

Involvement of PLD/mTOR signaling in differentiation of human epidermal keratinocytes

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Calcium has been known to be a major factor for triggering the differentiation of keratinocytes. In the current study, the involvement of mammalian target of rapamycin (mTOR) in the regulation of calcium-induced differentiation was examined using normal human epidermal keratinocytes (NHEK). Treatment of NHEK with calcium was found to cause marked decreases in p70 ribosomal S6 kinase (p70S6K) phosphorylation level. The activity of mTOR is essential for phosphorylation of p70S6K and the treatment of NHEK with rapamycin, a potent inhibitor of mTOR effectively potentiated calcium-induced differentiation. Moreover, treatment of NHEK with rapamycin caused marked decreases in protein level of cyclin D1, a cell cycle regulator. These results indicate that mTOR would be involved in the calcium-induced differentiation by modulating the expression of cyclin D1 in NHEK.