New discovery will inspire treatments for severe cancer pain

NTU scientists determined the underlying cause of the decrease in function of certain cancer painkillers, which will inspire the development of novel drugs

In clinical practice, a patient's tolerance for opioid painkillers is a consistently difficult issue to manage. This issue is particularly relevant for patients with serious cancer because the long-term use of opioids to alleviate their severe pain inevitably leads to decreased efficacy of the medication. To improve the quality of clinical treatment for these patients and to investigate the physiological reaction to opioid painkillers, a research team led by Dr. Chih-Peng Lin, Prof. Wei-Zen Sun and Prof. Wen-Mei Fu at the National Taiwan University College of Medicine has been studying this topic for more than three years. Their research led to the discovery of a cytokine signaling protein, CXCL1, in cancer patients' central nervous systems and that it influences the effects of opioid painkillers. This discovery could inspire the development of new drugs to inhibit the effects of CXCL1, which could stabilize the effects of opioid painkillers. These results were published in the most reputable anesthesia medical journal, Anesthesiology, in 2015.

First, the research team compared cerebrospinal fluid samples from two groups: opioid-tolerant cancer patients and opioid-naive subjects. They found that the amount of CXCL1 in the cerebrospinal fluid was significantly higher in the opioid-tolerant group. In addition, the CXCL1 level in the cancer patients increased as the opioid dose increased. Second, the research team conducted animal experiments to support their findings. After opioid painkillers were injected into the spines of rats, the spinal fluid levels of CXCL1 increased significantly within 48 hours. Additionally, administering a CXCL1 antibody to the rats, which neutralizes the effects of CXCL1, enhanced the effects of the opioid painkillers in the rats, demonstrating that CXCL1 is an important substance that affects live organisms' tolerance for opioid painkillers.

Dr. Lin and Prof. Sun have dedicated themselves to improving and creating innovations in the treatment of cancer pain for many years. In this study, they were responsible for the clinical care, the collection of cerebrospinal fluid and the data analysis. The pharmacology team was led by Prof. Fu, who specializes in animal research and novel drug development. This crucial study was accomplished through their expertise and teamwork.

Because the CXCL1 signaling pathway may be a novel target for the treatment of opioid tolerance, and because of the potential of this study in inspiring future drug development, it was elected by the American Society of Anesthesiologists (ASA) as the most important scientific discovery in its issue of the journal. This research provides a crucial scientific contribution and great benefit to society. Therefore, the ASA disseminated this study widely throughout both the scientific community and the media. For example, this scientific breakthrough was also published on the Forbes website.

Reference

Chih-Peng Lin, M.D., Kai-Hsiang Kang, Ph.D., Tzu-Hung Lin, Ph.D., Ming-Yueh Wu, Ph.D., Houng-Chi Liou, M.S., Woei-Jer Chuang, Ph.D., Wei-Zen Sun, M.D., Wen-Mei Fu, Ph.D.; Role of Spinal CXCL1 (GROδ) in Opioid Tolerance: A Human-to-rodent Translational Study. Anesthesiology 2015; 122(3):666-676. DOI:10.1097/ALN.0000000000000523.

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