ラット脊髄後根神経節細胞においてブラジキニンとインターロイキン -1b は RNA 結合タンパク質 HuR を介して相乗的にシクロオキシゲナーゼ -2 の発現を上昇する

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Neuroscience Letters, **694**, 215-219 (2019).

Bradykinin and interleukin-1b synergistically increase the expression of cyclooxygenase-2 through the RNA-binding protein HuR in rat dorsal root ganglion cells

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ABSTRACT: Synergistic expression of cyclooxygenase-2 (COX-2) by interleukin-1b (IL-1b) and bradykinin (BK) in peri-sensory neurons results in the production of prostanoids, which affects sensory neuronal activity and responsiveness and causes hyperalgesia. To evaluate the effects of pro-inflammatory mediators on COX-2 expression, cultured rat dorsal root ganglion (DRG) cells were treated with IL-1b and BK, which caused persistent increased COX-2 expression. Co–treatment increased COX-2 transcriptional activities in an additive manner by a COX-2 promoter luciferase assay. Immunoprecipitated HuR, an RNA-binding protein, in co-treated DRG cells contained more COX-2 mRNA than that of the control. The synergistic effects of IL-1b and BK on COX-2 expression may be a result of RNA stabilization mediated by HuR in peri-sensory neurons. Multiple pro-inflammatory cytokines and mediators are produced during neurogenic inflammation and aberrant control of COX-2 mRNA turnover may be implicated in diseases including chronic inflammation, which results in inflammation-derived hyperalgesia around primary sensory neurons.

抄録　ラット DRG 細胞における IL-1b と BK による相乗的な COX-2 発現の機序について検討した結果、薬物処置によって HuR が核内から細胞質へシャトリングし、そこで COX-2 mRNA を安定化することを見出した。