FRESH SKELETAL MUSCLE FIBERS AS INTERNAL FILLER OF CHITOSAN TUBES FOR NERVE REPAIR

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Chitosan tubes have shown promising results for peripheral nerve repair. Nevertheless, when severe lesions occur, hollow tubes not always lead to a complete functional recovery and nerve regeneration. For this reason, efforts must be done to further improve the outcome.
In this study, we enriched the hollow chitosan tube with fresh skeletal muscle fibers, which have been previously demonstrated to be a good filler in the muscle-in-vein paradigm, because of their structural and trophic role.
Rat median nerve gaps were repaired with 10mm chitosan tubes filled with a longitudinal piece of *pectoralis major* muscle (muscle-in-tube) and we compared it with hollow chitosan tubes and autologous nerve grafts, two techniques whose regeneration efficiency has already been demonstrated. Regenerating nerve samples were harvested at early (up to 28 days) and late (12 weeks) time-points for the biomolecular and morphological analysis and, for the functional and stereological analysis, respectively.
Functional assay and stereological analysis, performed on the distal part of regenerated nerve 12 weeks after nerve repair, demonstrate that the muscle-in-tube promotes functional recovery and nerve regeneration well as the hollow chitosan tube. Besides, biomolecular analyses performed on *in vitro* degenerating muscle and *in vivo* at early time points show that the fresh skeletal muscle produces and releases high levels of soluble isoforms of Neuregulin1. Neuregulin1 is a key factor for Schwann cell survival and dedifferentiation, and it is absent in the hollow tube during the early phase of regeneration, when Schwann cells did not yet colonize the hollow tube. Therefore, we suggest that muscle-in-tube, which spontaneously releases Neuregulin1, might be a promising strategy to repair injuries when hollow conduits are not effective.