SERINE RACEMASE ACTIVITY: REGULATION BY PKC

Vargas-Lopes, C.[1], Couto, I.A. [1], Assad-Kahn, S. [1], De Freitas, M.S.[2], Ferreira, S.T.[3], Panizzutti, R.[1]

[1]Departamento de Anatomia, ICB, Universidade Federal do Rio de janeiro, RJ; [2]Departamento de Farmacologia e Psicobiologia, IBRAG, Universidade do Estado do Rio de Janeiro, RJ; [3]Instituto de Bioquímica Médica, Universidade Federal do Rio de janeiro, RJ.

Serine racemase (SR) is a brain-enriched enzyme that catalyzes the conversion of L-serine to D-serine and pyruvate, an endogenous co-agonist of NMDA receptors. Sequencing of SR showed consensus sites for protein kinase C (PKC) phosphorylation, a serine-threonine kinase that participates in different brain functions, including learning process. Therefore, the present study analyzes a possible role of PKC regulating SR activity by changes in the phosphorylation state of the racemase. It was observed that purified recombinant SR and immunoprecipitated PKC interact causing a decrease of D-serine and pyruvate production. Treatment of astrocyte and neuronal cultures with BIM, a PKC inhibitor, increases D-serine levels, although the PKC activator PMA had no effect. By immunoblotting assay it was confirmed that the PKC effects on SR activity was correlated to differences in serine residues phosphorylation levels in the racemase. Finally, immunocytochemical analysis showed colocalization of SR and PKC in both neuronal and astrocyte cultures. Taking together these results suggest that SR is a potential target molecule for PKC, controlling both racemase and eliminase activities. This interaction can be relevant for the modulation of NMDA receptors activity and neuro-glial communication.

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