Lipid Mediators and Pain Signaling

Foreword

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A number of lipid mediators play various roles in health and disease. It has long been known that arachidonic acid-derived lipid mediators including prostanoids and leukotrienes (LTs) are implicated in inflammatory events. Prostaglandin E₂ (PGE₂) and some other prostaglandins appear to play major roles in peripheral and also possibly central processing of inflammatory pain. The analgesic effects of non-steroidal anti-inflammatory drugs (NSAIDs) result from reduced production of mainly PGE₂ following inhibition of cyclooxygenase-1 (COX-1) and/or COX-2. Recently, increasing evidence suggests that LTs and other lipid mediators including lysophosphatidic acid (LPA) and platelet-activating factor (PAF) might contribute to regulation of pain signals. There is also evidence that dietary fat might be associated with pain sensation. Most actions of these lipid mediators are mediated by G-protein-coupled receptors (GPCRs), and the development of selective antagonists for each receptor and of specific receptor-knockout mice has shed new light on roles of lipid mediators in regulation of pain signals. Thus, “Lipid Mediators and Pain Signaling” is a rapidly developing research area, and is a timely topic to be updated.

LPA is one of the most interesting lipid mediators that regulate pain signals. Nerve injury-induced intensive excitation of spinal neurons increases LPA production, and subsequent activation of both LPA₁ and LPA₃ receptors in the dorsal root ganglion (DRG) plays key roles in the initiation for neuropathic pain. PAF may also function as a pain mediator, particularly after tissue injury, and the PAF/PAF receptor system appears to play a role in the development and maintenance of neuropathic pain. LTs, generated in peripheral tissues, have long been known as an important inflammatory mediator in a variety of allergic/inflammatory diseases. Interestingly, there is evidence that, after nerve injury or following the development of peripheral inflammation, LT synthesis via the 5-lipoxygenase pathway increases in the spinal cord, and LT receptors are upregulated in DRG. Thus, LTs might be involved in the neuropathic and inflammatory pain.

PGE₂ is one of well-known lipid mediators for inflammatory pain. Recent studies focus on the downstream signals of activation of PGE₂ receptors, suggesting possible involvement of multiple ion channels in the pronociceptive effect of PGE₂. Further, there is evidence that dietary fats, especially polyunsaturated fatty acids (PUFA), are associated with pain and/or analgesia. Interestingly, G-protein-coupled receptor 40 (GPR40) and GPR120 are considered to function as receptors for certain free fatty acids, and might be involved in regulation of pain signals.

In the Current Topics entitled “Lipid Mediators and Pain Signaling,” qualified experts from five distinct research groups update information concerning the roles of LPA, PAF, LTs, PGE₂ and PUFA in processing of pain signals.