

**HEPARAN MIMETICS (RGTA) MODULATE CALPAIN ACTIVITY
AND EXPRESSION DURING MYOBLAST PROLIFERATION AND
DIFFERENTIATION *IN VITRO***

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Mammalian skeletal muscle shows a remarkable ability to regenerate following various kinds of injury. Satellite cells (muscular stem cells) are responsible for the muscle's ability to regenerate. When they are activated, these cells proliferate, then fuse into myotubes, which may undergo a maturation into muscular fibers. These fibers restore, at least in part, muscular architecture and function. Tissue remodelling that occurs during muscle regeneration is a process which involves several growth factors and proteases. This process is strongly enhanced by a derivatized dextran polymer named RGTA.

Dextran derivatives were obtained by controlled successive substitution of carboxymethyl, carbomethyl-benzylamide and carboxymethyl-benzylamide sulfonate groups on glucose residues. RGTA mimicked some of the properties of heparin or heparan sulphate to stabilise and protect heparin-binding growth factors such FGF and TGT- β . Some of these growth factors have been described as involved in myogenesis control. In previous studies, we have shown that muscle regeneration in adults could be greatly enhanced *in vivo* by treatment with RGTA. Since muscle regeneration occurs through the activation of satellite cells, in this study, we used primary cultures of rat satellite cells and foetal myoblast and treated them with the heparan sulphate analogue RGTA or heparin, in order to stimulate their growth and differentiation. We also studied the effect of this substance on calpain activity, expression and localization in cell cultures.

RGTA and heparin were shown to have an effect on satellite cell and foetal myoblast proliferation and differentiation. RGTA stimulated proliferation. Heparin used at concentrations similar to those of RGTA was less efficient at stimulating proliferation. The results obtained also showed that RGTA could modify the activity and expression of calpain.

These results suggest that the *in vitro* improvement of cell proliferation and differentiation induced by RGTA may be partly mediated by altering calpain activity.