DOI: 10.66069/ojspub.27450715

Research Progress of Traditional Chinese Medicine Moxibustion in Tumor Treatment and Rehabilitation Based on Modulation of Tumor Immune Microenvironment

Xuerong Zhang[1], Haijuan Xiao[2,3,*]

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Integrated Traditional Chinese and Western Medicine Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang, China
[3]Oncology Hospital, Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China
**Correspondence Author*

Abstract: ***The immunosuppressive state of the tumor immune microenvironment (TIME) is one of the core drivers of tumor progression, therapeutic resistance, recurrence and metastasis, and represents a major research hotspot in the field of oncology. As a classic external therapy of traditional Chinese medicine characterized by "thermal stimulation-acupoint regulation-systemic response", moxibustion exhibits promising application prospects in remodeling the tumor immune microenvironment. This paper systematically elaborates on the TCM theoretical basis, modern molecular mechanisms, preclinical experimental evidence and clinical studies concerning moxibustion-mediated regulation of the tumor immune microenvironment. It further summarizes recent research data regarding moxibustion's modulatory effects on immune cell subsets, cytokine networks and immune checkpoint pathways, and explores the unique advantages of moxibustion in enhancing anti-tumor efficacy and alleviating toxic and side effects induced by radiotherapy and chemotherapy.***

Keywords: Moxibustion, Tumor, Tumor Immune Microenvironment, Immunoregulation, Integrated Chinese and Western Medicine Therapy.

1. Introduction

1.1 Clinical Significance and Therapeutic Dilemma of Tumor Immune Microenvironment

The tumor immune microenvironment (TIME) is a dynamically regulable network composed of tumor cells, immune cells, stromal cells, cytokines and other components. Interactions between these elements exert pro- or anti-tumor effects and form a dynamic balance that ultimately determines the overall direction of anti-tumor immune responses [1]. Effective anti-cancer immune responses rely on a series of sequential, iterative processes collectively termed the "cancer-immunity cycle" [2]. This cycle terminates in two divergent outcomes: complete tumor clearance or the onset of tumor immune escape [3]. In cancer patients, the cancer-immunity cycle frequently malfunctions: tumor antigens may evade detection; dendritic cells (DCs) and T cells may recognize antigens as self rather than foreign antigens, triggering responses from regulatory T cells (Tregs) instead of effector T cells; T cells may fail to migrate to tumor sites or be suppressed from infiltrating tumor tissues; most critically, soluble factors within the TIME can blunt the function of mature effector T cells [4]. In addition to the aforementioned mechanisms, decreased cytotoxic activity of natural killer (NK) cells, M2 polarization of tumor-associated macrophages (TAMs) [5], and upregulated expression of immune checkpoint molecules such as programmed death receptor 1 (PD-1) and programmed death ligand 1 (PD-L1) [6]all contribute to tumor immune escape and compromise the efficacy of anti-tumor therapies including chemotherapy, radiotherapy and immunotherapy. Even immune checkpoint inhibitors (ICIs), a landmark immunotherapeutic modality, only yield clinical benefits in 20%–40% of patients, while approximately 40% of recipients develop immune-related adverse events of varying severity [7]. Modulating the immunosuppressive TIME to restore robust anti-tumor immunity has become a core priority in oncological research. Therefore, identifying safe, effective and cost-efficient interventions to remodel the TIME carries profound clinical value.

1.2 Research Basis of Moxibustion Intervention Against the Tumor Immune Microenvironment

The Huangdi Neijing (Huangdi's Internal Classic) states that "moxibustion is indicated for ailments unresponsive to acupuncture". As an external therapy in traditional Chinese medicine (TCM), moxibustion delivers thermal stimulation and infrared radiation generated by burning moxa wool to acupoints to warm and unblock meridians [8]. Modern biomedical research confirms that moxibustion alleviates common adverse effects of chemo-radiotherapy in cancer patients, including gastrointestinal toxicity and myelosuppression, and relieves cancer-related fatigue, pain and postoperative lymphedema [9]. It also potentiates the anti-tumor activity of conventional Western therapies to exert indirect anti-cancer effects [10]. Preclinical studies indicate that moxibustion enhances anti-tumor immunity by modulating multiple immune cell subsets within the TIME: moxibustion significantly elevates peripheral $CD4^+$ T cell counts and the $CD4^+/CD8^+$ T cell ratio in rats with precancerous hepatic lesions, reduces pro-inflammatory cytokine levels, and balances systemic immune homeostasis [11]. Compared with conventional Western anti-tumor therapies, moxibustion features convenient operation, low cost and high biosafety. Its holistic regulatory property aligns

well with the dynamic immune equilibrium of the TIME, offering novel strategies for integrated TCM-Western oncoimmunotherapy.

2. Theoretical Basis of Moxibustion for Remodeling the Tumor Immune Microenvironment

TCM theory attributes tumor initiation and progression to "deficiency of vital qi and accumulation of pathogenic toxins" [12]. The pathological microenvironment formed by the intermingling of deficiency, phlegm, blood stasis and cancer toxins corresponds to the TIME in modern medicine, which drives tumor proliferation, invasion and metastasis [13]. Accordingly, the immunosuppressive state of the TIME falls under the TCM pathogenesis of "insufficient vital qi and stagnant qi-blood". The Bianque Xinshu (Bian Que's Heart Book) emphasizes that "moxibustion ranks first among health-nourishing moxibustion", highlighting its unique capacity to tonify vital qi in severe illnesses. Targeting the core pathogenesis of vital qi deficiency, the warming nature of moxibustion tonifies yang and reinforces vital qi. Stimulating acupoints such as Zusanli (ST36) invigorates the spleen and boosts qi-blood production to supply material support for pathogen resistance [14], embodying the "strengthening body resistance" principle. Meanwhile, thermal stimulation warms meridians, dispels cold and resolves blood stasis [15], ameliorates local stagnation of qi and blood in tumor lesions, and restricts the proliferation and dissemination of pathogenic toxins to fulfill the "eliminating pathogenic factors" therapeutic purpose. Collectively, moxibustion remodels the TIME and inhibits tumor growth by regulating systemic immune function. Its characteristic of "strengthening resistance without retaining pathogens, eliminating pathogens without damaging resistance" balances therapeutic efficacy and safety, avoiding excessive immune activation and subsequent adverse events induced by single-agent Western immunotherapy. From a modern biomedical perspective, thermal stimulation from moxibustion activates transient receptor potential vanilloid 1 (TRPV1) at acupoints, which transmits signals through somatic and autonomic nerves to coordinate the neuro-immune-endocrine network [16]. This "local stimulation-central regulation-systemic response" signaling cascade provides a physiological framework to explain moxibustion-mediated TIME remodeling.

3. Moxibustion-Mediated Remodeling of the Tumor Immune Microenvironment

3.1 Reprogramming Immune Cell Subsets

Immune cells constitute the core functional components of the TIME. Moxibustion ameliorates the immunosuppressive microenvironment and exerts anti-tumor effects by regulating the proportion and effector function of diverse immune cell populations [17].

3.1.1 Balancing T Lymphocyte Subsets

Tumor-infiltrating lymphocytes (TILs) are the primary mediators of anti-tumor immune responses. Upon stimulation by multiple cytokines, T cells differentiate into $CD4^+$ helper T cells, $CD8^+$ cytotoxic T lymphocytes (CTLs) and Tregs. Among these populations, $CD8^+$ CTLs serve as the central effector cells that recognize and eliminate malignant cells. Within the $CD4^+$ T compartment, type 1 helper T cells (Th1) secrete interferon-gamma (IFN-γ) to activate $CD8^+$ CTLs; IFN-γ further promotes CTL recruitment to tumor parenchyma and sustains their effector function to suppress tumor progression [18]. Preclinical animal experiments in Lewis lung carcinoma models demonstrate that moxibustion at Zusanli (ST36) elevates intratumoral $CD4^+$ T cell proportion by 8. 3%, raises the $CD4^+/CD8^+$ ratio from 0.82 ± 0.15 to 1.23 ± 0.18 (within the physiological normal range of 1.2–2.0), and reduces Treg infiltration by 18. 6% [19]. Combination therapy with cisplatin and moxibustion augments tumor infiltration of $CD8^+$ CTLs, $CD4^+$ T cells and Th1 cells, and upregulates gene expression of CD69 (a key marker of T cell activation) and the effector cytokine IFN-γ. In sarcoma xenograft models, moxibustion also significantly increases intratumoral $CD4^+$ and $CD8^+$ T cell abundance [20]. Clinical research conducted by Wei Qiaoling et al. [5] further validates that gastric cancer patients receiving moxibustion alongside chemotherapy exhibit higher peripheral $CD3^+$, $CD4^+$ T cell counts and $CD4^+/CD8^+$ ratios than control subjects, with sustained regulatory effects persisting from chemotherapy to seven days postoperatively, indicating durable immunomodulatory activity of moxibustion on T cell subsets.

3.1.2 Activating Innate Immune Cells

NK cells and macrophages are potent innate lymphocytes that eliminate malignant cells and constrain metastatic dissemination, serving as critical sentinels of tumor immune surveillance [21]. In early-stage tumorigenesis, M1-polarized macrophages eliminate tumor cells and secrete chemokines to recruit and activate other effector immune cells. As tumors progress, soluble mediators within the TIME skew infiltrating macrophages toward the immunosuppressive M2 phenotype [22]. A pooled meta-analysis confirms that NK cell counts are significantly higher in patients receiving adjuvant moxibustion relative to control groups, proving moxibustion preserves systemic innate immune function [23]. Independent mouse studies conducted by Hu Dan et al. report that moxibustion at Zhongwan (CV12) and Guanyuan (CV4) enhances NK cell cytotoxicity in hepatocellular carcinoma xenograft models. Tumor-associated macrophages secrete abundant immunosuppressive mediators including macrophage colony-stimulating factor (M-CSF), interleukin-4 (IL-4), IL-13, IL-10 and prostaglandin E2, which collectively drive tumor proliferation [24]. Published research [20] reveals that moxibustion reduces serum IL-4 and IL-10 concentrations and suppresses intratumoral IL-10 transcription in sarcoma-bearing mice. In breast cancer xenograft models, moxibustion at Zusanli (ST36) lowers circulating IL-10 levels, implying moxibustion alleviates TIME immunosuppression by modulating TAM polarization.

3.2 Regulating the Cytokine Signaling Network

Moxibustion breaks the immunosuppressive TIME via bidirectional modulation of cytokine networks to foster a tumor-rejecting microenvironment. Tumor-associated inflammation is a hallmark of the TIME; pro-inflammatory

cytokines such as tumor necrosis factor-alpha (TNF-α) and IL-6 facilitate tumor angiogenesis and metastasis while inhibiting effector immune cell function [25] [26]. In rodent models, moxibustion at Tianshu (ST25) and Shangjuxu (ST37) suppresses the NF-κB signaling pathway and markedly reduces inflammatory cell infiltration [27]. A clinical trial by Wang Wen et al. enrolling gastric cancer patients with malignant ascites applies moxibustion at Shenque (CV8) and Guanyuan (CV4). The moxibustion intervention group achieves significantly higher ascitic IL-2 concentrations and NK cell activity compared with patients receiving intraperitoneal chemotherapy alone, verifying the positive immunomodulatory effects of acupoint moxibustion on IL-2 and NK cell function [28]. Zhao Zeda et al. [29] propose that moxibustion balances immune homeostasis by regulating cytokine-mediated immune cascades and restraining excessive inflammatory responses.

During solid tumor progression, malignant cells remodel complex molecular signaling crosstalk to drive aberrant angiogenesis and establish an immunosuppressive TIME [30]. Vascular endothelial growth factor A (VEGF-A), a master regulator of physiological angiogenesis and vascular maturation [31], also acts as a central driver of TIME immunosuppression [32] [33]. Targeted VEGF-A inhibition to normalize tumor vasculature and simultaneously activate anti-tumor immunity represents a synergistic therapeutic strategy [34]. Preclinical research by Xie Tianle [35] using gastric cancer-bearing rats confirms that moxibustion downregulates VEGF-A expression, reduces intratumoral microvessel density, increases pericyte coverage, reconstructs aberrant vascular architecture, and alleviates intratumoral hypoxia and elevated interstitial fluid pressure within the TIME.

3.3 Intervening Immune Checkpoint Signaling Pathways

Aberrant activation of immune checkpoint pathways constitutes a core mechanism of tumor immune escape and a major barrier to effective immunotherapy [36]. Emerging preclinical and clinical evidence demonstrates that moxibustion reinvigorates anti-tumor immunity by downregulating immune checkpoint molecule expression. In Lewis lung carcinoma mice receiving combined cisplatin and moxibustion, intratumoral PD-L1 expression and PD-1 levels on $CD8^+$ T cells are suppressed, accompanied by elevated tumor-infiltrating $CD8^+$ T cell proportions [19]. A clinical trial enrolling patients with advanced non-squamous non-small cell lung cancer sets a control arm of ICIs plus chemotherapy, while the experimental arm adds adjuvant moxibustion. The objective tumor response rate reaches 58. 06% in the moxibustion group versus 51. 61% in controls; patients receiving moxibustion exhibit significantly prolonged progression-free survival (PFS) and reduced risk of disease progression, confirming the synergistic anti-tumor value of moxibustion combined with ICI regimens and improved immune function [37]. Mild moxibustion attenuates immunosuppressive hepatic myeloid macrophage infiltration, promotes intratumoral accumulation and activation of $CD8^+$ T cells, restores colorectal carcinoma sensitivity to anti-PD-1 therapy, and ultimately inhibits hepatic metastasis of colorectal cancer [38]. Research conducted by Zhang Feicheng et al. [39] demonstrates that moxibustion combined with chemotherapy preserves body weight, reduces tumor volume, improves tumor histopathological morphology, and suppresses intratumoral expression of PD-1, T-cell immunoglobulin and mucin-domain containing molecule 3 (TIM-3), and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). These findings identify checkpoint downregulation as a mechanistic basis for moxibustion-chemo combination therapy and provide theoretical support for pairing moxibustion with ICIs. Additional clinical observations further validate that heat-sensitive moxibustion generates robust anti-tumor efficacy when combined with immunotherapy or targeted agents [40].

4. Application of Moxibustion in Tumor Rehabilitation

4.1 Alleviating Adverse Reactions of Anti-Tumor Therapy

Chemotherapy-induced gastrointestinal toxicity, including nausea and vomiting, ranks among the most prevalent treatment-related adverse events in clinical oncology [41]. Clinical trials report that mild moxibustion at Zusanli (ST36), Guanyuan (CV4), Qihai (CV6) and salt-partitioned moxibustion at Xiawan (CV10) effectively mitigates chemotherapy-induced nausea, vomiting and constipation in breast cancer patients. Mechanistically, this intervention downregulates pepsinogen I (positively correlated with gastric acid secretion), pepsinogen II (a biomarker of chronic gastric mucosal inflammation), and gastrin-17 (a non-invasive marker of gastric mucosal structural integrity) [42]. Another clinical study [43] verifies that moxibustion at back-shu acupoints alleviates chemotherapy-triggered nausea and vomiting, alongside concurrent toxicities including headache, general fatigue, constipation and somnolence. Chemotherapy-induced myelosuppression and subsequent severe infectious complications (notably neutropenia) are major contributors to cancer-associated morbidity and mortality [23]. Xiao Xianhui et al. [44] report that moxibustion at Zusanli (ST36) reduces the incidence of myelosuppression in patients receiving platinum-based chemotherapy; peripheral white blood cell, granulocyte and platelet counts are significantly higher in the moxibustion group on day 10 post-chemotherapy. A randomized controlled trial of lung cancer patients further confirms that ginger-partitioned moxibustion elevates leukocyte and platelet counts following chemotherapy [45].

4.2 Improving Quality of Life

Heat-sensitive moxibustion administered to elderly patients with malignant tumors improves appetite, reinforces immune function and elevates overall quality of life, with prolonged survival benefits correlated with robust deqi sensation during moxibustion therapy [46]. A comprehensive meta-analysis reveals that moxibustion-combined regimens achieve superior pain relief, lower numerical pain scores, faster onset and longer duration of analgesic effects, alongside elevated global quality of life scores and reduced reliance on analgesic medication [47]. Research by Zhang Man et al. [48] demonstrates that conventional moxibustion, infrared moxibustion, thunder-fire moxibustion and thunder-fire moxibustion combined with Ziwu Liuzhu theory produce superior improvements in sleep disturbance among cancer patients compared with standard supportive care. Collectively,

these clinical findings establish that moxibustion creates a positive therapeutic cycle of enhanced anti-tumor efficacy, alleviated symptomatic burden and improved quality of life, delivering comprehensive supportive care for cancer rehabilitation.

5. Summary

Conventional Western anti-tumor therapies exert direct cytotoxicity against tumor lesions yet frequently damage endogenous vital qi. Multiple modern TCM oncologists attribute tumor pathogenesis to underlying vital qi deficiency complicated by intermingled phlegm, blood stasis and cancer toxins [49] [50] [51]. Moxibustion centers on the therapeutic principles of warming yang to strengthen resistance and unblock collaterals to resolve stasis, which aligns perfectly with the core TCM pathogenesis of malignant tumors. Modern translational research confirms that moxibustion remodels the TIME through multi-layered regulatory mechanisms: balancing the relative proportions of $CD4^+$ T cells, $CD8^+$ T cells and Tregs [52], and modulating the secretion of pro- and anti-tumor cytokines [53]. Photothermal stimulation from moxibustion improves local microcirculation, activates multiple molecular signaling targets to mediate signal transduction, and modulates inflammatory cytokine expression [54]. Clinical practice corroborates that moxibustion synergizes conventional Western anti-tumor regimens to boost therapeutic efficacy [55] while comprehensively ameliorating patients' quality of life [56]. Emerging novel moxibustion modalities including heat-sensitive moxibustion and electronic moxibustion further expand the clinical scope of moxibustion in tumor treatment and rehabilitation. Current research in this field still faces prominent limitations: insufficient integration between TCM theoretical frameworks and molecular mechanistic research, lack of unified standardized protocols for clinical moxibustion intervention in oncology, and scarcity of long-term follow-up data to evaluate long-term prognostic outcomes. Future investigations should integrate TCM syndrome differentiation theory with cutting-edge immunological experimental techniques, establish standardized operating specifications for tumor-targeted moxibustion, systematically dissect the immune regulatory pathways underlying the "strengthening resistance and resolving stasis" therapeutic principle, and construct standardized clinical application systems for moxibustion. This will provide a safe, mild, clinically effective and cost-efficient adjuvant therapeutic option for cancer patients.

References

[1] Bingzhe L, Yunpeng W, Dongjiang M, et al. Immunotherapy: Reshape the Tumor Immune Microenvironment [J]. Frontiers in Immunology, 2022, 13: 844142.

[2] Chen S D, Mellman I. Oncology Meets Immunology: The Cancer-Immunity Cycle [J]. Immunity, 2013, 39(1): 1-10.

[3] Vinay S D, Ryan P E, Pawelec G, et al. Immune evasion in cancer: Mechanistic basis and therapeutic strategies [J]. Seminars in Cancer Biology, 2015, 35(S): S185-S198.

[4] Asher M. New checkpoint inhibitors ride the immunotherapy tsunami [J]. Nature Reviews Drug Discovery, 2013, 12(7): 489-492.

[5] WEI Qiao-ling, PANG Yong-hui, ZUO Hong-qun, et al. Effects of Moxibustion Combined with Immune Enteral Nutrition on the Nutritional Status, Immune Function and HSP70 in Gastric Cancer Patients Undergoing Neoadjuvant Chemotherapy [J]. Shanghai Journal of Acupuncture and Moxibustion, 2020, 39(05): 541-545.

[6] Huichen Zhao, Huihui Hu, Yishu Xing, et al. Research progress on immune checkpoint PD-1/PD-L1 inhibitor combination therapy for advanced gastric cancer [J]. Chinese Journal of Clinical Oncology, 2022, 49(18): 958-962.

[7] Keam S, Turner N, Kugeratski G F, et al. Toxicity in the era of immune checkpoint inhibitor therapy [J]. Frontiers in Immunology, 2024, 15: 1447021.

[8] Jiang Jinfeng, Wang Lingling, Xu Bin, et al. Anti-inflammatory: effect mechanism of warming-dredging in moxibustion [J]. Chinese Acupuncture & Moxibustion, 2013, 33(9): 860-864.

[9] Zhang H W, Lin Z X, Cheung F, et al. Moxibustion for alleviating side effects of chemotherapy or radiotherapy in people with cancer [J]. The Cochrane Database of Systematic Reviews, 2018, (11): CD010559.

[10] Xie Li, Diao Benshu, Diao Canyang, et al. Fuzheng Jiandu Kang'ai decoction combined with moxibustion in the treatment of NSCLC after radiotherapy [J]. Shaanxi Journal of Traditional Chinese Medicine, 2016, 37(2): 161-163.

[11] Yan Yanan, Wang Ning, Wang Zhuoyu, et al. Effects of Direct Moxibustion of "Ganshu" (BL 18) on the Contents of T cells in Peripheral Blood in Rats with Precancerous Lesion of Primary Hepatocellular Carcinoma [J]. Acupuncture Research, 2016, 41(4): 321-326.

[12] WANG Qi. Classification and diagnosis basis of nine basic constitutions in Chinese medicine [J]. Journal of Beijing University of Traditional Chinese Medicine, 2005, 28(4): 1-8.

[13] XIE Xiaomei, ZHAO Weihan, RAN Jingchun, et al. Prevention and Treatment of Gastric Cancer by Chinese Medicine Based on Tumor Immune Microenvironment [J]. Acta Chinese Medicine, 2019, 34(11): 2329-2334.

[14] ZHOU Ting, LI Wen-tao, YU Jian-chun, et al. Impacts of moxibustion at Zusanli (ST 36) on the improvements in the quality of life in patients with advanced malignant tumor [J]. Chinese Acupuncture & Moxibustion, 2019, 39(2): 133-136.

[15] Shi J, Zhang X, Chen J, et al. Acupuncture and moxibustion therapy for cognitive impairment: the microbiome–gut–brain axis and its role [J]. Frontiers in Neuroscience, 2024, 17: 1275860.

[16] Bruno B, Valérie S, Sonia P. Therapeutic Potential of Vagus Nerve Stimulation for Inflammatory Bowel Diseases [J]. Frontiers in Neuroscience, 2021, 15: 650971.

[17] Zhang Qufei, Li Lixia, Lin Guohua, et al. Effect of direct moxibustion at Sihua points on cytokine of chemotherapy patients with lung cancer [J]. Chinese Acupuncture & Moxibustion, 2013, 33(3): 207-210

[18] GROOM J R, LUSTER A D. CXCR3 ligands: redundant, collaborative and antagonistic functions [J]. Immunology and Cell Biology, 2011, 89(2): 207-215.
[19] Bin W, Jin H, Shanshan L, et al. The Combinatorial Effect of Cisplatin and Moxibustion on Tumor Growth Inhibition with Special Reference to Modulation of the Immune Microenvironment in Lewis Lung Cancer Mice [J]. Evidence-Based Complementary and Alternative Medicine, 2020, 2020: 3170803.
[20] Jun L L, Chong Y S, Xiang M L, et al. Effects of moxibustion on Treg cells in sarcoma microenvironment [J]. Journal of Integrative Medicine, 2021, 19(3): 251-257.
[21] Glasner A, Levi A, Enk J, et al. NKp46 Receptor-Mediated Interferon-γ Production by Natural Killer Cells Increases Fibronectin 1 to Alter Tumor Architecture and Control Metastasis [J]. Immunity, 2018, 48(2): 396-398.
[22] QIU Xiaowei, LAI Baoyong, NIU Wenquan, et al. Effects of Moxibustion on Lymphocytes and Its Subsets in Patients after Radiotherapy and Chemotherapy: A Systematic Review and Meta-analysis [J]. Liaoning Journal of Traditional Chinese Medicine, 2021, 48(10): 162-167.
[23] Shanshan L, Bin W, Jiaqi W, et al. Moxibustion for the Treatment of Cancer and its Complications: Efficacies and Mechanisms [J]. Integrative Cancer Therapies, 2023, 22: 15347354231198089.
[24] Dan H, Weiming S, Chenyuan G, et al. Grain-sized moxibustion promotes NK cell antitumour immunity by inhibiting adrenergic signalling in non–small cell lung cancer [J]. Journal of Cellular and Molecular Medicine, 2021, 25(6): 2900-2908.
[25] Chen X, Lin L, Wu Q, et al. Tumor Necrosis Factor-α Promotes the Tumorigenesis, Lymphangiogenesis, and Lymphatic Metastasis in Cervical Cancer via Activating VEGFC-Mediated AKT and ERK Pathways [J]. Mediators of Inflammation, 2023, 2023(1): 5679966.
[26] Huseni M A, Wang L, Klementowicz J E, et al. CD8+ T cell-intrinsic IL-6 signaling promotes resistance to anti-PD-L1 immunotherapy [J]. Cell Reports Medicine, 2023, 4(1): 100878.
[27] ZHU Shan-shan, WANG Jiao-jiao, ZOU Ling, et al. Anti-inflammation effect of moxibustion for rats with diarrhea-predominant irritable bowel syndrome based on multiple miRNAs regulating NF-κB signal pathway [J]. Chinese Acupuncture & Moxibustion, 2022, 42(6): 654-662.
[28] WANG Wen, SI Wentao, YANG Ping, et al. Clinical Observation on 40 Cases of Ascites with Spleen and Kidney Yang Deficiency Syndrome Treated by External Application of Xiaozhang Lishui Powder (消胀利水散) and Moxibustion [J]. Journal of Traditional Chinese Medicine, 2019, 60(16): 1389-1394.
[29] ZHAO Ze da, YAO Sheng Wang, XIN Wen, et al. Research progress on effect-enhancing and toxic-reducing mechanism of indirect moxibustion combined with cancer immunotherapy [J]. Biomedical Engineering and Clinical Medicine, 2024, 28(3): 438-444.
[30] Simone B, Harald S, Thomas B, et al. Dynamic EMT: a multi-tool for tumor progression [J]. The EMBO Journal, 2021, 40(18): e108647.
[31] Claesson-Welsh L, Welsh M. VEGFA and tumour angiogenesis [J]. Intern Med. 2013, 273 (2): 114-127.
[32] Thibault V, Orianne C, Elie M, et al. VEGF-A modulates expression of inhibitory checkpoints on CD8+ T cells in tumors [J]. The Journal of experimental medicine, 2015, 212(2): 139-148.
[33] Bourhis M, Palle J, Galy-Fauroux I, et al. Direct and indirect modulation of T cells by VEGF-A counteracted by anti-angiogenic treatment [J]. Frontiers in Immunology, 2021, 12: 616837.
[34] Fukumura D, Kloepper J, Amoozgar Z, et al. Enhancing cancer immunotherapy using antiangiogenics: opportunities and challenges [J]. Nature Reviews Clinical Oncology, 2018, 15(5): 325-340.
[35] Xie Tianle. Effect of moxibustion regulating VEGF-A expression on tumor vascular normalization and immune microenvironment in gastric cancer rats [D]. Changsha: Hunan University of Chinese Medicine, 2025.
[36] Deng X, Xiong F, Li X, et al. Application of atomic force microscopy in cancer research [J]. Journal of nanobiotechnology, 2018, 16(1): 102.
[37] YE Zhifeng, HUANG Ting, HU Keke, et al. Clinical Study on Moxibustion Combined with Immune Checkpoint Inhibitors and Chemotherapy for Advanced Non-Squamous Non-Small Cell Lung Cancer [J]. New Chinese Medicine, 2024, 56(16): 129-135.
[38] ZHUANG Yi, SUN Jianhua, JIANG Shiyuan, et al. Mild Moxibustion Inhibiting Hepatic Metastasis of CRC [J]. Acta Chinese Medicine, 2024, 39(06): 1182-1187.
[39] ZHANG Feicheng, GAO Tianyu, ZHANG Chenxi, et al. Effect of moxibustion combined with chemotherapy on immune checkpoints in tumor tissue of breast cancer-bearing mice [J]. Acupuncture Research, 2025, 50(03): 319-326.
[40] HUANG Xianbao, XIE Dingyi, CHEN Rixin. CHEN Rixin's academic view of "synergistic effect of moxibustion combined with medication" and its application in tumor rehabilitation [J]. Chinese Acupuncture & Moxibustion, 2024, 44(9): 1057-1061.
[41] ZHANG Hui, ZHANG Ping, GUO Ru, et al. Establishment and validation of a risk prediction model for nausea and vomiting during postoperative chemotherapy in gastric cancer patients [J]. Journal of Clinical Surgery, 2024, 32(5): 484-488.
[42] LI Wanying, LI Liuning. Effect of moxibustion on prevention and treatment of nausea and vomiting caused by cisplatin in lung cancer [J]. Chinese Acupuncture & Moxibustion, 2018, 38(7): 695-699.
[43] ZHU Linglan, CAI Yahong, ZHANG Bibi. Exploring the Clinical Effect of Moxibustion on Back-Shu Points in Preventing Chemotherapy-Induced Nausea and Vomiting Based on the “Regulating Shu Points to Regulate the Pivot” Theory [J]. Journal of Zhejiang Chinese Medical University, 2025, 49(5): 611-616.
[44] XIAO Xianhui, JIA Runmiao, LI Hongke, et al. Clinical Study on Efficacy of Moxibustion at Zusanli (ST36) to Treat Myelosuppression in Patients Receiving Chemotherapy in the Treatment of Advanced Non-small Cell Lung Cancer [J]. Clinical Journal of Traditional Chinese Medicine, 2019, 31(2): 339-342.
[45] ZHANG Lei, WANG Ya-ling, FU Rui-yang, et al. Ginger-partitioned moxibustion in the prevention of nausea and vomiting induced by chemotherapy in lung

cancer:a randomized controlled trial [J]. Acupuncture Research, 2020, 45(7): 574-577+582.
[46] YU Ting, LIU Huawei, LIU Zuqin, et al. Heat-sensitive moxibustion assisted in palliative treatment to improve the quality of life in elderly patients with malignant tumor: a randomized controlled trial [J]. Chinese Acupuncture & Moxibustion, 2025, 45(02): 167-172.
[47] Li Y, Hong E, Ye W, et al. Moxibustion as an Adjuvant Therapy for Cancer Pain: A Systematic Review and Meta-Analysis [J]. Journal of Pain Research, 2023, 16: 515-525.
[48] ZHANG Man, YUN Jie, WU Ting-ting, et al. Mesh Meta-analysis of moxibustion in improving sleep quality in cancer patients [J]. Chinese Journal of Convalescent Medicine, 2024, 33(08): 11-16.
[49] YANG Zhu, TANG Dongxin, GUO Bin, et al. Data Mining Analysis of Medication Experience of LIU Shangyi in Treating Cancer [J]. Journal of Traditional Chinese Medicine, 2016, 57(19): 1641-1645.
[50] SONG Jing-ru, SUN Ming-yu. TCM master LIU Jia-xiang's experience of strengthening the body to treat postoperative breast cancer [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2022, 37(4): 2020-2024.
[51] YI Dan, DU Mengnan, JIA Yingjie. Analysis of academic thought in treating cancer tumors with 'Chuzhuo Peiben' theory [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2024, 39(7): 3470-3473.
[52] Tan Jing, Lin Yaping, Zhao Huan, et al. Effects of Moxibustion on CD4+ and CD4+CD25+T Lymphocytes in Peripheral Blood of Rats with Gastric Tumor [J]. World Chinese Medicine, 2019, 14(3): 515-520.
[53] K S B, Alberto M. Macrophage plasticity and interaction with lymphocyte subsets: cancer as a paradigm [J]. Nature Immunology, 2010, 11(10): 889-896.
[54] HU Jing, YANG Hua-yuan. Conduction pathway and function of physical signals of moxibustion stimulus [J]. Chinese Acupuncture & Moxibustion, 2021, 41(5): 577-581.
[55] LI Ji-juan, ZHANG Chen-xi, LIANG Xin-yue, et al. Moxibustion enhances the antitumor efficacy of Trametinib in breast cancer-bearing mice via MEK/ERK signaling pathway [J]. Acupuncture Research, 2026, 51(4): 474-483.
[56] WANG Ying, ZHANG Ming, LI Xiangqi. Effects of Moxibustion on T Lymphocyte Subsets and Quality of Life in Patients with Triple-Negative Breast Cancer Undergoing Neoadjuvant Chemotherapy [J]. Chinese Journal of Traditional Medical Science and Technology, 2025, 32(4): 626-629.