SNACC

SOCIETY FOR NEUROSCIENCE IN ANESTHESIOLOGY AND CRITICAL CARE

ARTICLE OF THE MONTH

Up-regulation of Cathepsin G in the Development of Chronic Postsurgical Pain: An Experimental and Clinical Genetic Study

Liu X, Tian Y, Meng Z, Chen Y, Ho IH, Choy KW, Lichtner P,
Wong SH, Yu J, Gin T, Wu WK, Cheng CH, Chan MT
Anesthesiology. 2015 Oct;123(4):838-50.
PMID: 26270939

In this October edition of the SNACC Article of the Month, we explore an article of great interest to those who think about the molecular mechanisms behind chronic postsurgical pain. While not in the realm of what we commonly associate with clinical neuroanesthesia, this study does deal with modulation of the nervous system in nociceptive states and is an important step in understanding concepts which may affect our patients who undergo surgeries associated with significant postoperative and chronic pain states (e.g., complex spine surgery). Liu and colleagues have delved into the phenomenon of central sensitization, by which the nervous system is "upregulated" to develop chronic postsurgical pain. They identified a mediator by the name of cathepsin G that modulates such pain, and a protease that blocks the effects of cathepsin G and provides analgesia in a rodent model. Their study also explored genetic polymorphisms in cathepsin G which are applicable to humans. Expounding on this article is Dr. Guy Kositratna, who is a visiting scholar in Neuroanesthesia at the University of Pennsylvania. Please enjoy his insights, and please join us at the SNACC Annual Meeting in San Diego this month. Hope to see you there! As always, chime in on th ***SNACC LinkedIn Feed*** with your thoughts.

~John F. Bebawy, MD

Commentary

Guy Kositratna, MD
Visiting Scholar in Neuroanesthesia
University of Pennsylvania

Protease enzymes have been found to play an important role in central sensitization, resulting in the development of chronic pain. Liu X and colleagues recently identified cathepsin G (CTSG) as a novel protease that also modulates spinal pain signaling. Their discovery has led to a possibility that targeting at the proteases may represent a new approach to regulate spinal nociceptive transmission.

The authors conducted a microarray analysis of the dorsal spinal horn in rat models and found that the CTSG was the most up-regulated gene following persistent hyperalgesia caused by an intraplanar injection of complete

Freund's adjuvant (CFA). An increase in neutrophils and release of inflammatory mediators such as interleukin 1β were observed after the hyperalgesia had developed; whereas they were found to be significantly decreased when specific CTSG inhibitor (CatGI) had been intrathecally injected. These findings led to an assumption that the CTSG may contribute to an increase in pain hypersensitivity by its chemotactic properties.

The clinical relevance of CTSG gene polymorphisms in the development of chronic pain in humans was also demonstrated in the study. Patients carrying homozygous allele of SNPs rs2070697 and rs2236742 in the CTSG gene were associated with a lower risk of chronic post-surgical pain assessed at 12 months postoperatively. The authors concluded that the CTSG has a potential of becoming a new target for chronic pain intervention. Also, preoperative determination of CTSG gene polymorphisms may assist physicians in planning a prevention plan for the chronic post-surgical pain syndrome.