

ARACHIDONIC ACID POTENTIATES NATIVE AND RECOMBINANT P2X7-MEDIATED ERK1/2, BUT NOT JNK AND p38 PHOSPHORYLATION IN CULTURED CORTICAL ASTROCYTES AND HUMAN EMBRYONIC KIDNEY 293 CELLS

Barbieri Raffaella¹, Alloisio Susanna¹, Ferroni Stefano² and Nobile Mario¹

¹Institute of Biophysics, CNR, 16149 Genoa, Italy

²Dept. of Human and General Physiology, University of Bologna, 40127 Bologna, Italy

Astrocytes are involved in normal and pathological brain functions, where they become activated and undergo reactive gliosis. Astrocytes have been shown to respond to extracellular nucleotides via the activation of P2 receptors, either G protein-coupled P2Y receptors or P2X receptors that are ligand-gated ion channels. ATP is an intercellular signalling transmitter that is released in both trauma and inflammation and P2X7 receptors are involved in immune system signalling. In this study, we have examined the manner in which activation of the P2X7 receptor, can lead to the phosphorylation of mitogen activated protein kinases. Furthermore, arachidonic acid (AA), a second messenger molecule that is released by ligand-stimulated phospholipase A₂ and it is involved in many inflammatory processes is also investigated. The results showed that ATP and the P2X7 receptor agonist 2, 3'-O- (4-benzoyl) benzoyl-ATP (Bz-ATP) induced mitogen-activated protein kinases (MAPKs) ERK1/2, JNK and p38 phosphorylation. A concentration-dependent stimulation of ERK1/2, JNK and p38 phosphorylation was also obtained by extracellular AA. The effect was just obtained at AA concentration that not involve AA-dependent Ca²⁺ entry. Finally, a significant potentiation of ERK1/2 phosphorylation was elicited by the simultaneous presence of BzATP and AA, whereas no differences were observed on JNK or p38 phosphorylation. The synergistic effect of AA and Bz-ATP was also observed in human embryonic kidney (HEK) 293 cells stably expressing rat P2X7, but not in rat P2X2. Interestingly, the ERK1/2 activation by BzATP and AA was in any case independent from Ca²⁺ entry whereas the ERK1/2 potentiation was Ca²⁺-dependent. The results suggest that ERK1/2 could be the most important mediators of the biological actions of P2X7 receptors and AA in type-1 cortical astrocytes. *Supported by MIUR (Italy)*