Souza GR, Cunha TM, Silva RL, Lotufo CM, Verri WA Jr, Funez MI, Villarreal CF, Talbot J, Sousa LP, Parada CA, Cunha FQ, Ferreira SH. Involvement of nuclear factor kappa B in the maintenance of persistent inflammatory hypernociception. (2015). *Pharmacol Biochem Behav*, 134:49-56.

The pathophysiology of chronic inflammatory pain remains poorly understood. In this context, we developed an experimental model in which successive daily injection of prostaglandin E2 (PGE2) for 14days into rat hind paws produces a persistent state of hypernociception (i.e. decrease in mechanical nociceptive threshold). This state persists for more than 30days after discontinuing PGE2 injection. In the present study, we investigated the participation of nuclear factor kappa B (NF-κB), in the maintenance of this process. Mechanical hypernociception was evaluated using the electronic von Frey test. Activation of NF-κB signaling was measured through the determination of NF-κB p65 subunit translocation to the nucleus of dorsal root ganglion neurons (DRG) by immunofluorescence and western blotting. Herein, we detected an increase in NF-κB p65 subunit translocation to the nucleus of DRG neurons along with persistent inflammatory hypernociception compared with controls. Intrathecal treatment with either dexamethasone or PDTC (NF-κB activation inhibitor) after ending of the induction phase of the persistent inflammatory hypernociception, curtailed the hypernociception period as well as reducing NF-κB p65 subunit translocation. Treatment with antisense oligonucleotides against the NF-κB p65 subunit for 5 consecutive days also reduced persistent inflammatory hypernociception. Inhibition of PKA and PKCε reduced persistent inflammatory hypernociception, which was associated with inhibition of NF-κB p65 subunit translocation. Together these results suggest that peripheral activation of NF-κB by PKA and PKC in primary sensory neurons plays an important role in maintaining persistent inflammatory pain.