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Anti-apoptotic function of PDZRN3 protein in myoblasts

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We previously demonstrated that PDZRN3 is an important protein for myogenic differentiation from myoblasts to myotubes. In regeneration of injured skeletal muscle *in vivo*, stem cells induce MyoD expression and differentiate into myoblasts, which expand through proliferation. We reported that PDZRN3 is upregulated along with MyoD during regeneration of injured muscle. In this study, we aimed to clarify a role of PDZRN3 in proliferation of myoblasts. When exposed to serum deprivation stress, PDZRN3-depleted C2C12 myoblasts by RNAi showed higher levels of apoptotic markers as compared with those of control cells. PDZRN3-depletion also suppressed the activation of anti-apoptotic Akt, indicating the involvement of PDZRN3 in apoptotic regulation. We found that the abundance of cyclin A2 was reduced in PDZRN3-depleted C2C12 myoblasts, as was that of Mre11, which plays an important role in the repair of DNA damage. The activation of p53 was enhanced in PDZRN3-depleted cells due to the DNA damage accumulation. Overexpression of cyclin A2 restored the expression of Mre11 and attenuated caspase-3 cleavage in PDZRN3-depleted C2C12 cells subjected to serum deprivation. These results thus indicate that PDZRN3 restrains apoptosis in myoblasts through maintenance of cyclin A2 expression.