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Inflammatory hyperalgesia is a complex process that depends on the sensitization of primary nociceptive neurons triggered by proinflammatory mediators, such as interleukin 1β (IL-1β). Recently, the peripheral activation of caspase-1 (previously known as IL-1β-converting enzyme) was implicated in the induction of acute inflammatory pain by promoting the processing of IL-1β from its precursor form, pro-IL-1β. Caspase-1 activation in several systems requires the assembly of an intracellular molecular platform called an inflammasome. Inflammasomes consist of 1 nucleotide-binding oligomerization domain-like receptor (NLR), the adapter molecule apoptosis-associated speck-like protein containing a C-terminal caspase recruitment domain (ASC), and caspase-1. NLRP3 and NLRC4 inflammasomes are well described. However, the identity of the inflammasome that is involved in the peripheral activation of caspase-1 that accounts for acute inflammatory hyperalgesia has not been described. The present findings demonstrated that mice deficient in NLRC4 or ASC, but not in NLRP3, present reduced mechanical and thermal acute inflammatory hyperalgesia induced by carrageenan. The reduced hyperalgesia was accompanied by significant impairments in the levels of mature forms of IL-1β (p17) and caspase-1 (p20) compared to wild-type mice at the inflammatory site. Therefore, these results identified the inflammasome components NLRC4 and ASC as the molecular platform involved in the peripheral activation of caspase-1 and IL-1β maturation, which are responsible for the induction of acute inflammatory pain. In conclusion, our study provides new therapeutic targets for the control of acute inflammatory pain.