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A novel DAG-dependent mechanism links PKCα and cyclin B1 regulating the G2/M progression of cell cycle

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Protein kinase C α has been reported to regulate cell cycle in several cell lines. Most of the reports describe a role for PKC α in G1/S transition but little is known about its possible involvement in G2/M progression. Our studies on the effects of PKC inhibitors, PKC α silencing and overexpression demonstrated a novel and positive role for PKC α in cyclin B1 regulation in human erythroleukemia cell line, K562. On the other hand, using PKC inhibitors and a PKC α inactive mutant, we could report that PKC α activity was not necessary for cyclin B1 regulation. Moreover, immunoprecipitation and immunocytochemistry experiments showed that these two proteins could physically interact each other and enter into the nuclei during G2/M progression. In order to better understand this mechanism, we investigated how PKC α could be attracted into the nuclei. We found a high increase of nuclear DAG during the G2/M phase. Then, using PMA and PLC inhibitors, we showed that PKC α translocation was due to the increase in nuclear DAG. Surprisingly, we saw the same effect on cyclin B1. Finally, in order to discover which PLC was involved, we silenced the nuclear localized PLCβ1 founding a decrease in PKC α and cyclin B1 nuclear amount. Taken together, our data demonstrate the existence of a novel DAG dependent mechanism linking PKC α and cyclin B1 which can regulate their entry into the nuclei during the G2/M phase of cell cycle.

References

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Key words

PKC α, Cyclin B1, Cell Cycle, PLCβ1, Nuclear lipid signalling.