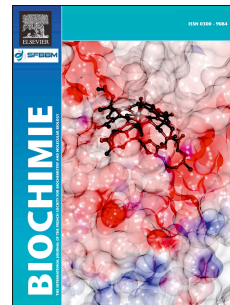


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Diacylglycerol kinase δ controls down-regulation of cyclin D1 for C2C12 myogenic differentiation

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1 Abstract

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

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