Review > Int Rev Neurobiol. 2009;85:165-77. doi: 10.1016/S0074-7742(09)85013-7.

PPAR and Pain

Takehiko Maeda [1], Shiroh Kishioka

Affiliations

PMID: 19607969 DOI: 10.1016/S0074-7742(09)85013-7

Abstract

Peroxisome proliferator-activated receptors (PPARs) are ligand-activated transcription factor belonging to a nuclear hormone receptor superfamily, containing three isoforms (alpha, beta/delta, and gamma). PPARs play a critical physiological role as a primary lipid sensor and regulator of lipid metabolism. Thus, its ligands are clinically used for treatment of type 2 diabetes and hyperlipidemia. On the other hand, PPAR ligands exert the antineuroinflammatory activity through preventing upregulation of inflammatory mediators in animal models for neurodegenerative disease and autoimmune disease. Neuropathic pain and inflammatory pain, clinically important one, are chronically progressed and underlain by neuroinflammation. In a few years, some studies using experimental models emerge that administration of PPAR ligands reduces inflammatory pain and neuropathic pain. PPAR ligands repress expression of genes for inflammatory mediators involved in both pains, such as proinflammatory cytokines, by a molecular mechanism termed ligand-dependent direct transrepression. Alternative mechanism is independent of transcriptional regulation of target genes, such as inhibition of activity of ion channels involved in the development of inflammatory pain and neuropathic pain, and therefore the analgesic effect occurs with rapid onset. The effects of PPAR ligands on neuroinflammation in animal models suggest their possible use for treating human inflammatory pain and neuropathic pain.