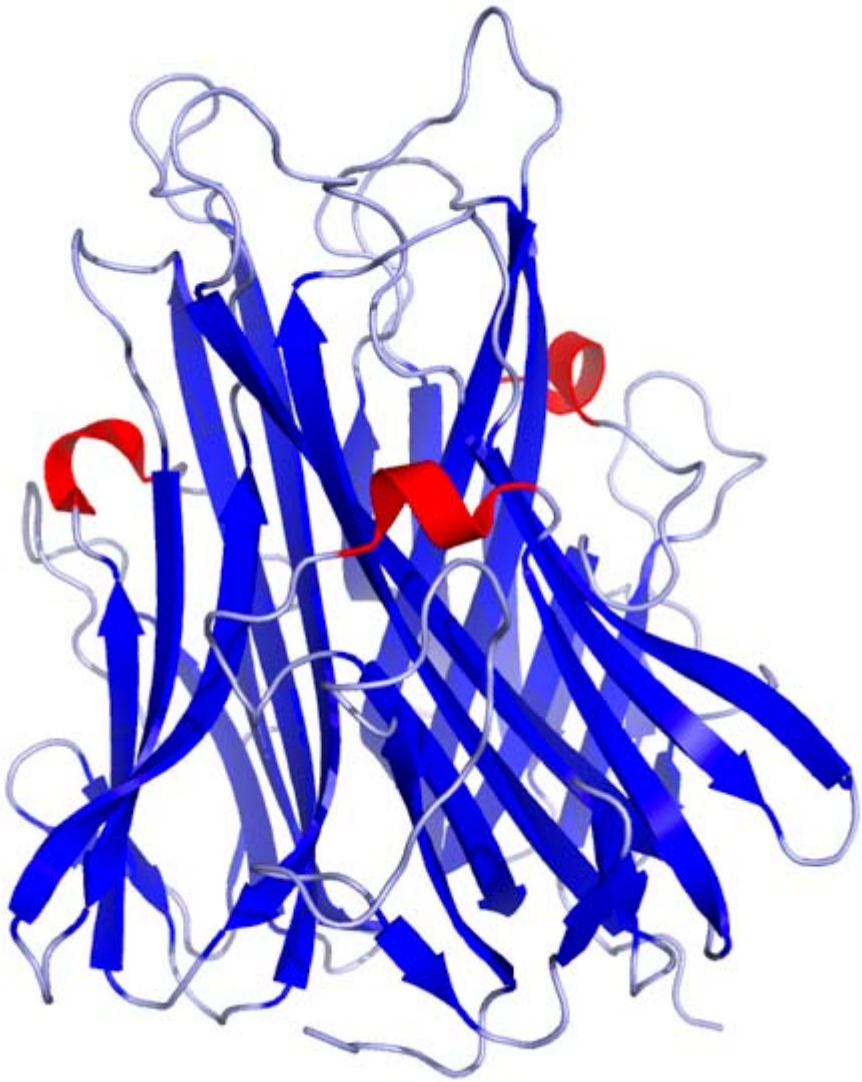
Acupuncture Anti-inflammatory Marker Found

Published by *HealthCMI* on February 3, 2017

Acupuncture reduces inflammation and researchers have discovered how it works. In a laboratory controlled scientific investigation, a key biological marker has been identified, quantified, and directly correlated with the application of acupuncture. Acupuncture successfully downregulates a proinflammatory biochemical (tumor necrosis factor alpha), which results in anti-inflammatory responses. In addition, the researchers have mapped the neural pathways by which acupuncture signaling stimulates anti-inflammatory effects.



Crystal Structure of TNF-α

Researchers in Korea have identified a mechanism by which acupuncture stimulation at the acupoint ST36 (Zusanli) has an anti-inflammatory effect. By downregulating tumor necrosis factor alpha (TNF-α), acupuncture relieves systemic inflammation. By testing the effects that a splenic neurectomy and vagotomy have on TNF-α levels in the spleen and the brain, Lim et al. found that the anti-inflammatory

effects of ST36 (Zusanli) rely on the vagus nerve pathway. Both manual acupuncture stimulation (MAC) and electroacupuncture (EAC) induce c-Fos protein generation. However, only manual acupuncture stimulation has the effect of downregulating TNF-α; electroacupuncture has the opposite effect when applied to ST36.

Chronic inflammation is involved in a variety of disease processes. Inflammation is part of the body's natural response to injuries, but if the condition persists it can lead to further damage. There are a number of factors related to chronic inflammation, including TNF-α. As an endogenous pyrogen, TNF-α is primarily involved in the regulation of immune cells. It is able to induce fever, inflammation, apoptosis, inhibit tumor growth, and inhibit virus replication. [1] However, its dysregulation is implicated in the processes of a number of diseases including major depression, cancer, psoriasis, Alzheimer's disease, and inflammatory bowel disease (IBD). [2] The researchers in this study used lipopolysaccharide (LPS) to induce TNF-α production in lab mice. Next, they performed a real-time polymerase chain reaction (PCR) DNA analysis, which "showed that TNF-α mRNA was highly induced in the spleen following LPS administration and was downregulated by MAC." [3]

The researchers also gave the mice either a splenic neurectomy or a vagotomy to discern which nerve pathway was responsible for transmitting the anti-inflammatory responses induced by the acupuncture treatments. They found that the TNF-α levels decreased with MAC but were re-elevated in mice with a splenic neurectomy and vagotomy, suggesting that "TNF-α induced in the spleen and the serum after LPS administration may be modulated by AS [acupuncture stimulation]." [4] Another trial showed that CNQX (AMPA receptor blocker) and PPADS (selective purinergic antagonist) — which both inhibit the dorsal vagal complex (DVC) — also decreased splenic TNF-α, which implies the direct involvement of the vagus nerve in the modulation of TNF-α. [5]

The vagus nerve is a cranial nerve best known for innervating the viscera. However, "growing bodies of evidence indicate that vagus nerve activity is important not only for homeostatic regulation of internal organs but also for the regulation of pathologic inflammatory reactions; thus, the vagus nerve acts as a bridge between the neural and immune systems. Notably, VNS can activate the a7 nicotinic acetylcholine receptor on the macrophages in the spleen." [6]

The cholinergic response, mediated by the vagus nerve, directly controls a proinflammatory response by way of the inflammatory reflex. Several inflammatory diseases are regulated by the 'cholinergic anti-inflammatory reflex,' including rheumatoid arthritis, diabetes, and obesity. [7] Additionally, previous research finds that insulin resistance is caused by chronic inflammation resulting from immune and metabolic dysregulation; in addition, a decrease in vagus nerve activity is correlated with obesity. [8] "Selective cholinergic activation within the efferent vagus nerve-mediated arm of the inflammatory reflex can suppress obesity-associated inflammation and reverse metabolic complications. These findings raise the intriguing possibility that dysregulation of vagus nerve-mediated signaling might contribute to the pathogenesis of obesity and its related comorbidities." [9]

Obesity has reached epidemic levels in many countries and is a precursor for many chronic diseases, including diabetes. Chronic inflammation is "a critical step in the pathogenesis of insulin resistance and type 2 diabetes mellitus. Cholinergic mechanisms within the inflammatory reflex have, in the past 2 years, been implicated in attenuating obesity-related inflammation and metabolic complications. This knowledge has led to the exploration of novel therapeutic approaches in the treatment of obesity-related disorders." [10]

The anti-inflammatory effect of ST36 (Zusanli) has also been explored by other researchers. A study at Rutgers University (New Jersey) found that "stimulating ST36 (Zusanli) with an electrical current passed

through an acupuncture needle activated two nerve tracts in mice that led to the production of a biochemical that quieted a sepsis-like inflammatory reaction that had been induced in mice" [11] by stimulating a release of the anti-inflammatory neurotransmitter dopamine from the adrenal glands. When the Rutgers University researchers traced the nerve pathway, they found that it led up the sciatic nerve — near the location of ST36 (Zusanli) — to the spinal cord and the brain, and back down the vagus nerve to the adrenal glands.

Another study, conducted at Daejeon University (South Korea), finds that the incidence of collagen-induced arthritis (CIA), which is most commonly used to study the effects of rheumatoid arthritis, "was reduced and histological destruction of joint was prevented by EA [electroacupuncture] at ST36 (Zusanli). These results suggested that EA at ST36 (Zusanli) may reduce arthritis incidence and prevent joint destruction in CIA." [12] By decreasing inflammation, further damage is preventable.

Chronic inflammation is related to a wide variety of health concerns, many of which increase morbidity; therefore, finding ways to relieve inflammation is of great importance. According to the aforementioned research, splenic factors affect inflammation. This is consistent with Traditional Chinese Medicine (TCM) theory; regulation of the spleen is understood to resolve what is termed 'dampness', which can manifest in the body in a variety of ways, including inflammation and obesity.

The researchers here have illuminated the mechanism of action by which the spleen affects systemic inflammation and the complex nature of the neural pathways that these signals travel. This study provides a solid groundwork for further trials; having a serum marker (TNF-α) for chronic inflammation provides researchers with an objective measurement to gauge the effects of acupuncture treatments on the modulation of chronic inflammatory diseases. Using TNF-α measurements to understand the effects of acupuncture on inflammation, acupuncturists gain a greater understanding of the systemic biochemical changes induced by acupuncture treatments.

In related research, Lin et al. from the University of South Florida (Tampa) and the Fujian University of Traditional Chinese Medicine (Fuzhou) prove that acupuncture alleviates pain, at least in part, by regulation of microglial cells. Lin et al. demonstrate that acupuncture reduces "microglial and astrocytic proliferation coupled with improved functional recovery after SCI [spinal cord injury] …. acupuncture exerts a remarkable analgesic effect on SCI by also inhibiting production of microglial cells through attenuation of p38MAPK and ERK activation." [13] Their study finds "clinical evidence demonstrating that acupuncture is capable of producing analgesia in neuropathic pain by suppressing microglial activation." Funding for the research was provided by the US Department of Defense, University of South Florida Neurosurgery and Brain Repair, and the James and Esther King Biomedical Research Foundation. Lin et al. also note that acupuncture prevents damage to structures of the brain. The researchers note that electroacupuncture reduces oxidative damage to the hippocampus by "preventing microglial activation."

Lin et al. note that their research is not isolated. The researchers cite several examples demonstrating that specific therapeutic biochemical reactions are stimulated by acupuncture. One citation presents hope for integration of acupuncture into conventional medical protocols for the purposes of pain management. Lin et al. note that University of Maryland (Baltimore) researchers conclude that, "Electroacupuncture blocks pain by activating a variety of bioactive chemicals through peripheral, spinal, and supraspinal mechanisms. These include opioids, which desensitize peripheral nociceptors and reduce proinflammatory cytokines peripherally and in the spinal cord, and serotonin and norepinephrine, which decrease spinal N-methyl-d-aspartate receptor subunit GluN1 phosphorylation." [14]

The aforementioned research gives us important scientific measures regarding the specificity of acupuncture point stimulation. Scientists demonstrate that acupuncture produces biological responses that

are both anti-inflammatory and analgesic. The objective data quantifies specific actions and helps us gain a greater understanding as to how acupuncture exerts beneficial responses.

Notes

1 en.wikipedia.org/wiki/Tumor_necrosis_factor_alpha
2 en.wikipedia.org/wiki/Tumor_necrosis_factor_alpha
3 HD Lim et al., "Anti-Inflammatory Effects of Acupuncture Stimulation via the Vagus Nerve," PloS one. 11, no. 3 (March 19, 2016), accessed February 3, 2017, pp 4-5. ncbi.nlm.nih.gov/pubmed/26991319
4 Lim et al., Anti-Inflammatory Effects of Acupuncture Stimulation via the Vagus Nerve, Pg 5
5 Lim et al., Anti-Inflammatory Effects of Acupuncture Stimulation via the Vagus Nerve,Pg 1
6 Lim et al., Anti-Inflammatory Effects of Acupuncture Stimulation via the Vagus Nerve, Pg 7
7 Lim et al., Anti-Inflammatory Effects of Acupuncture Stimulation via the Vagus Nerve, Pg 7
8 Valentin A. Pavlov and Kevin J. Tracey, The Vagus Nerve and the Inflammatory Reflex—linking Immunity and Metabolism, 8, no. 12, accessed February 3, 2017, ncbi.nlm.nih.gov/pmc/articles/PMC4082307/
9 Pavlov et al, The Vagus Nerve and the Inflammatory Reflex
10 Pavlov et al, The Vagus Nerve and the Inflammatory Reflex
11 blogs.scientificamerican.com/talking-back/can-acupuncture-reverse-killer-inflammation/
12 Yun-Kyoung Yim et al., Electro-Acupuncture at Acupoint ST36 Reduces Inflammation and Regulates Immune Activity in Collagen-Induced Arthritic Mice, 4, no. 1 (August 18, 2006), accessed February 3, 2017, ncbi.nlm.nih.gov/pmc/articles/PMC1810363/
13 Lin, Lili, Nikola Skakavac, Xiaoyang Lin, Dong Lin, Mia C. Borlongan, Cesar V. Borlongan, and Chuanhai Cao. "Acupuncture-induced analgesia: the role of microglial inhibition." Cell transplantation 25, no. 4 (2016): 621-628.
14 Zhang, Ruixin, Lixing Lao, Ke Ren, and Brian M. Berman. "Mechanisms of acupuncture–electroacupuncture on persistent pain." The Journal of the American Society of Anesthesiologists 120, no. 2 (2014): 482-503.