The N-terminal peptide of α-smooth muscle actin Ac-EEED inhibits myofibroblast contraction: therapeutic implications

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It is well accepted that connective tissue remodeling during wound healing, fibromatoses and fibrotic diseases depends on myofibroblast contractile activity. Myofibroblast are characterized by the neo-expression of α-smooth muscle (SM) actin (SMA), the actin isoform typical of vascular SMCs. Experimental work has shown that α-SMA expression is responsible for tension production by myofibroblasts. Our laboratory has produced a specific antibody for α-SMA whose epitope is the N-terminal sequence Ac-EEED unique for this protein. This sequence, microinjected in myofibroblasts or administered to cultured myofibroblasts by means of a cell penetrating peptidic sequence, displaces α-SMA from stress fibers and reduces myofibroblast contractility. We have also tested the action of Ac-EEED in vivo using a model of splinted wound. When the peptide is administered once a day from the 8th to the 10nth day after producing a 2 by 2 cm splinted wound on the dorsal region of rats it results on a significant reduction of wound contraction 24 hours after removal of the splinting frame. These results show that Ac-EEED can influence myofibroblast contraction in vitro and wound contraction in vivo and suggest that this peptide represents a new candidate for the treatment of inappropriate connective tissue remodeling in several pathological situations, including Dupuytres's disease.