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Tai Chi and Its Impact on Immune Mechanisms: A Comprehensive Review

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Abstract

Tai Chi, a mind-body exercise that combines slow, deliberate movements with meditation, is widely practiced to promote health. Studies indicate that the active stretching inherent in Tai Chi can, through mechanical transmission via the fascia network, modulate immune cell activity by reducing pro-inflammatory cytokines (e.g., IL-6, TNF-α) and enhancing the expression of anti-inflammatory cytokines (e.g., IL-10, TGF-β). Additionally, Tai Chi may optimize immune balance by regulating the hypothalamic-pituitary-adrenal (HPA) axis and influencing epigenetic pathways, alleviating chronic inflammatory conditions. Future research should explore its long-term immunological effects and potential applications in precision medicine, ultimately informing its integration into preventive and integrative healthcare strategies [1].

Keywords

Tai Chi, Immune Regulation, Fascia, HPA Axis, Epigenetic Modulation, Inflammation, Integrative Medicine, Aging

1. Introduction

1.1. Background and Significance

Over the past two decades, mind-body therapies (MBTs), including Tai Chi, meditation, and yoga, have increasingly attracted scientific interest [2]. Among these, Tai Chi is a traditional Chinese practice that combines meditation and physical movement. Slow, flowing motions, balance training, postural adjustments, and mental focus characterize it. Initially rooted in martial arts, Tai Chi is widely recognized for its potential in health promotion and immune modulation.

Unlike other mind-body exercises, Tai Chi emphasizes "active stretching",

which applies stable and controlled mechanical forces to body tissues. This process activates both biomechanical and immunological pathways. Research suggests that Tai Chi can influence immune cell function through mechanical transmission via the fascial system, thereby regulating the balance between pro-inflammatory and anti-inflammatory mediators and optimizing immune homeostasis [3].

Recent research has begun to uncover the immunomodulatory potential of biomechanical interventions, particularly those involving active stretching. Tu *et al.* (2022) demonstrated that when murine macrophages were cultured on flexible membranes and subjected to cyclic mechanical strain up to 15% for 8 hours, there was a significant increase in NF-κB activation and pro-inflammatory cytokine secretion. This response was shown to be mediated through activation of the RhoA/ROCK/NF-κB signaling axis, which regulates cytoskeletal remodeling and enables cellular responses to external mechanical cues, including migration, motility, and polarity shifts. Notably, this process promoted macrophage polarization toward the anti-inflammatory M2 phenotype [4].

Further, Berrueta *et al.* (2023) applied short-duration daily active stretching in a murine subcutaneous inflammation model. They observed reduced lesion size and elevated levels of pro-resolving lipid mediators such as 17-HDHA. Single-cell transcriptomic profiling revealed enhanced activity of both M2-related (Arg1-expressing) and M1-related (Nos2-expressing) gene programs, indicating that stretching modulates the pro-inflammatory response and facilitates inflammation resolution, thus supporting tissue homeostasis [5].

Furthermore, Babaniamansour *et al.* (2024) employed a pharmacological approach combining TRPV4 inhibition with mechanical strain. Even low-magnitude cyclic strain (3%) could shift M1-like macrophages toward a reparative phenotype. Meanwhile, moderate strain (6%) further influenced the behavior of M2 macrophages, emphasizing the role of mechanical tension as a fine-tuned immunoregulatory cue [6].

These findings suggest that Tai Chi's active stretching component may establish a graded, integrin-dependent biomechanical microenvironment contributing to tissue remodeling, immune cell plasticity, and inflammation resolution. This reinforces the hypothesis that, as a non-pharmacological, low-impact intervention, Tai Chi holds promise in addressing chronic inflammation, immune dysregulation, and related health conditions. Future studies should integrate biomechanics, immunology, and neuroscience to comprehensively elucidate the multilayered mechanisms by which Tai Chi influences immune homeostasis.

1.2. Objectives

This review investigates how Tai Chi affects immune function through its biomechanical properties. The objective is to elucidate the mechanisms of immune modulation by analyzing the key biomechanical characteristics of Tai Chi, such as postural stability and muscle tension regulation. Particular attention is given to its

cellular-level impacts, including fibroblast regeneration, macrophage-mediated regulation of inflammatory responses, and neuroimmune cell enhancement in anti-inflammatory processes. Additionally, Tai Chi's potential role in epigenetic regulation is examined, noting that while it does not alter DNA sequences, it can modulate gene expression through epigenetic modifications such as DNA methylation and histone acetylation [7] [8].

1.3. Methods

This review systematically integrates 315 peer-reviewed articles published between 2000 and 2024 on the biomechanical, immunological, and epigenetic effects of Tai Chi. The databases searched included PubMed, Web of Science, and Scopus, using the following keywords: "Tai Chi", "active stretching", "immune modulation", "mechanotransduction", "epigenetics", and "fascial system".

Inclusion Criteria:

The study subjects were Tai Chi or Tai Chi-based interventions related to biomechanical properties, immune modulation, or epigenetic regulation.

- Research subjects include human, animal, and in vitro cell models.
- Randomized controlled trials (RCTs), observational studies, mechanistic studies, or systematic reviews.
- Articles published in English between 2000 and 2024.
- Publications in peer-reviewed journals.

Exclusion Criteria:

- Studies focusing solely on martial arts performance without health-related outcomes.
- Studies that did not clearly distinguish Tai Chi from other mind-body practices (e.g., general exercise, yoga, or Qigong).
- Non-peer-reviewed articles include editorials, commentaries, conference abstracts, or unpublished data.
- Studies are not relevant to biomechanical, immunological, or epigenetic mechanisms.
- Articles are not available in full text.

Two independent reviewers screened the titles and abstracts of the 315 identified records for relevance. Full-text evaluations were subsequently conducted based on the inclusion and exclusion criteria, resulting in 64 studies being selected for data synthesis.

2. Biomechanical Characteristics of Tai Chi

2.1. Overall Perspective and Fascia Theory

The biomechanical stimulation in exercises such as Tai Chi is transmitted through the fascia, a connective tissue network that envelops muscles and organs and modulates tension throughout the body. A rodent study on fascia examined whether the active contractility of fascial cells could affect musculoskeletal dynamics [9]. This research supports that, as a form of biomechanical stimulation, Tai Chi in-

fluences fascia regulation, cellular responses, and immune system modulation, thereby contributing to overall bodily balance and health. Tai Chi-induced fascia activation also promotes synergistic actions between fibroblasts and macrophages, essential for mitigating chronic inflammation and maintaining immune regulation [10] [11].

Recent anatomical studies by Stecco (2025) further reinforce the concept of fascia as a unified mechanical continuum, structurally and functionally integrating the musculoskeletal, vascular, and nervous systems. She emphasized that fascial layers are not merely passive structures but also influence proprioception and interoception—key elements in the somatic awareness cultivated in Tai Chi. Her research on superficial fascia's heterogeneity and anisotropic biomechanical properties helps explain how Tai Chi's low-impact and multidirectional loading can elicit region-specific adaptive responses [12].

The principle of fascia integrity aligns closely with Tai Chi's foundational concepts of "relaxation, sinking, and stability". These principles emphasize full-body muscle relaxation, physical stability, and precise coordination of the entire fascial system. Fascia connects muscles and bones and forms a continuous tissue network across joints to regulate tension and distribute mechanical stress, thereby integrating the whole kinetic chain. For example, the Fascial Chain theory describes several myofascial networks:

- **Superficial Back Line (SBL):** Extending through the plantar fascia, gastrocnemius, hamstrings, sacrotuberous ligament, and erector spinae, this line is crucial in Tai Chi stance and gait control [13].
- **Functional Front Line (FFL):** Including the rectus abdominis, rectus femoris, and iliopsoas, this line participates in core stability and lower limb movement, enhancing the "dantian-driven" effect of Tai Chi [13].

The slow and flowing movements of Tai Chi coordinate these myofascial chains. The forces generated during muscle contraction are transmitted through surrounding fascial conduits, creating a natural mechanical feedback system that optimizes energy transfer and stabilizes movement.

Supporting this perspective, Robert Schleip's research reveals that fascia is capable of active contraction through the presence of myofibroblasts, suggesting that it plays a role in musculoskeletal dynamics beyond passive force transmission [12]. His findings indicate that the continuous and intentional movement in Tai Chi may activate these contractile properties of fascia, enabling the regulation of connective tissue tone and responsiveness throughout the body.

2.1.1. Role of Fascia Regulation

Tai Chi emphasizes a posture of "centered, relaxed, and stable." Its biomechanical features include:

- **Reducing joint load:** By adjusting the three points of support on the foot (ball of the big toe, little toe, and heel), weight is evenly distributed, reducing stress on the knee and hip joints.
- **Optimizing fascial tension:** This avoids over-tightening of local muscle

groups, ensuring mechanical tension is evenly transmitted along the myofascial chain, thus enhancing balance and coordination.

- **Enhancing remote effects of fascia:** Myofascial intervention can affect the mobility of distant tissues. For instance, relaxation of the plantar fascia may improve hamstring flexibility, thereby enhancing the range of motion (ROM) in the lumbar spine and hips. Research shows that fascial release and tension modulation in various regions can impact overall performance. Tai Chi's stretching and rotational movements influence distant muscles through the fascial chain, enhancing flexibility and rehabilitation outcomes [11] [13].

The slow and flowing movements of Tai Chi coordinate these myofascial chains. The forces generated during muscle contraction are transmitted through surrounding fascial conduits, creating a natural mechanical feedback system that optimizes energy transfer and stabilizes movement [11]. Supporting this perspective, Robert Schleip's research reveals that fascia is capable of active contraction through the presence of myofibroblasts, suggesting that it plays a role in musculoskeletal dynamics beyond passive force transmission [9]. His findings indicate that the continuous and intentional movement in Tai Chi may activate these contractile properties of fascia, enabling the regulation of connective tissue tone and responsiveness throughout the body [14].

2.1.2. Mechanical Conduction and Absorption

Tai Chi's concepts of "listening to the force" and "transforming the force" reflect the fascia system's role in absorbing and redirecting mechanical stress:

- **Listening to the force:** The fascial network perceives the direction and magnitude of external forces, allowing the body to adjust tension in real time and optimize load distribution.
- **Transforming the force:** The fascia stores and releases elastic energy, dispersing stress across muscles and minimizing injury risk. Mechanoreceptors such as integrins within fascia detect and respond to these stimuli, influencing cytoskeletal structure, inflammatory signaling, and tissue regeneration [13].

Through slow, continuous, active stretching, Tai Chi modulates fascial tension, enhances musculoskeletal coordination, and alters the microenvironment surrounding immune-related cells. Recent studies have highlighted the close association between the fascial system and immune regulation, indicating that imbalanced fascial tension may contribute to local inflammation. In contrast, tension release may help restore immune homeostasis. These mechanical changes can influence cellular function via integrin-mediated mechanotransduction, affecting key immune cells such as fibroblasts and macrophages.

In summary, combining Stecco's anatomical reconceptualization of fascia with Schleip's validation of its contractile potential, Tai Chi's biomechanical benefits derive not only from enhancing fascial elasticity but also from activating proprioceptive mechanisms and modulating connective tissue tone in an intelligent, dynamic manner. Therefore, Tai Chi may exert immunomodulatory effects through structural improvements in the fascia-joint system and mechanical regulation of

immune cells. The following section will explore these cellular-level responses, focusing on how Tai Chi influences macrophage polarization and contributes to immune regulation and inflammation resolution.

3. Mechanical Stimulation of Tai Chi and Immune System Regulation

As an integrative mind-body practice, Tai Chi generates significant mechanical stimulation at both the fascial and cellular levels through its slow and controlled active stretching movements. Research indicates that such stimulation enhances fascial elasticity and stability and is vital to immune system regulation. This section will explore how fascial tension modulation influences fibroblast responses, macrophage polarization, and the impact of inflammatory cytokine dynamics on immune cell function.

3.1. Regulation of Fascial Tension and Fibroblast Response

3.1.1. Activation of Fibroblasts by Stretching

The active stretching inherent in Tai Chi, transmitted through the myofascial chain, activates integrin receptors in fibroblasts, inducing cytoskeletal reorganization and promoting the synthesis of matrix proteins (e.g., collagen and hyaluronic acid). These changes enhance the elasticity and stability of the fascia and improve the structural integrity of connective tissue [15]. Research by Meltzer *et al.* using *in vitro* human fibroblast models showed that repetitive motion strain (RMS) and reactive stretching [15] affected cytokine release. The RMS group exhibited elevated secretion of the pro-inflammatory cytokine IL-6 and a 51% increase in proliferation compared with the 24RMS group ($P < 0.05$). After simulated reactive stretching [16], levels of pro-inflammatory factors significantly decreased while anti-inflammatory cytokines such as IL-10 increased [17].

3.1.2. Regulation of Inflammation through Active Stretching

Mind-body exercises such as Tai Chi profoundly affect myofascial and immune systems through slow and coordinated active stretching. Recent studies show that active stretching promotes mechanical adaptation of fascia and regulates the inflammatory response by influencing the release of anti-inflammatory cytokines (e.g., IL-10, TGF-β) and reducing IL-6 levels, thereby improving tissue repair and immune homeostasis. IL-6, which is involved in energy metabolism and is released from skeletal muscle during exercise, can stimulate lipolysis. Experimental evidence includes [18]:

1) A 2019 randomized controlled trial by Anna Sophie *et al.* demonstrated that exercise-induced changes in visceral adipose tissue mass were regulated by IL-6 signaling [19].

2) Studies by Irwin and Olmstead (2012, 2014) reported that Tai Chi reduced levels of pro-inflammatory cytokines, indicating that stretching-based exercises (such as yoga and Tai Chi) effectively lower circulating pro-inflammatory cytokines like IL-6 and TNF-α [8].

3) Studies from 2014 by Kiecolt-Glaser and Sarvottam (2013) found that stretching exercises can significantly reduce TNF-α and IL-1β levels, enhancing anti-inflammatory capacity [20].

Emerging evidence suggests that Tai Chi may regulate inflammatory processes via two principal mechanisms.

- **At the cellular level:** Fibroblasts secrete IL-10 and TGF-β after stretching while reducing IL-6 and TNF-α expression, thereby enhancing immune homeostasis [21].
- **At the tissue level:** In animal models, stretching reduced the thickness of inflammatory tissues and promoted the release of anti-inflammatory mediators such as RvD1, accelerating the resolution of inflammation [5].

Furthermore, studies have indicated that such modulation may improve stress-induced immunosuppression and help restore immune homeostasis. In a 2021 exploratory randomized controlled trial, Redwine *et al.* evaluated the effects of Tai Chi, resistance band training, and treatment as usual on inflammatory markers in older adults with heart failure. A total of 69 participants were enrolled and randomly assigned to a Tai Chi group (TC), resistance band group [22], or treatment-as-usual group [23], with an intervention period of 16 weeks [24].

- **Tai Chi group (TC):** 1.5 ± 0.8 pg/ml to 2.0 ± 1.4 pg/ml—a 33% ↑, $p < 0.05$.
- **Resistance Training group (RT):** 1.9 ± 0.9 pg/ml to 1.8 ± 1.6 pg/ml a 5% ↓ $p < 0.05$.
- **Control group [25]:** No significant changes were observed.

Despite the lack of significant differences among the groups in IL-6 levels, the authors noted improvements in cognitive function, suggesting that inflammation reduction may occur through alternative mechanisms, such as CRP reduction and alleviation of depressive symptoms, thereby indirectly affecting immune and mental status. While the study did not demonstrate a direct decrease in IL-6 through Tai Chi, the observed correlations with cognitive and psychological improvements indicate that Tai Chi may exert its effects through an integrated neuroimmune regulatory pathway rather than a single inflammatory marker.

3.1.3. Effects of Active Stretching on Cancer Cells

In recent years, researchers have begun to explore the potential immunological effects of active stretching, such as that involved in Tai Chi, within the tumor microenvironment. The gentle stretching movements characteristic of Tai Chi may help restore cytotoxic immune functions and act synergistically with mediators like RvD1 to inhibit tumor growth [26], Fascia not only regulates local immune responses through mechanotransduction but also contributes to the regulation of chronic inflammation by reducing neutrophil infiltration and enhancing the synthesis of specialized pro-resolving mediators, such as Resolvin D1 (RvD1) and Resolvin D2 (RvD2) [5].

Langevin *et al.* (2016) emphasized the biomechanical role of connective tissue in cancer biology. They proposed that fascial stiffness and fibrosis are key mechanical drivers of cancer progression. Body-based interventions—including

stretching, yoga, and manual therapies—may alleviate connective tissue inflammation and fibrosis, inhibiting tumor invasion and metastasis. Their study underscores the concept of fascia as a regulatory medium within the tumor niche, suggesting that mechanical changes induced by gentle physical activity may modulate local immune function and extracellular matrix structure. Such biomechanical modulation not only benefits patient quality of life but also offers a theoretical foundation for non-pharmacological strategies in integrative oncology [26].

Berrueta and Bergholz *et al.* (2018) conducted an experimental study using a murine model of breast cancer. They found that 10 minutes of daily gentle stretching significantly reduced inflammation and fibrosis in connective tissue and suppressed tumor progression. After four weeks of intervention, tumor volume in the stretching group was 52% smaller than in the non-stretched control group ($p < 0.001$), indicating a substantial anti-tumor effect. Although there are physiological differences between mice and humans regarding immune regulation and tumor microenvironments, murine models remain widely used for simulating human diseases. Inflammation-resolving pathways such as those involving RvD1 are highly conserved across species. Fascia not only regulates local immune responses through mechanotransduction but also contributes to the regulation of chronic inflammation by reducing neutrophil infiltration and enhancing the synthesis of specialized pro-resolving mediators, such as Resolvin D1 (RvD1) and Resolvin D2 (RvD2) [5]. Notably, the stretching protocol employed in the study (10 minutes per day within normal range of motion) approximates the intensity and duration of light to moderate stretching activities in humans, such as Tai Chi or yoga for 10 - 20 minutes [27].

In addition, inflammatory cytokine dynamics are inherently complex and bidirectional. While many studies have shown that mind-body practices—including Tai Chi—commonly reduce pro-inflammatory cytokines such as IL-6 and TNF-α, evidence also suggests that cytokines like IL-2, IL-4, IL-10, and IFN-γ may exhibit variable upregulation or downregulation depending on physiological state. This bidirectional regulation may reflect the immune system's effort to maintain homeostasis in the context of infection, injury, or tumor immunosurveillance [28].

For example, research on patients with multiple myeloma has shown that local pro-inflammatory cytokines, including IL-6, IL-1α, and IL-1β, are involved in T cell activation and enhancement of cytotoxic responses. Such pro-inflammatory signaling may support tumor immune surveillance [21]. These findings support the "parallel regulation" hypothesis, in which compensatory mechanisms across the cytokine network balance fluctuations in individual cytokines to maintain immune equilibrium [29].

Taken together, Tai Chi and similar active stretching practices may restore immune homeostasis by modulating cytokine expression and enhancing immune cell adaptability. Given that immune regulation also involves macrophage polarization, the next section will explore how fascial tension and mechanotransduction

influence macrophage phenotypic transformation and immune function.

3.2. Macrophage Polarization

3.2.1. Interactions between the Fascial System and Macrophages

Macrophages exhibit diverse activation phenotypes under various pathological conditions, ranging from pro-inflammatory (M1) to pro-repair (M2) states, accompanied by progressive changes in transcriptomic profiles and functional outputs [30]. Their polarization is governed by a complex interplay of soluble biochemical factors, metabolites, and signaling pathways [31] [32], including cytokines, chemokines, and lipid mediators. In addition to these chemical signals, physical components of the tissue microenvironment—such as extracellular matrix stiffness, spatial confinement, cell-cell interactions, and mechanical tension—also play critical roles in shaping macrophage behavior [33]-[35].

Spatial confinement and mechanical strain have been shown to influence macrophage transcriptional programming and functional states. Studies reveal that macrophages under spatial constraint display a biphasic M1 response: while early signaling events, such as TLR4 activation and downstream transcription factors like p65 and IRF3, remain largely unaffected, the expression of late-stage pro-inflammatory genes (e.g., IL-6, iNOS, TNF-α) is significantly downregulated several hours post-activation. This suppression is linked to chromatin condensation, elevated HDAC3 activity, and reduced MRTF-A-SRF coactivator complex signaling. Additionally, spatial restriction reduces phagocytic capacity and cytokine secretion, suggesting that physical constraints can reprogram macrophage immune phenotypes [36].

The fascial system is critical to the physical microenvironment as a body-wide tension-transmitting network. When fascial tension becomes imbalanced or remains chronically contracted, it may lead to abnormal mechanical signaling and spatial compression in localized tissues, thereby influencing adjacent macrophages' activation tendency and polarization fate. Tai Chi's slow, flowing movements facilitate the extensibility and redistribution of fascial tension, thereby improving local spatial microenvironments and the dynamics of mechanical signaling.

Based on this, it is hypothesized that Tai Chi may indirectly guide macrophages toward a pro-healing (M2) phenotype by modulating the mechanical signaling background provided by the fascial system, thus contributing to maintaining immune homeostasis and regulating inflammatory responses.

3.2.2. Mechanoregulation of M1/M2 Polarization through Tai Chi

The slow, sustained active stretching in Tai Chi movements (e.g., "cloud hands," "grasping the knee and twisting step") can release fascial tension, reshape spatial tension distributions, and optimize the physical microenvironment encountered by tissue-resident macrophages. Such low-intensity, long-duration mechanical stimulation has been shown to promote M2 polarization and suppress M1 activation through the following mechanisms:

- **RhoA/ROCK signaling pathway regulation:** Stretch-induced tension can ac-

tivate or modulate the RhoA-ROCK pathway, promoting the shift from M1 to M2 phenotypes and attenuating chronic inflammation [4].

- **Integrin and YAP/TAZ mechanotransduction axis:** (Figure 1) Mechanical stretching activates integrin signaling and YAP/TAZ transcriptional coactivators, enhancing M2 polarization and cytoskeletal tension remodeling [37].
- **PPARγ upregulation and chromatin remodeling:** The mechanical stimulation mimicked by Tai Chi movements increases the expression of PPARγ, which works in concert with reduced HDAC3 activity and chromatin reorganization to promote anti-inflammatory gene transcription [38].
- **Reduction of pro-inflammatory cytokine secretion:** Empirical studies of Tai Chi practitioners have demonstrated decreased levels of IL-6, TNF-α, and other pro-inflammatory cytokines, potentially due to the creation of a low-tension mechanical niche that mimics spatial confinement–induced suppression of late-phase M1 activation [39].

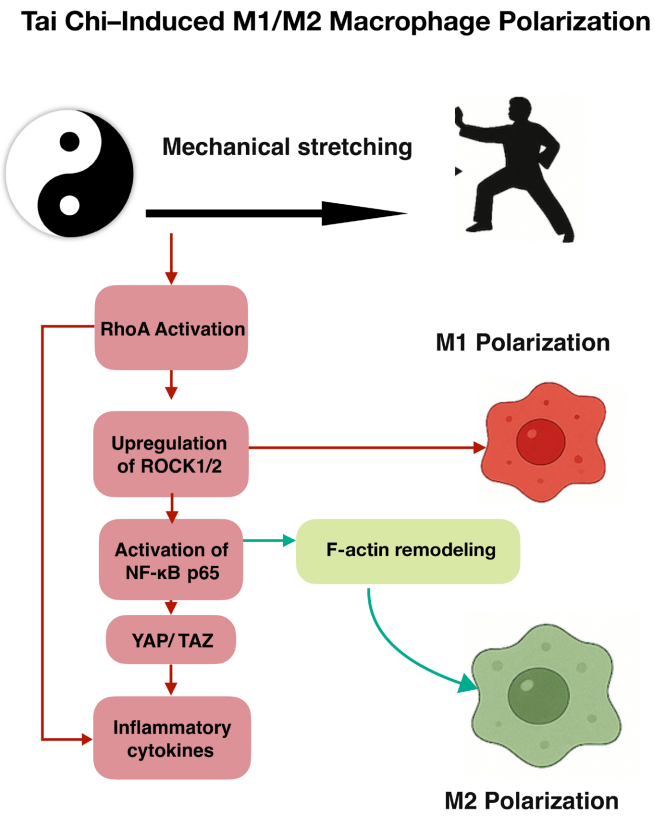

Figure 1. Tai Chi-mediated self-stretching induced immune polarization.

In summary, Tai Chi modulates immune function by adjusting fascial tension, creating a repair-supportive mechanical niche for macrophages, and influencing key signaling pathways such as RhoA/ROCK, YAP/TAZ, and PPARγ. These biomechanical effects promote anti-inflammatory M2 polarization and may further involve epigenetic mechanisms like chromatin remodeling and transcriptional

regulation.

However, immune regulation extends beyond local tissue mechanics. Systemic factors—particularly stress and neuroendocrine activity—also play a critical role. Tai Chi may exert dual effects as a holistic mind-body practice: biomechanically shaping the local immune microenvironment while concurrently modulating systemic responses through the HPA axis and epigenetic pathways. The following chapter explores this systemic dimension of Tai Chi's immunoregulatory potential.

3.3. Fascial Tension and Regional Immune Regulation

Following myocardial infarction, fibroblasts located in the infarct zone are subjected to significantly greater mechanical strain compared to those in remote, non-infarcted myocardial regions, In 2020, Rogers *et al.* developed a fibroblast mechanochemical signaling network model, which demonstrated that mechanical tension not only modulates the magnitude of fibroblast responses to biochemical stimuli such as TGF-β1, norepinephrine (NE), and IL-1, but can also amplify, suppress, or even reverse those responses depending on the level of applied strain [40]. The model further predicted that inhibition of the IL-6 and Akt/mTOR pathways in low-tension zones could effectively downregulate the expression of profibrotic matrix proteins [40].

Experimental findings support these computational predictions. For instance, IL-1 has been shown to reverse the myofibroblast phenotype of valvular interstitial cells cultured on stiff substrates, and pressure overload in wild-type mice has been reported to exacerbate fibrotic remodeling in a TGF-β1-dependent manner [41].

This mechanical environment holds therapeutic potential by suppressing pathological collagen deposition in remote myocardial regions while preserving essential matrix support in the infarct zone. Tai Chi, therefore, may serve as a non-pharmacological mechano-adaptive strategy to support regional antifibrotic remodeling.

This chapter reviewed how Tai Chi modulates immune function at the local level by activating cellular mechanotransduction through muscle stretching and fascial tension. The moderate mechanical stimuli generated by Tai Chi effectively influence the activation states and cytokine expression profiles of key immune cells such as fibroblasts and macrophages, thereby facilitating tissue remodeling and inhibiting fibrotic progression, particularly in pathological conditions such as post-myocardial infarction. Additionally, the biomechanical signals induced by Tai Chi may enhance the stability of immune responses through epigenetic mechanisms. However, it is essential to emphasize that immune regulation is not determined solely by local mechanical environments; systemic factors such as psychological stress and neuroendocrine activity also play pivotal roles. As an integrative practice that combines physical movement with mental regulation, Tai Chi modulates local immune microenvironments via biomechanical pathways and may also influence systemic immune responses through the hypothalamic-pituitary-adrenal (HPA) axis and epigenetic regulation.

Furthermore, recent research has highlighted the potential of Tai Chi as a non-pharmacological intervention for cancer prevention and treatment, as well as a primary strategy for both preventing myocardial infarction and supporting post-infarction recovery. The next chapter will explore the mechanisms and current research on Tai Chi's role in systemic immune modulation.

4. HPA Axis and Epigenetic Immune Regulation

Epigenetics refers to how the genome interacts with environmental factors to regulate gene expression and function without altering the underlying DNA sequence. Through epigenetic modifications such as DNA methylation and histone modifications, cells can respond to internal and external stimuli (e.g., environment, stress, exercise), thereby modulating the spatiotemporal dynamics of gene expression and biological functions [42] [43]. Epigenetics represents the interface between the environment and the genome by triggering complex molecular mechanisms to adjust gene expression in response to a wide range of positive and negative stimuli.

As a mind-body exercise, Tai Chi has been shown to reduce stress-induced immune suppression through modulation of the HPA axis. It may also optimize immune gene expression via epigenetic pathways [44]. Tai Chi may also influence signaling cascades involved in skeletal muscle physiology, metabolism, and contractile function. Recent studies confirm that epigenetic modifications, particularly DNA methylation and histone changes, play essential roles in exercise adaptation and immune regulation [45].

4.1. The Function of the HPA Axis and the Impact of Tai Chi

4.1.1. Role of the HPA Axis in Stress Response

The hypothalamic-pituitary-adrenal (HPA) axis is a central neuroendocrine regulator that orchestrates stress responses and modulates immune function. When the body encounters stress, the HPA axis releases adrenocorticotropic hormone (ACTH) and glucocorticoids (such as cortisol), triggering a cascade of physiological changes, including immune suppression and inflammation regulation. However, overactivation of the HPA axis is closely linked to chronic diseases, immune dysregulation, and neuroinflammation, which can lead to serious health issues [46] [47].

Neuroimaging research has shown that areas such as the amygdala, anterior cingulate cortex [48], and medial prefrontal cortex (PFC) play key roles in initiating stress responses. Connectivity between the right amygdala and ACC has been positively correlated with physiological stress reactivity, highlighting the importance of these neural circuits in regulating HPA activity and the "fight-or-flight" response [49].

4.1.2. Studies on Tai Chi's Regulation of the HPA Axis

The HPA axis is central to managing stress responses and immune function; its prolonged activation leads to increased levels of pro-inflammatory cytokines (such as IL-6 and TNF-α), which can trigger chronic inflammation. Studies have shown that through relaxation and rhythmic movements, Tai Chi effectively reg-

ulates the HPA axis, reducing the negative impact of chronic stress on the immune system. This includes lowering circulating glucocorticoid levels, reducing pro-inflammatory cytokines, and restoring serotonin levels [50]. Tai Chi and Qigong practices have also been associated with increased endorphin levels and decreased ACTH and cortisol levels [51].

Additional findings suggest that Tai Chi helps reverse glucocorticoid resistance in older adults, reduce oxidative stress markers, and restore serotonergic balance—all of which contribute to improved HPA function and immune resilience [52]. For example, in studies of breast cancer survivors and elderly individuals, Tai Chi was found to reduce the expression of pro-inflammatory genes (e.g., NF-κB), lower circulating levels of IL-6 and TNF-α, and enhance IL-10 expression in peripheral blood mononuclear cells (PBMCs). Transcriptome-wide analyses also revealed downregulation of hundreds of inflammation-related genes and upregulation of antibody response genes (e.g., CD19, IGS) [53].

Moreover, Tai Chi may enhance glucocorticoid receptor sensitivity, allowing more effective negative feedback regulation of the HPA axis and suppression of systemic inflammation. Longitudinal studies report reductions in salivary cortisol and improved neuroendocrine-immune dynamics among Tai Chi practitioners.

In summary, Tai Chi positively affects stress responses and immune regulation by lowering cortisol levels, reducing HPA axis overactivation, enhancing immune resilience, and decreasing systemic inflammation.

4.2. Epigenetic Regulation by Tai Chi

Tai Chi also contributes to immune balance by influencing epigenetic processes such as DNA methylation and histone modifications.

4.2.1. DNA Methylation

Studies on DNA methylation patterns in Tai Chi practitioners have revealed significant differences compared to non-practitioners. One study involving 60 CpG sites found that women practicing Tai Chi exhibited a significantly slower methylation loss or gain rate at six key sites, with 5% and 70% changes. These alterations may be associated with the anti-aging and anti-inflammatory effects of Tai Chi. Genes related to energy metabolism and immune function in Tai Chi practitioners demonstrate a more stable methylation pattern, potentially reducing the expression of pro-inflammatory cytokines while enhancing anti-inflammatory mediator levels [42].

4.2.2. Histone Modifications

Tai Chi has also been linked to increased histone acetylation (e.g., H3 and H4), which loosens chromatin structure and facilitates the transcription of anti-inflammatory genes (**Table 1**). This epigenetic shift suppresses NF-κB signaling and enhances tissue repair responses. Pharmacological studies indicate that histone deacetylase (HDAC) inhibition promotes IL-10 expression while suppressing IL-6 and other pro-inflammatory cytokines [54] [55].

Significant downregulation of HDAC2, HDAC3, and HDAC9 expression was observed in short-term interventions, alongside increased H4ac and H3K4me3 modifications. These changes were associated with reduced inflammatory gene markers, including RIPK2 and COX2.

Table 1. Clinical evidence.

Epigenetic Mechanism	Key Findings	Clinical Evidence	Health Impact
DNA Methylation	Reduced methylation loss at aging-related CpG sites, delaying epigenetic aging and stabilizing immune function.	A study of 237 Tai Chi practitioners showed lower rates of methylation change at key CpG sites compared with controls, demonstrating anti-inflammatory and anti-aging effects [56].	Stabilized immune function; reduced aging rate; lower risk of age-related diseases.
Histone Modifications	Increased acetylation of histones H3 and H4 enhances chromatin openness and promotes transcription of anti-inflammatory genes.	Increased histone acetylation was associated with higher IL-10 expression and reduced IL-6, proving Tai Chi's anti-inflammatory role [24].	Improved muscle recovery and flexibility; better overall inflammatory status.

5. Tai Chi's Role in Immunosenescence

5.1. Impact on the Epigenetic Clock

The epigenetic clock is a robust biomarker of biological aging. Cumulative lifetime stress and chronic age-related diseases accelerate immunosenescence—the decline of immune system function, which includes chronic inflammation, T cell senescence, and epigenetic alterations. Recent studies suggest that Tai Chi may delay the aging process of the immune system by modulating the epigenetic clock. Its mechanisms include:

- **DNA Methylation:** Genomic DNA methylation patterns change with age, affecting gene expression and aging processes [57]. Tai Chi may optimize immune cell function by modulating methylation at age-related CpG sites, thereby slowing epigenetic aging [48].
- **Histone Modifications:** Exercise can promote demethylation of H3K9 and H3K27, enhancing the expression of anti-inflammatory genes [42]. Tai Chi might use similar mechanisms to improve immune homeostasis.
- **miRNA Regulation:** Tai Chi may alter the expression of miRNAs in tissues, which in turn regulate various inflammatory cytokines such as IL-1β, IL-8, IL-6, and TNF-α [58]. This bidirectional regulation forms a complex network that influences immune cell function. Taichi may modulate specific miRNAs (e.g., miR-146a, miR-21) to suppress chronic inflammation and improve immune balance [59].

Research indicates that lifestyle factors such as diet, exercise, and meditation can modulate the epigenetic clock, slowing aging. These findings suggest that as an integrative mind-body practice, Tai Chi may play a protective role in immunosenescence [60].

One study investigating the impact of Tai Chi on DNA methylation found that women who practiced Tai Chi long-term exhibited reduced age-related DNA methylation loss. Another study reported that long-term meditation practitioners showed a slower progression of the epigenetic clock and methylation changes in genes related to immune cell metabolism and inflammation [45].

In summary, these studies support the notion that Tai Chi may help delay aging by modulating epigenetic mechanisms and exerting protective effects against immunosenescence.

5.2. Impact on Biomarkers of Immunosenescence

Tai Chi may improve biomarkers of immunosenescence through several mechanisms:

- **Reducing Chronic Inflammation:** Regular practice has been shown to significantly reduce pro-inflammatory cytokines such as IL-6 and TNF-*α*, while simultaneously upregulating the expression of anti-inflammatory cytokines like IL-10, thereby alleviating inflammaging. A study conducted by de Oliveira Silva *et al.* (2024) demonstrated that elderly participants who engaged in a 12-week physical activity program, comprising three 45-minute sessions per week, exhibited notable improvements in inflammatory biomarkers [61]:
- IL-6 levels decreased by **32.4%**
- TNF-*α* levels decreased by **28.7%**
- IL-10 expression increased by **41%**

These findings suggest that consistent participation in aerobic and tension-regulating exercise effectively modulates cytokine expression, facilitating a shift in the immune milieu from a pro-inflammatory to an anti-inflammatory state. This transition not only helps reduce chronic low-grade inflammation but also holds the potential to counteract immunosenescence by promoting immune homeostasis and enhancing tissue repair capacity in older adults.

- **Enhancing Vaccine Response:** A study by Yang *et al.* (2007) found that older adults who engaged in a 5-month Tai Chi and Qigong program showed significantly higher antibody titers by 173%, 130%, and 109% at 3, 6, and 20 weeks post-vaccination, compared to controls. This suggests that such mind–body practices can enhance adaptive immune responses and improve vaccine efficacy in the elderly [62].
- **Improving T Cell Senescence:** With age, an increase in $CD28^-$ T cells and a decrease in the CD4+/CD8+ T cell ratio contribute to immune dysfunction. Research suggests that Tai Chi may modulate these markers, delaying T cell senescence and enhancing immune system performance [62].

Horvath's (2013) "epigenetic clock" theory indicates that DNA methylation age

accurately predicts physiological aging, and accelerated epigenetic aging is linked to shortened lifespan and increased chronic disease risk. Accumulated stress and trauma can accelerate epigenetic aging, while interventions such as exercise and meditation may reverse these changes [57].

Recent studies have shown that lifestyle interventions—including meditation and physical exercise—can reverse this process and slow down epigenetic aging [63]. Therefore, Tai Chi may help delay immunosenescence and promote healthy aging by modulating DNA methylation patterns, reducing inflammation, and regulating immune cell function, offering a potential mechanistic basis for its effects.

5.3. Applications and Challenges in Immune Regulation

5.3.1. Intervention in Depression, Inflammation, and Cancer Survival

Tai Chi has been demonstrated to modulate cytokine levels and cortisol secretion, thereby reducing systemic inflammation and alleviating stress-induced immune suppression. For instance, Irwin *et al.* (2014) found that a 3-month Tai Chi intervention in breast cancer survivors led to significant reductions in pro-inflammatory markers, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), as well as decreased expression of genes associated with inflammation [18]. These findings suggest that Tai Chi can enhance psychological well-being and improve quality of life in individuals with chronic conditions, such as cancer survivors

5.3.2. Intervention in Immunosenescence

Immunosenescence, characterized by the gradual decline of immune function with age, poses significant health challenges, including increased susceptibility to infections, reduced vaccine efficacy, and chronic inflammation. Regular physical activity, such as Tai Chi, has positively affected the immune system. A study by Długosz *et al.* (2021) indicated that physically active older adults exhibited higher counts of naïve CD4+ T lymphocytes (CD4+CD45RA+) and a more favorable CD4+CD45RA+/CD4+CD45RO+ ratio compared to inactive individuals, suggesting a rejuvenation of the immune system [64]. These results imply that Tai Chi may help counteract immunosenescence by enhancing thymic activity, modulating inflammatory cytokine expression, and reducing chronic low-grade inflammation, promoting healthy aging.

5.3.3. Current Challenges and Limitations

Despite its promising potential for immune modulation, research on Tai Chi faces several challenges. One major issue is the lack of standardized intervention protocols, with variations in practice styles, frequencies, and intensities leading to heterogeneity in study outcomes. Additionally, many studies have small sample sizes and lack long-term follow-up data, limiting the generalizability of findings. Future research should aim to develop standardized Tai Chi intervention models and incorporate comprehensive assessments, including immunological biomarkers and epigenetic evaluations, better to understand its role in immune regulation and aging.

6. Discussion and Future Directions

This review has demonstrated that as a mind-body integrative practice combining physical movement, breath regulation, and meditative awareness, Tai Chi exerts multi-dimensional and multi-pathway immunoregulatory effects. Across levels of fascial biomechanics, immune cell polarization, HPA axis modulation, epigenetic remodeling, and the mitigation of immunosenescence, Tai Chi engages a complex interplay of biomechanical, neuroendocrine, and molecular-epigenetic mechanisms to promote immune homeostasis. Notably, Tai Chi has been shown to reduce inflammatory burden, optimize T cell function and antibody production, and reprogram immune-related gene expression patterns—all of which contribute to healthier immune aging.

Despite these promising findings, current research on Tai Chi and immune regulation remains limited by several methodological and conceptual gaps. Many existing studies are constrained by small sample sizes, short intervention durations, and a lack of standardized Tai Chi protocols, leading to substantial heterogeneity across trials. Additionally, the absence of well-designed active control groups in some studies makes it difficult to isolate the unique therapeutic effects of Tai Chi from nonspecific benefits related to social interaction or general physical activity. Mechanistic studies remain in their infancy, and critical questions persist regarding the relative contribution of different components of Tai Chi, such as biomechanical stimulation, breathing patterns, mindfulness, and social engagement, in mediating its immunological effects. While changes in biomarkers such as IL-6, TNF-α, IL-10, and antibody titers are encouraging, the long-term clinical implications, such as reduced infection rates, enhanced vaccine efficacy, or attenuation of chronic inflammatory disease progression, are yet to be conclusively demonstrated.

Tai Chi, positioned at the intersection of traditional self-cultivation and modern precision medicine, still lacks definitive mechanistic characterization. Whether its immunoregulatory effects are primarily mediated by mechanical signaling, neuroendocrine integration, or the synergy of mind-body interaction remains to be determined. Furthermore, the relative weight of its elements—physical movement, breath coordination, and mindfulness—in different clinical or aging contexts has not been rigorously compared. These uncertainties must be addressed if Tai Chi is to be translated into a standardized, evidence-based therapeutic modality.

Future research should focus on the following key areas:

- **Larger and Longer-Term Trials**: Conduct multi-site, well-powered randomized controlled trials (RCTs) across diverse populations to validate the sustained effects of Tai Chi on immune health over time.
- **Dose-Response and Standardization**: Determine the optimal frequency and duration of practice, and establish standardized Tai Chi intervention protocols to improve reproducibility and comparability across studies.
- **Mechanistic Investigations**: Apply advanced genomic, proteomic, and cellular assays to elucidate the specific molecular pathways through which Tai Chi influences immune function.

- **Comparative Effectiveness Research**: Compare Tai Chi to conventional exercise, yoga, mindfulness meditation, and other interventions to identify its unique contributions to immunological resilience.
- **Clinical Applications and Synergistic Strategies**: Explore the use of Tai Chi as an adjunctive therapy in clinical contexts such as vaccination programs and chronic inflammatory disease management, and evaluate its synergistic potential when combined with pharmacological treatments.

Addressing these research priorities will strengthen the evidence base for Tai Chi's immunomodulatory capacity and facilitate its integration into clinical care and community-based health strategies. Given its low risk profile, accessibility, and multifaceted health benefits, Tai Chi holds substantial potential as a scalable public health intervention to enhance immune resilience and overall well-being in aging populations and beyond.

7. Conclusion

7.1. Main Findings

Tai Chi is a holistic, low-risk mind-body intervention that integrates traditional Eastern movement practices with contemporary immunological science. This review highlights its capacity to modulate immune function through multilayered and interconnected mechanisms.

At the **biomechanical level**, Tai Chi's active stretching and fascial tension modulation activate fibroblasts, rebalance local tissue tension, and enhance perfusion and nutrient delivery, attenuating localized inflammation. These mechanical stimuli foster a favorable immune microenvironment by upregulating anti-inflammatory cytokines (e.g., IL-10, TGF-β), downregulating pro-inflammatory mediators (e.g., IL-6, TNF-α), facilitating M2 macrophage polarization, and promoting the synthesis of inflammation-resolving mediators such as Resolvin D1.

At the systemic level, Tai Chi has been shown to downregulate hypothalamic-pituitary-adrenal (HPA) axis activity, reduce cortisol secretion, and alleviate stress-induced immune suppression. In parallel, long-term practice may induce epigenetic adaptations, including stabilized DNA methylation patterns and increased histone acetylation, which help sustain anti-inflammatory gene expression and support immune homeostasis. These mechanisms collectively contribute to a reduction in inflammaging and a delay in immunosenescence.

In summary, the immunoregulatory pathway of Tai Chi can be conceptualized as follows: **Figure 2**.

Tai Chi practice → fascial tension modulation → local cellular behavioral shifts → improved immune microenvironment → optimization of HPA axis and epigenetic regulation → enhancement of immune system homeostasis.

This multilevel interaction positions Tai Chi as a scientifically supported, multitargeted approach with significant potential to improve immune resilience and support healthy aging.

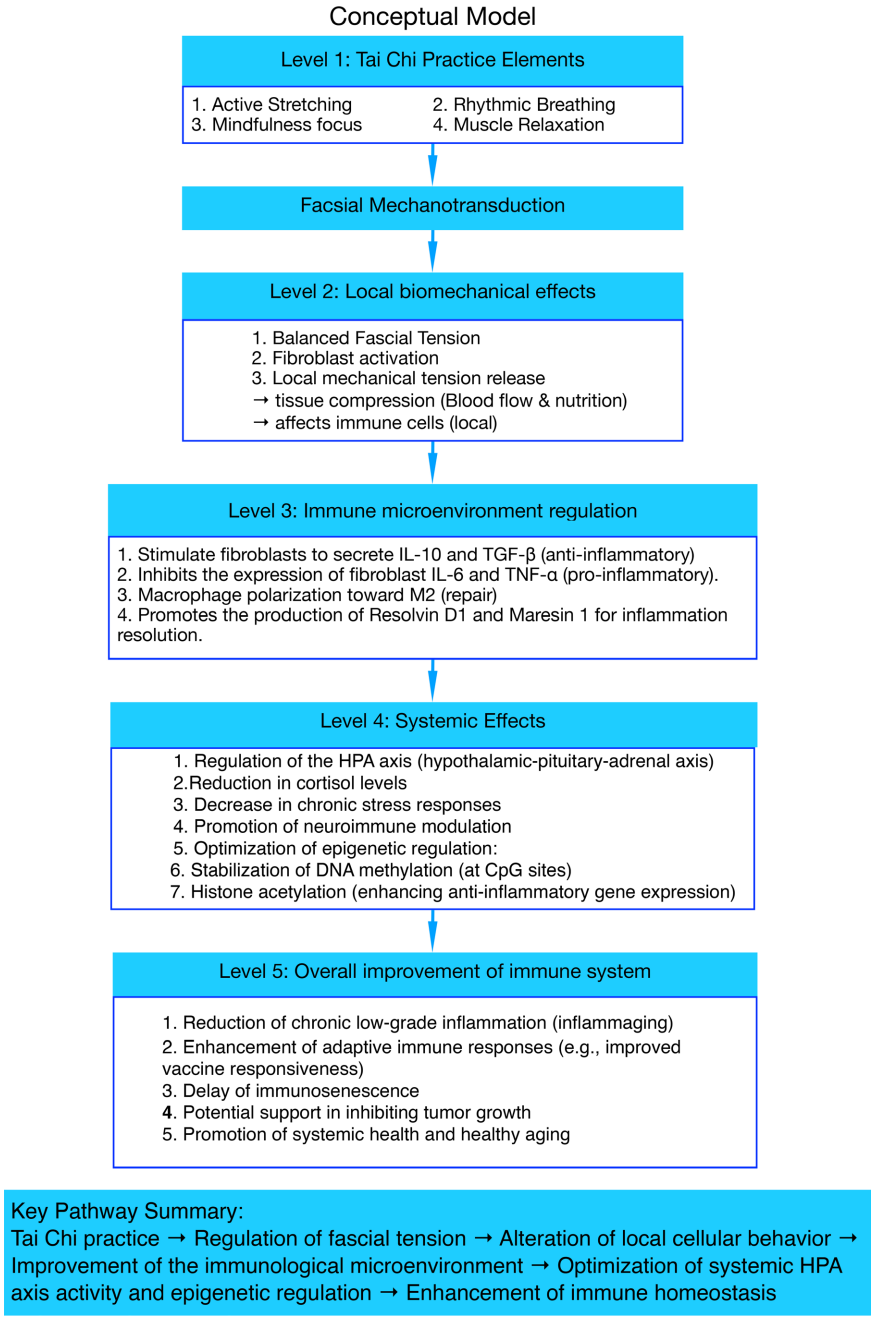

Figure 2. Multilevel immune modulation by Tai Chi: A conceptual framework.

7.2. Clinical Implications

Clinical evidence suggests that Tai Chi can reduce pro-inflammatory biomarkers, enhance immune cell function, and improve vaccine responsiveness, particularly in aging and chronically ill populations. Additional benefits related to emotional regulation, physical function, and mental well-being further support its value as a complementary therapeutic strategy. However, it is essential to emphasize that Tai Chi should be used as a supplement, not a replacement, for conventional medical treatment.

7.3. Future Directions

Future research should emphasize interdisciplinary collaboration, integrating immunology, exercise physiology, neuroscience, epigenetics, and clinical medicine. Well-designed, large-scale, and long-term randomized controlled trials are needed to standardize Tai Chi intervention protocols and elucidate dose-response relationships. In-depth mechanistic investigations will further clarify how Tai Chi modulates immune function and advance its integration into personalized immunoregulatory and preventive medicine frameworks.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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