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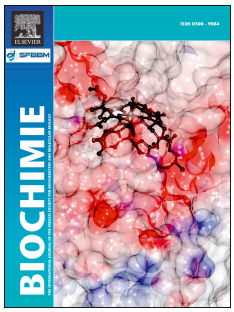

Diacylglycerol kinase δ controls down-regulation of cyclin D1 for C2C12 myogenic differentiation

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Abstract

Diacylglycerol kinase (DGK) is a lipid-metabolizing enzyme that phosphorylates diacylglycerol (DG) to produce phosphatidic acid (PA). DGKδ is highly expressed in the skeletal muscle, and a decrease in DGKδ expression increases the severity of type 2 diabetes. However, the role of DGKδ in myogenic differentiation is still unknown. The present study demonstrated that DGKδ expression was down-regulated in the early stage of C2C12 myogenic differentiation almost concurrently with a decrease in cyclin D1 expression. The knockdown of DGKδ by DGKδ-specific siRNAs significantly increased the levels of cyclin D1 expression at 48 h after C2C12 myogenic differentiation. In contrast, at the same time, the knockdown of DGKδ decreased the levels of myogenin expression and the number of myosin heavy chain (MHC)-positive cells. These results indicate that DGKδ regulates the early differentiation of C2C12 myoblasts via controlling the down-regulation of cyclin D1 expression. Moreover, the suppression of DGKδ expression increased the phosphorylation levels of conventional and novel protein kinase Cs (cnPKCs). Furthermore, DGKδ suppression increased the levels of cyclin D1 and phospho-cnPKCs even at the first 24 h of myogenic differentiation. These results suggest that DGKδ controls the down-regulation of cyclin D1 expression by attenuating the PKC signaling pathway for C2C12 myogenic differentiation.