PPAR-α AGONISTS CAUSE ANALGESIA THROUGH IKca AND BKca POTASSIUM CHANNELS ACTIVATION

La Rana Giovanna, Russo R., Sasso O., D'Agostino G. and Calignano A.

Dip. Farmacologia Sperimentale, Facoltà di Farmacia, via D. Montesano 49-Napoli.

Palmitoylethanolamide (PEA), the naturally occurring amide of palmitic acid and ethanolamine, modulates pain and inflammation (1). We identify PPAR-α (peroxisome proliferator-activated receptor-α) as the target of PEA responsible for these actions. PEA activated PPAR-α in vitro and attenuated acute pain in wild-type mice, but not in mice lacking PPAR-α (PPAR-$\alpha^{-/-}$)(2). The synthetic PPAR-α agonists GW7647 and Wy-14643 also exerted potent analgesic effects, which were contingent on PPAR-α expression and indipendent on PPAR-α-induced anti-inflammation. PPAR-α induced analgesia occurred within minutes from agonist administration and was regulated by calcium-operated BKca and IKca potassium channel antagonist (3). Our finding show that PPAR-α mediates the acute analgesic actions of PEA trough the control of potassium channels, suggesting a role for this nuclear receptor in the control of pain initiation.

References

1) Calignano A., La Rana G., Giuffrida A., Piomelli D. (1998) Nature 394: 277-281.
2) Lo Verme J, Fu J, Astarita G, La Rana G et al. (2005) Mol Pharmacol ,67: 15.
3) LoVerme J, Russo R, La Rana G, Fu J, Farthing J, Mattace-Raso G, Meli R, Hohmann A, Calignano A, Piomelli D. J Pharmacol Exp Ther. (2006) 319:1051.