

DISCUSSION ON THE MECHANISM OF TCM PREVENTION AND TREATMENT OF "INFLAMMATION-CANCER" TRANSFORMATION

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Abstract: Cancer worldwide has a high incidence rate and a high case fatality rate, causing a serious disease burden on humans. It is of great significance to slow down the risk of cancer, to study the treatment of cancer and to clarify the target of cancer to improve the prognosis of patients with cancer. Chronic inflammation can lead to the occurrence of cancer, and the mechanism of inflammation leading to the occurrence and development of cancer is not very clear. Traditional Chinese medicine (TCM) can prevent inflammatory cancer transformation by inhibiting inflammatory reaction. This paper discusses the mechanism of TCM prevention and treatment of inflammatory cancer transformation, which is helpful to further explain the pharmacological effect of compound TCM prescriptions and active ingredients, in order to provide new ideas for the wider and more accurate application of TCM in clinical practice.

Keywords: Traditional Chinese medicine; Inflammation-cancer transformation; Epithelial-mesenchymal transition; Tumor-associated macrophages; Cancer stem cells

1 INTRODUCTION

Cancer worldwide has a high incidence rate and a high case fatality rate, resulting in a serious disease burden on humans. Cancer is also one of the main problems that threaten the health of our population. In recent years, the incidence and mortality of cancer in China have increased significantly [1]. It is of great significance to slow down the risk of cancer, study the therapeutic drugs to prevent and treat cancer, and clarify the relevant therapeutic targets to improve the prognosis of cancer patients.

Chronic inflammation can lead to the occurrence of cancer, such as colitis-associated colorectal cancer (CAC) caused by inflammatory bowel disease (IBD), liver inflammation can then induce liver cancer, and chronic inflammation of gastric mucosa can gradually lead to gastric cancer. However, at present, the mechanism of inflammation leading to the occurrence and development of cancer is not very clear. TCM is one of the important means of cancer treatment in China. Its therapeutic advantages are mainly reflected in regulating the inflammatory environment in tumor lesion tissues, regulating the influencing factors related to tumor inflammatory environment, so as to inhibit the growth of tumor cells and prevent the metastasis of cancer cells from blood tract and lymph. It is found that compound TCM prescriptions can prevent inflammatory cancer transformation by inhibiting inflammatory response, and its mechanism of action involves nuclear transcription factor- κ B (NF- κ B), Wnt / β -catenin and other signaling pathways [2]. This paper discusses the mechanism of TCM prevention and treatment of inflammatory cancer transformation, which is helpful to further explain the pharmacological effect of compound TCM prescriptions and active ingredients, in order to provide new ideas for the wider and more accurate application of TCM in clinical practice.

2 EPITHELIAL-MESENCHYMAL TRANSITION (EMT)

EMT is closely related to the occurrence and progression of malignant tumors, which is one of the important mechanisms of tumor invasion, metastasis and drug resistance. While TCM and active ingredients can act on tumor EMT to inhibit the proliferation, invasion and migration of cancer cells. Vimentin-mediated NLRP3 (NOD-, LRR- and pyrin domain- containing protein3) / Caspase-1 signaling, TGF- β 1-induced EMT process, and the arachidonic acid-HETEs metabolic pathway activated by Gq proteins. All three pathways are involved in the regulation of inflammation, Vimentin, NLRP3, Caspase-1 are the core targets, Vimentin Is an important molecule linking the transformation of inflammatory carcinoma, It can participate in the regulation of tumor inflammation microenvironment through many aspects; NLRP3, Caspase-1 are involved in the formation of the NLRP3 inflammasome, The latter is one of the inflammasome with the largest number of ligands found to date, Its activation is not only able to promote the cleavage maturation of the inflammatory mediators pro-IL-1 β and pro-IL-18, Be secreted outside the cell to exert various inflammatory effects, Can also induce Caspase-1-dependent cell pyroptosis, Make the cells die under inflammatory and stressed pathological conditions [3].NLRP3 inflammasome is involved in diverse inflammatory diseases. However, the endogenous regulatory mechanisms of NLRP3 inflammasome are still less defined. β -catenin, which is the central mediator of the canonical Wnt/ β -catenin signaling, promotes NLRP3 inflammasome activation [4]. It was found that the TCM (composed of Astragalus, ganoderma lucidum and mountain mushroom) could inhibit EMT remodeling of tumor immune microenvironment [5]. Luo Yang found that Chutan Jiedu Decoction (composed of such as Dangshen, Atractylodes, and Poria) could regulate the expression of in EMT related proteins twist, fibronectin, and

Snail and vimentin. Qinghua Yichang Formula can inhibit the activation of NLRP3 inflammasome, reduce the activation of Caspase-1 and GSDMD proteins, regulate the immune balance, and reduce the expression of proinflammatory factors in [6-8]. Experimental studies have shown that β -lupinene can inhibit the proliferation, invasion and migration of lung cancer cells by inhibiting the EMT, stem cell-like properties and self-renewal ability of lung cancer cells. Taking the mechanism of EMT of TCM as the starting point, the paper aims to analyze the transcription level mechanism of the sequence evolution process of "inflammation-dysplasia-cancer" and the changes of key signaling pathways and molecules in the regulatory network of "inflammation-cancer", so as to provide a theoretical basis for the pathogenesis of the transformation and clinical diagnosis and treatment of inflammatory cancer.

3 TUMOR-ASSOCIATED MACROPHAGES (TAMS)

The tumor microenvironment has the largest proportion of numerous inflammatory cells with associated macrophages, with about 30%-50% [10]. Macrophages can be divided into two types: classically activated macrophages (M1) and selectively activated macrophages (M2). M1 can secrete immune regulatory factors such as IL-12, IFN and TNF- α , and make cytotoxic T lymphocytes in the tumor immune system; M2 is induced by IL-4 and IL-10 from the tumor environment, suppressing the anti-tumor immune response, accelerating the development of tumor, and directly or indirectly promoting cancer metastasis. According to relevant studies, Tumor-Associated Macrophages (TAMs) and their secreted factors are important components of the inflammatory microenvironment, and also play a very important role in the formation of tumor microenvironment and tumor development and development. The study found that [11], composed of astragalus, atractylodes, yunling and other Chinese medicine can reduce inflammatory necrosis of liver cells and liver cancer tissue gene expression, the main mechanism of prevention and treatment of liver cancer through downregulation of TGF- β 1 induced liver cancer EMT process, Gq protein activation of arachidonic acid-HETEs metabolism pathway and Vimentin mediated NLRP3/Caspase-1 pathway, involved in the regulation of liver cancer inflammation microenvironment, inhibit the occurrence and development of liver cancer. The herbal prescription, the treatment of stress colitis, can affect JAK / STAT signaling pathway to reduce the serum inflammatory factors IL-4 and IL-10 in mice, promote the transformation of M2 macrophages into M1 macrophages, improve the tumor immune microenvironment under chronic stress, and inhibit the development of colorectal cancer [12].

4 NUCLEAR FACTOR κ B (NF- κ B)

NF- κ B is the joint point, which can affect every link of cell homeostasis, thus triggering tumors. As the core protein of inflammatory response, in the process of inflammatory cancer transformation, the production mechanism and role of NF- κ B are particularly important in the study of tumor inflammatory microenvironment. It is found that the compound TCM prescriptions coix seed can inhibit the release of pro-inflammatory factors and promote the release of anti-inflammatory factors by regulating NF- κ B signaling pathway, so as to prevent the occurrence of colon cancer [13]. Paeonol, the active ingredient of TCM, can relieve CAC [14] by regulating the levels of TNF- α , IL-6, IL-1 β , IL-10, STAT-3, and NF- κ B p65 in mice.

5 CANCER STEM CELL (CSC)

CSC is key cells for tumor initiation and can lead to tumor malignancy and their recurrence, metastasis, as well as cancer cell heterogeneity. Wnt/ β -catenin signaling pathway plays a very important role in EMT and is also one of the key points in maintaining CSC. The release of β -catenin from the cell membrane upon activation by specific ligands promotes the transcription of [15] from genes involved in the induction of the mesenchymal phenotype and maintenance of CSC.

It was found that the active components of TCM could inhibit the EMT process and CSC [16] simultaneously by inhibiting the PI3K / AKT, Notch1 and EZH 2 signaling pathways. According to TCM, CSC is the root cause of the "cancer toxicity" hidden in the cancer microenvironment, and CSC is in the tumor microenvironment of healthy qi deficiency, with both blood stasis and sputum [17]. "Cancer poison" and is closely related to tumor inflammatory microenvironment, the formation of "cancer poison" main pathological factors, blood stasis and tumor inflammatory microenvironment inflammatory factors, chemokines, tumor inflammatory microenvironment promote tumor metastasis EMT way also accord with the "cancer poison" phlegm stasis damp and heat through the pathogenic characteristics of [18].

At present, there are more and more studies on the role of compound TCM prescriptions and TCM active ingredients in regulating inflammatory factors and inhibiting CSC and related mechanisms. "inflammation-tumor stem cell" may become an important research direction for the prevention and treatment of the "inflammation-cancer" transformation in TCM.

COMPETING INTERESTS

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