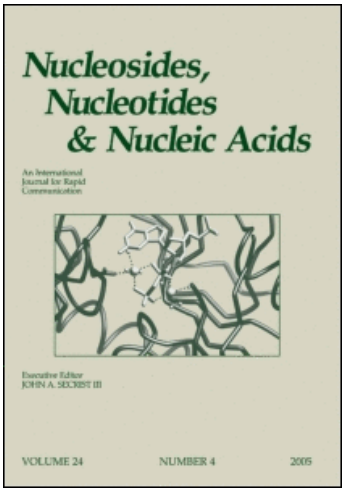

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Influence of Phospholipase A_2-Prostaglawdin System Linked to A1 Adexosine Becepmb on Protein Kinase C Activity of Cultubed Glial Cells

R. Ciccarelli[a]; M. Di Muzio[a]; P. Di Iorio[a]; P. Ballerini[a]; F. Caciagli[a]
[a] Institute of Neuroscience, Chair of Pharmacology. University of Chieti. Medical School, Chieti, Italy

To cite this Article Ciccarelli, R. , Muzio, M. Di , Iorio, P. Di , Ballerini, P. and Caciagli, F.(1991) 'Influence of Phospholipase A_2-Prostaglawdin System Linked to A1 Adexosine Becepmb on Protein Kinase C Activity of Cultubed Glial Cells', Nucleosides, Nucleotides and Nucleic Acids, 10: 5, 1235 — 1236
To link to this Article: DOI: 10.1080/07328319108047289
URL: http://dx.doi.org/10.1080/07328319108047289

NUCLEOSIDES & NUCLEOTIDES, 10(5), 1235-1236 (1991)

INFLUENCE OF PHOSPHOLIPASE A_2-PROSTAGLANDIN SYSTEM LINKED TO A_1 ADENOSINE RECEPTOR ON PROTEIN KINASE C ACTIVITY OF CULTURED GLIAL CELLS

Ciccarelli R.*, Di Muzio M., Di Iorio P., Ballerini P. and Caciagli F.
Institute of Neuroscience, Chair of Pharmacology. University of Chieti.
Medical School. Via dei Vestini 31. 66013 Chieti. Italy.

Abstract: In cultured astrocytes phospholipase A_2 seems to be functionally linked to G_i protein of A_1 adenosine receptors. Phospholipase A_2 inhibition and A_1-linked G_i protein inactivation resulted in purine release increase due to protein kinase C activation.

Glial cells exert an ionic buffer role in the CNS and support neuronal activities by releasing various substances with different functional targets. Our previous findings pointed out that cultured glial cells, able to release purines (P)[1], are provided with an autoregulatory mechanism involving A_1 and probably A_2 subtype of adenosine (ado) receptors[2]. An enhanced P outflow, equivalent to that observed in presence of a selective A_1 antagonist (8-cyclopenyl-1,3-dipropylxanthine), was assayed both in cultures pretreated with N-ethylmaleimide (NEM), a drug able to uncouple G_i protein from A_1 receptor sites, and in cultured astrocytes with completely inhibited phospholipase A_2-prostaglandin (PLA_2-PG) system[2]. Thus PLA_2-PG system seems to be involved in the regulation of P release from glial cells and probably its activation is functionally linked to A_1 ado receptor stimulation. Since it was pointed out that protein kinase C regulates hormone and neurotransmitter release from different tissues[3] and its activity (pkC-a) can be influenced by the products of PLA_2-PG system activation[4], we investigated the possible changes of pkC-a related to those pharmacological manipulations of both PLA_2-PG system and A_1-mediated ado receptor activity able to modulate P release[2]. The pkC-a was determined according to Kikkawa et al. method[5], in both the supernatant (sf) and particulate fractions (pf) of rat striatum cultured astrocytes at the 14th day of culture. In control cells approximately 80% of the total

pkC-a was found in the sf, the specific enzyme activity being 0.118±0.09 nmol phosphate transferred/min/mg protein. In these cells, cultured for 14 days, the assayed specific pkC-a was less 10% of that found in adult rat cortex[5, 6]. The specific pkC-a progressively increased in astrocytes cultured for 21 and 28 days, reaching 25.1±1.6% and 68.3±9.8% respectively of the pkC-a assayed both in the adult rat brain[5] and in glial cells cultured for 6-8 weeks[7]. However, the ratio between specific pkC-a of the sf and that of pf was not significantly changed. 400 nM phorbol 12-myristate 13-acetate, administered to the cultures for 30 min, very strongly increased pkC-a in the pf while remarkably reduced that of sf. In 28 days old cultured astrocytes the full responsiveness of pkC-a was reached (283.7±33.6% of control), while at the 14th day of culture a satisfactory responsiveness (71.8±6.1% of the maximal one) was assayed. In 14 days old cultures treated with 1 μM dexamethasone, daily administerd for 3 days to obtain a complete inhibition of PLA_2-PG system[2], a significant increase of pkC-a in the pf (+70.3±5.9%) was observed too. A similar trend of pkC-a was measured in the pf (+58.1±7.2% of control) deriving from 100 μM NEM pretreated astrocytes. NEM addition to dexamethasone pretreated cultures produced no further effect on pkC-a. These results underline that PLA_2-PG system is functionally connected with G_i protein linked to A_1 ado receptor sites. Furthermore, the previously observed increase of P release from cultured astrocytes, induced by A_1-linked G_i protein inactivation[2] or by PLA_2-PG system complete inhibition[2], could be related to a pkC activation.

REFERENCES

1) Caciagli, F., Ciccarelli, R., Di Iorio, P., Ballerini, P., & Tacconelli, L. (1988) **Pharmacol.Res.Commun. 20(11)**, 935-947

2) Caciagli, F., Ciccarelli, R., Di Iorio, P., Tacconelli, L., & Ballerini, P. (1989) **Pharmacol.Res. 21(3)**, 271-283

3) Kaczmarek, L.K. (1987) **TINS 10**, 30-34

4) Mc Phail, L.C., Clayton, C.C., & Snyderman, R. (1985) **Science 224**, 622-624

5) Kikkawa, U., Takai, Y., Minakuchi, R., Inhoharas, S., & Nishizuka, Y. (1982) **J.Biol.Chem. 257**, 13341-13348

6) Mobley, L.P., Scott, S.L., & Cruz, E.G. (1986) **Brain Res. 398**, 366-369

7) Neary, J.T., Norenberg, L.B., & Norenberg, M.D. (1986) **Brain Res. 385**, 420-424