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Can predictive biomarkers of chronic pain find in the immune system?

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Chronic pain is a significant global health problem. In the 2012 National Health Interview Survey in United States, 25 million adults reported daily chronic pain and 23 million more complained of severe pain [1]. Similarly, 19% of adult Europeans reported chronic pain of moderate to severe intensity, seriously compromising quality of life [2]. In addition, a recent study documented that the annual cost of chronic pain is more than the yearly costs for heart disease, cancer, and diabetes [3]. Taken together, chronic pain is a major health care problem worldwide, that needs to be taken more seriously.

Chronic pain has been recognized as pain that persists beyond the period of the normal healing process and was defined as persistent or recurrent pain lasting longer than 3 months [4]. Chronic pain can arise from various causes, including tissue or nerve damage, inflammation, and ongoing illness, but there may also be no any obvious cause. This is the reason why chronic pain can be very hard to treat and can have negative impacts on the patient's daily activities and quality of life.

In many preclinical and clinical studies, it is well known that an immune system is closely linked to the development and maintenance of various chronic pain conditions, such as rheumatic arthritis, osteoarthritis, fibromyalgia, and complex regional pain syndrome [5]. In response to tissue damage or nerve injury, mast cells or macrophages are activated and neutrophils or natural killer (NK) cells are recruited to the site of injury. Immune cells initiate the sensitization of peripheral nociceptors by release of inflammatory cytokines or other mediators. In addition, microglia or astrocytes also make an integrated network with the neurons and immune cells that coordinate immune responses and modulate the excitability of pain pathways [6]. In a recent study, Massart et al. [7] demonstrated that chronic pain can change the deoxyribonucleic acid (DNA) in the brain and immune system, showing a positive correlation between the changes of DNA methylation and persistent pain in both the prefrontal cortex and peripheral T cells of rats.

In this issue of the Korean Journal of Pain, Yoon et al. [8] investigated the changes on NK cell cytotoxic activity and the subset population of NK cells in the peripheral blood of patients with chronic pain. In this study, the cytotoxic activity of NK cells in patients with chronic pain was not different from that in normal patients. This finding is in agreement with those of previous studies with chronic low back pain, fibromyalgia, and complex regional pain syndrome, in which the percentage of NK cells did not differ between chronic pain conditions and controls [9-11]. These results showed that it is not easy for findings from

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preclinical studies to be translated into clinical practice.

The immune system has a critical role in pain transmission and modulation. In addition, chronic pain can also affect the innate immune system. Based on insight into the role of interaction between the immune system and pain modulation, further studies should be focused on finding potential candidates for blood-based pain biomarkers.

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