

The application of traditional Chinese medicine against the tumor immune escape

Jing Xu, Jingjing Zhang, Jing Wang

Department of Hematology and Oncology, Dongzhimen Hospital,
Beijing University of Chinese Medicine, Beijing, China

INTRODUCTION

Tumor immune escape happens when tumor cells are not detected, recognized, and killed by the body's immune system. It is often under the protection of the tumor microenvironment, which refers to a complex network composed of tumor cells, immune cells, endothelial cells, stromal cells, fibroblasts and various cytokines. By interacting with stromal cells and immune cells, or by secreting cytokines, tumor cells can get rid of the recognition and attack, and suppress the immune response of the host, so as to transform the tumor microenvironment into a microenvironment conducive to tumor survival, growth and uncontrollable proliferation, eventually causing immune escape of tumor cells.^[1-2] Among them, macrophages, dendritic cells, regulatory T cells, myeloid-derived suppressor cells and NK cells are the main immune regulatory cells. Traditional Chinese medicine (TCM), widely used by patients with cancers in China, can reverse the immune escape of tumor by modifying the microenvironment and enhancing the function of immune cells.

According to TCM, the occurrence of tumor is related to the deficiency of healthy *qi* and the hyperactivity of evil *qi* in the body. It is the major principle of TCM in the treatment of malignant tumors to strengthen the healthy *qi* and disperse the evil *qi*, tonify the spleen and resolve the dampness, clear heat and detoxify. Strengthening the healthy *qi* and dispersing the evil *qi* method can play an

anti-tumor role by regulating immune cell mediated tumor immune escape in tumor microenvironment. On the one hand, it can promote the secretion of tumor suppressor factors by macrophages, and inhibit the formation of tumor-related macrophages.^[3-4] Epimedium koreanum Nakai polysaccharides are an important active component of Epimedium. It can promote secretion of cytokines such as IFN- γ and TNF- α , and activate CD4+T cells differentiation to enhance the anti-tumor effect of the body.^[5] On the other hand, it can suppress the effect of myeloid derived suppressor cells (MDSCs) and reduce the angiogenesis of tumors. MDSCs are abundantly present in the tumor microenvironment, and are an important cell population that causes tumor immune escape and has immunosuppressive effects.^[6-7] By examining the level of MDSCs in peripheral blood of 31 breast cancer patients, it was found that the level of MDSCs in peripheral blood was closely related to disease progression. Shuganjianpi formula alone or combined with gemcitabine chemotherapy could inhibit the proliferation of MDSC cells and improve the immunity of the body.^[8-9]

Many studies have repeatedly proven the key anti-cancer mechanism of TCM lies in regulating immune cells and mediating tumor immune escape. Pang *et al.*^[10] studied the mechanism of Bufei Decoction against Non-Small Cell Lung Cancer (NSCLC) and found that tumor-associated macrophages was essential in the progression of NSCLC and were related to tumor cell immune suppression. Su *et al.*^[11] established a mouse

Address for Correspondence:
Dr. Jing Wang, MD/PhD, No.5
Haiyuncang, Dongcheng District, Beijing,
100700, China.
E-mail: Jing.Wang@bucm.edu.cn

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4T1 breast cancer model and found that Xihuang Pill, a patent Chinese medicine of heat clearing and detoxification function, could promote apoptosis of Treg cells in the tumor microenvironment. Another study pointed out that Astragalus polysaccharide (APS), main component of *qi* tonifying herb *Astragalus membranaceus*, inhibited the expression of Foxp3 mRNA through cytokine and matrix repair, hampered SDF-1's recruitment of Treg cells in the micro-environment of liver cancer, and reduces the immunosuppressive effect of Treg cells.^[12] Other research of Wolfberry, *Scutellaria barbata*, and *Coix lacryma-jobi* also showed their different properties to improve anti-tumor immunity.^[13-15]

The wisdom of TCM method is in symphony with the most recent understanding of anti-cancer strategy. A comprehensive database of TCM on immuno-oncology has been established based on the chemical ingredients of herbs that interact with the immune-oncology targets.^[16] It provides us a new tool for potential herbs with immune regulating properties, yet all results need to be confirmed with further experiments and trials. Up to now, the scientific explanation of TCM for cancer is still rather preliminary. It calls for more rigorous experiments and clinical trials in order to decipher the capacity of TCM in the anti-tumor immunity.

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Conflict of Interest

None declared.

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