Antigen-induced inflammatory mechanical hypernociception in mice is mediated by IL-18

Recent reports indicate that IL-18 participates in mediating several inflammatory diseases including rheumatoid arthritis (RA) (1). In RA patients, IL-18 induces and sustains articular Th1 cell responses, and promotes tumor necrosis factor-alpha (TNF-α) production (2). In rats, IL-18 induces mechanical hypernociception, a clinical sigh of RA (3). In ovalbumin (OVA) challenge-induced hypernociception among immunized mice, IL-15 stimulates the sequential production of interferon-γ (IFN-γ), endothelin-1 (ET-1), prostaglandin E2 (PGE2), and ultimately sensitizes the nociceptors (4). The OVA challenge-induced hypernociception and production of IFN-γ were significantly reduced in IL-18−/− mice (5). On the other hand, IL-18-induced hypernociception was diminished in naive mice pretreated with ET receptors antagonists and cyclooxygenase inhibitor as well as in IFN-γ−/− mice (5). In addition, the OVA challenge-induced ET-1 production was both restrained in IL-18−/− and IFN-γ−/− mice (5). Therefore, IL-18 mediates OVA challenge-induced hypernociception via the same downstream signal pathway (IFN-γ → ET-1 → PGE2 → nociceptor sensitization) as IL-15 (5).