Spred2 inhibits TGF-?1-induced urokinase type plasminogen activator expression, cell motility and epithelial mesenchymal transition

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TGF-?1 is a potent inductor of malignance in cancer cells. TGF-?1 stimulates the expression of extracellular matrix degrading proteases, cell migration and it is also involved in the epithelial-mesenchymal transition (EMT). In the present work, we analyzed the role of Spred2 in the urokinase-type plasminogen activator (uPA) stimulation, EMT and cell migration by TGF-?1. We found that both the expression of mRNA and the protein level of Spred2 were lower in transformed keratinocytes PDV compared with immortalized keratinocytes MCA-3D. The transient ectopic expression of Spred2 in PDV cells inhibited the TGF-?1-transactivated SRE-Luc reporter which is related with the ERK1,2 signal. The stable ectopic expression of Spred2 in PDV cells (SP cells) led to the loss of ERK 1,2 activation by TGF-?1, although Smad2 activation was not affected, and the knockdown of Spred2 enhanced the activation of ERK1,2 signal by TGF-?1. The increment of uPA expression induced by TGF-?1 was suppressed in SP ce