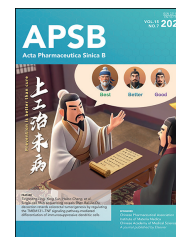




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EDITORIAL

Traditional Chinese medicine in the early prevention of colorectal cancer from the perspective of tumor microenvironment



KEY WORDS

Colorectal cancer;
Early prevention;
Tumor microenvironment

Colorectal cancer (CRC), a globally prevalent malignancy, typically evolves through the adenoma-carcinoma sequence *via* intricate interplay of genetic, environmental, and metabolic factors¹. The current clinical and basic research predominantly focuses on the treatment of CRC, while insufficient attention has been paid to the precancerous lesions and early intervention². The historical account of Bian Que and his brothers in ancient Chinese medicine reveals the TCM theory of “preventive treatment of diseases”, emphasizing that disease prevention is better than cure. The theory of “preventive treatment of diseases” includes three levels: prevention before disease, prevention of the development of the existing disease, and prevention of the recrudescence of disease. This theory remarkably aligned with modern concepts of tumor primary and secondary prevention³. However, TCM has the characteristics of “multi-component, multi-pathway and multi-target”⁴. How to apply modern scientific systems to interpret the “preventive treatment of diseases” theory of TCM and its anti-cancer mechanisms still faces many challenges.

A recent study by Cheng’s team published in *Acta Pharmaceutica Sinica B* (APSB) has systematically delineated the changes in the tumor microenvironment (TME) and elucidated the molecular mechanisms underlying the Shen-Bai-Jie-Du decoction’s (SBJDD’s) suppression of colorectal

adenoma–carcinoma transition (Fig. 1, Created in BioRender, Agreement number: XP28D4EEY0)⁵. They demonstrated that SBJDD significantly retards colorectal tumorigenesis in *Apc*^{Min/+} mice and in clinical patients. Single-cell RNA sequencing depicted a dynamic cellular landscape during colorectal adenoma–carcinoma transition and SBJDD treatment, revealing significant enrichment of *Nlrp3*⁺ TAMs, neutrophils, stem cells, *Ccl22*⁺ DCs, *Spp1*⁺ macrophages, *Cd4*⁺ regulatory T cells (Tregs), and *Cd4*⁺ Th17 cells throughout tumorigenesis. Integrated analysis with The Cancer Genome Atlas cohort identified *Ccl22*⁺ DCs as the pivotal cell subtype exhibiting dual-modulation during both colorectal adenoma–carcinoma transition and SBJDD treatment. Pseudotime trajectory analysis traced the ontogeny of *Ccl22*⁺ DCs to *Wdfy4*⁺ DCs precursors. Combinatorial cellular interaction analysis, multiplex immunohistochemistry, and flow cytometry demonstrated that *Ccl22*⁺ DCs promote colorectal tumorigenesis *via* Tregs-mediated immunosuppression. Mechanistically, berberine (an active compound of SBJDD) suppressed *Ccl22*⁺ DC differentiation and their immunosuppressive function by targeting TMEM131, a transmembrane regulatory protein governing TNF signaling pathway activation.

This study established a close connection between the two complex systems of TCM and TME through single-cell sequencing, which not only deepened the understanding of the dynamic evolution of colorectal TME, but also highlighted the potential of TCM in the early prevention of CRC. In addition, this study also identified *Ccl22*⁺ DCs-TMEM131 as potential therapeutic targets, indicating that normalization of the TME may be a safer strategy for tumor prevention and treatment, and providing a new paradigm for research on the mechanisms of modern TCM compounds.

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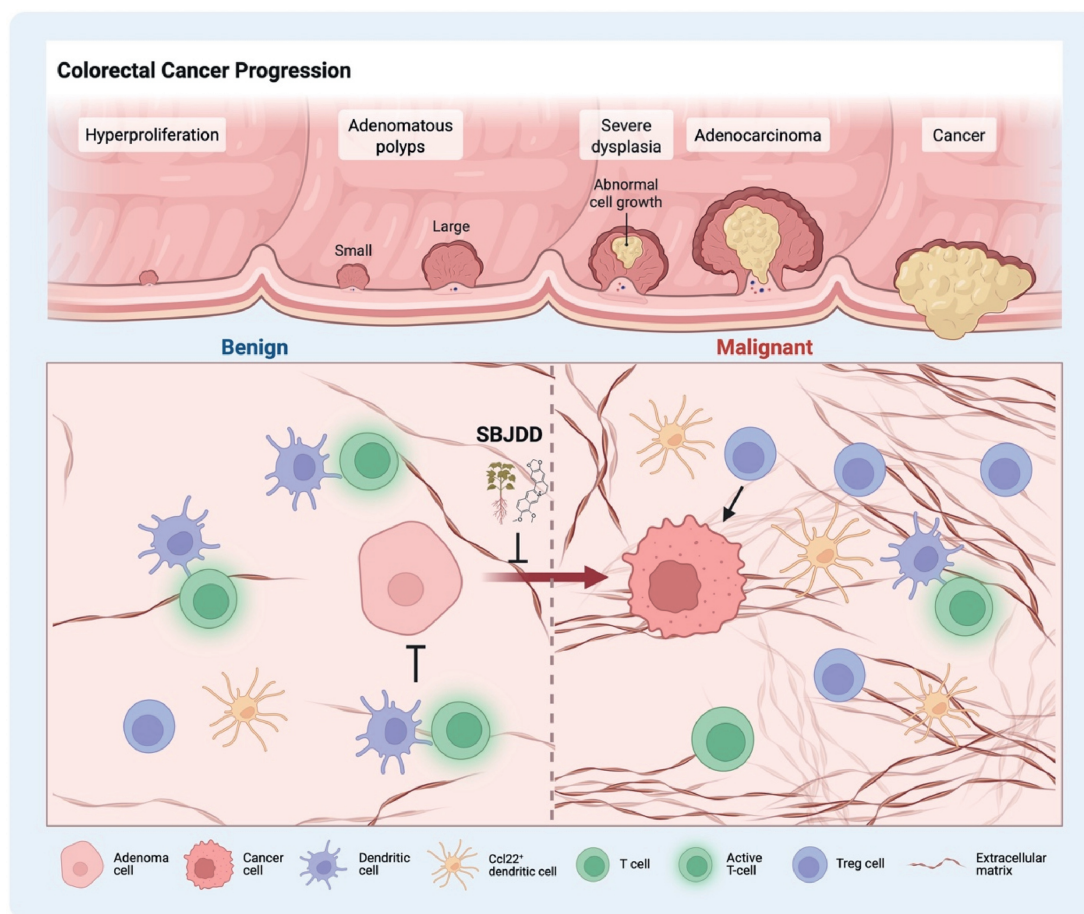


Figure 1 Dynamic cellular landscape during colorectal adenoma-carcinoma transition and Shen-Bai-Jie-Du decoction (SBJDD)'s treatment.

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