proliferation and apoptosis, signal transduction, stem cell biology, developmental biology, gene regulation and epigenetics, cancer biology, immunity and infection, neuroscience, disease-specific animal models, gene and cell-based therapies, and regenerative medicine.

Scopus CiteScore: 7.3 | Impact Factor: 6.9

# # # # # #

More information: https://www.keaipublishing.com/en/journals/genes-and-diseases/

Editorial Board: https://www.keaipublishing.com/en/journals/genes-and-diseases/editorial-board/

All issues and articles in press are available online in ScienceDirect

(https://www.sciencedirect.com/journal/genes-and-diseases).

Submissions to Genes & Disease may be made using Editorial Manager (https://www.editorialmanager.com/gendis/default.aspx).

Print ISSN: 2352-4820
eISSN: 2352-3042
CN: 50-1221/R
Contact Us: editor@genesndiseases.com

X (formerly Twitter): @GenesNDiseases (https://x.com/GenesNDiseases)

Genes & Diseases Editorial Office
Genes & Diseases
+86 23 6571 4691
email us here
Visit us on social media:
Facebook
X
LinkedIn
Instagram
YouTube
Other
