

Abstract

J Neurosci. 2008 Feb 6;28(6):1320-30.

Cysteine-rich protein 2, a novel downstream effector of cGMP/cGMP-dependent protein kinase I-mediated persistent inflammatory pain.

Schmidtko A, Gao W, Sausbier M, Rauhmeier I, Sausbier U, Niederberger E, Scholich K, Huber A, Neuhuber W, Allescher HD, Hofmann F, Tegeder I, Ruth P, Geisslinger G.

Pharmazentrum Frankfurt/ZAFES, Institut für Klinische Pharmakologie, Klinikum der Johann Wolfgang Goethe-Universität Frankfurt, 60590 Frankfurt am Main, Germany.

BACKGROUND: The cGMP/cGMP-dependent protein kinase I (cGKI) signaling pathway plays an important role in spinal nociceptive processing. However, downstream targets of cGKI in this context have not been identified to date.

OBJECTIVE: Using a yeast two-hybrid screen, we isolated cysteine-rich protein 2 (CRP2) as a novel cGKI interactor in the spinal cord. CRP2 is expressed in laminae I and II of the mouse spinal cord and is colocalized with cGKI, calcitonin gene-related peptide, and isolectin B4. Moreover, the majority of CRP2 mRNA-positive dorsal root ganglion (DRG) neurons express cGKI and peripherin. CRP2 is phosphorylated in a cGMP-dependent manner, and its expression increases in the spinal cord and in DRGs after noxious stimulation of a hindpaw.

METHODS: To elucidate the functional role of CRP2 in nociception, we analyzed mice with a targeted deletion of CRP2.

RESULTS: CRP2-deficient (CRP2^{-/-}) mice demonstrate normal behavioral responses to acute nociception and after axonal injury of the sciatic nerve, but increased nociceptive behavior in models of inflammatory hyperalgesia compared with wild-type mice. Intrathecal administration of cGMP analogs increases the nociceptive behavior in wild-type but not in CRP2^{-/-} mice, indicating that the presence of CRP2 is important for cGMP-mediated nociception.

CONCLUSION: These data suggest that CRP2 is a new downstream effector of cGKI-mediated spinal nociceptive processing and point to an inhibitory role of CRP2 in the generation of inflammatory pain.

PMID: 18256252

