

Prostaglandin E₂ increases expression of mRNA for cyclooxygenase-2 and microsomal prostaglandin E synthase-1 in microglia.

Takayuki Nagano, Naohiko Tsuda, Kenichi Fujimura, Yuji Ikezawa, Yuki Higashi, Shinya H. Kimura, Motohiko Takemura

Dept. Pharmacol., Hyogo Col. Med.

Prostaglandin E₂ (PGE₂) plays an important role in modulating microglial function. In the present study, we have found that PGE₂ increases expression of mRNA for cyclooxygenase-2 (COX-2) and microsomal prostaglandin E synthase-1 (mPGES-1), which are involved in PGE₂ synthase in cultured rat microglia.

COX-2 and mPGES-1 mRNA levels were increased by PGE₂ at 10⁻⁶ M for 3 h in microglia. The increase of these mRNA levels was inhibited by PF-04418948 (EP₂ antagonist), but not by ONO-8713 (EP₁ antagonist), ONO-AE3-240 (EP₃ antagonist), or ONO-AE3-208 (EP₄ antagonist) at 10⁻⁶ M. In addition, ONO-AE1-259-01 (EP₂ agonist), also increased COX-2 and mPGES-1 mRNA levels in a dose dependent manner, and these mRNA levels were not affected by ONO-DI-004 (EP₁ agonist), ONO-AE-248 (EP₃ agonist), or ONO-AE1-329 (EP₄ agonist) at 10⁻⁶ M. Moreover, PGE₂ at 10⁻⁶ M for 3 h decreased expression of mRNA for microsomal prostaglandin E synthase-2, and did not affect expression of mRNA levels for cyclooxygenase-1 or cytosolic prostaglandin E synthase, which are also involved in PGE₂ synthase.

Therefore, activation of EP₂ receptor results in the increase of COX-2 and mPGES-1 mRNA levels in microglia.