A rat model for reconstruction of ablated muscle

Vindigni Vincenzo, Mazzoleni Francesco, Salviati Alessandro, Rossini Katia (1), Carraro Ugo (1)

Plastic Surgery Clinic and (1) Translational Myology Lab of the Interdepartmental Research Center of Myology, Department of Biomedical Science, University of Padua, Italy.
E-mail: vincenzo.vindigni@unipd.it

Abstract

The goal of this study was to apply a step-by-step approach to identify factors favoring the survival of autologous satellite cells and, thus, muscle regeneration ("guided healing"). Muscle regeneration in free grafts is also determined by the size of the muscle being transplanted, because the speed at which new blood vessels penetrate into the mass of an avascular necrotic tissue will determine the extent of fibrosis. Auto-grafting of the middle third of the rectus abdominis muscle results in scar. In a rat model of full-thickness rectus abdominis muscle ablation, when autologous myoblasts were isolated from the explanted rectus abdominis and seeded in a homologous acellular matrix, the only regenerated myofibers are confined to the border of the patch. We succeed in regenerating myofibers in the graft by injecting marcaine in both the auto-graft and the surrounding muscles. Three weeks after surgery, the patch was paved by young centrally nucleated myofibers intermixed to early myofibers and myotubes, both expressing embryonic myosin. Muscle regeneration seems to be the result of co-ordinate migration of angioblasts and satellite cell–derived myoblasts from the muscles surrounding the patch, suggesting that (neo)vascularization of the scaffold followed by co-ordinate proliferation of seeded cells are mandatory events to allow myoblasts to migrate into the patch and differentiate up to myofiber stage.

Key Words: rat muscle, rectus abdominis, guided healing, reconstruction of ablated muscle, auto-grafting.

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Studies in mice, rats, and humans show that the efficiency of muscle regeneration in grafts is determined in part by the thickness of the muscle being transplanted, because the speed at which new blood vessels penetrate into the mass of avascular necrotic tissue will determine the extent of fibrosis.

The goal of this study was to apply a step-by-step approach to identify factors favoring the survival of autologous satellite cells and, thus, muscle regeneration ("guided healing"). In a rat model of full-thickness rectus abdominis muscle ablation, autologous myoblasts were isolated from the explanted rectus abdominis and seeded in a homologous acellular matrix immediately after wall reconstruction (group 1, five animals). In group 2 (five animals), the ablated rectus abdominis was autografted in situ. In a third group of ten rats, marcaine is injected in the autograft (5 animals) or acellular muscle matrix (5 animals), and into the surrounding abdominal wall muscle at the time of surgery.

Histological (haematoxylin-eosin stain) and immunofluorescence (antibody to embryonic myosin) analysis were performed three weeks after surgery (figure 1). Patches have the mechanical properties to support the abdominal organs (survival rate 100%, hernia rate 0%). Auto-grafting of the middle third of the rectus abdominis muscle results in scar. When autologous myoblasts are seeded in a homologous acellular matrix, the only regenerated myofibers are confined to the border of the patch. We succeed in regenerating myofibers in the graft by injecting marcaine in both the auto-graft and the surrounding muscles. Three weeks after surgery, the patch was paved by young centrally nucleated myofibers intermixed to early myofibers and myotubes, which express embryonic myosin.

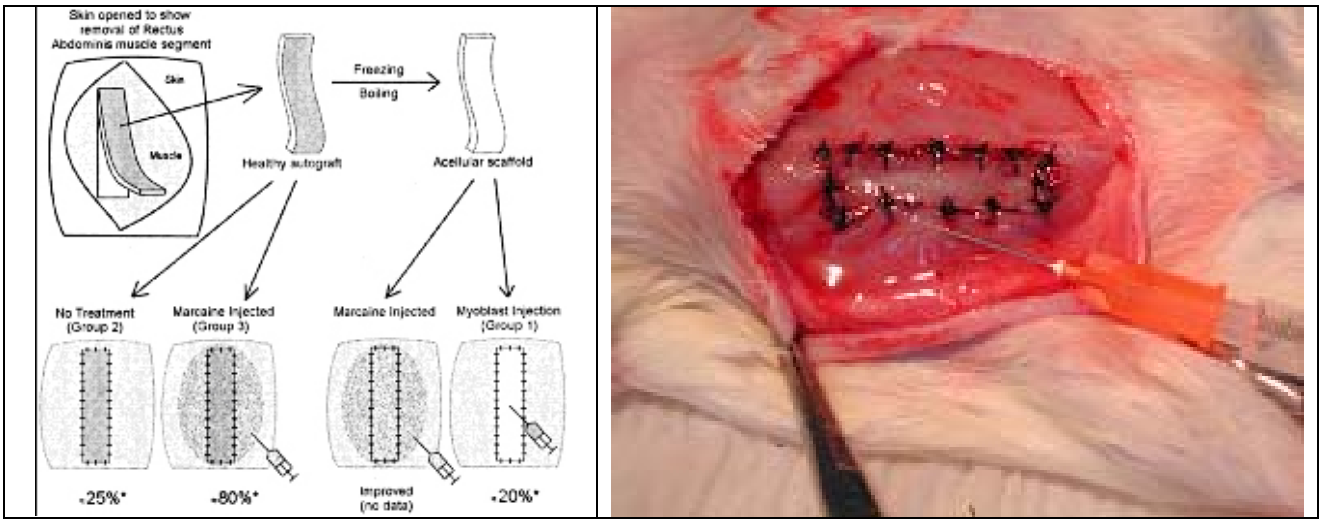

Figure 1. *Summary of the experimental procedure and main groups. The dimensions of the grafted muscle segment are 24 mm long, 8 mm wide, and up to 3 mm thick*

Muscle regeneration seems to be the result of co-ordinate migration of angioblasts and satellite cell–derived myoblasts from the muscles surrounding the patch. The results strongly suggest that vascularization of the scaffold followed by co-ordinate proliferation of the seeded cells are mandatory events to allow myoblasts to migrate into the patch and differentiate up to myofiber stage.

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