Peripheral nerve regeneration

Peripheral nerve regeneration comprises the formation of axonal sprouts, their outgrowth as regenerating axons and the reinnervation of original targets.

Existing series indicate that genitoplasty patients experience faster and more complete recovery than any other peripheral nerve regeneration scenarios. However, there are many potential confounding factors in assessment and reporting, and more consistent and reproducible measure endpoints measures are needed. Further research is needed to better understand both the basic science and clinical science of peripheral nerve regeneration in genitoplasty, which may change fundamental aspects of current paradigms of peripheral nerve regeneration [1)].

The strategy of using multipotential stem cells like bone mesenchymal stromal cells (BMSCs) for nerve tissue engineering is proven feasible. The promotion effects on neural transdifferentiation of BMSCs from factors including nerve growth factor (NGF), laminin and Electrostimulation (ES) have been reported, while it is not known if these factors can achieve a strong synergetic impact when the cells are cultured on conductive substrates.

In a study of Jing et al., it was identified that any single factor (NGF, laminin, or conductive substrate) combined with ES demonstrated the capacity to induce BMSCs transdifferentiating into neural cells, while the efficiency was found in the order of NGF > laminin > conductive substrate. The combination of any two of the factors would be more efficient in inducing the neural transdifferentiation than individual factor. As expected, the strongest promotion in inducing BMSCs to transdifferentiate into neural cells was identified when BMSCs were cultured on laminin-treated conductive nanofibrous mesh in the presence of NGF and under proper ES simultaneously, showing significant synergetic efficiency from these multiple factors. Studies on the Notch-1 signaling pathway, a main negative regulator of neurogenesis, revealed these factors sharing a similar molecular mechanism in regulating the neural transdifferentiation of BMSCs. The results suggested that satisfactory nerve regeneration might be achievable if these synergetic multiple factors could be involved in nerve guidance conduit design, especially, when BMSCs were applied as co-implanted cells [2)].

The success of peripheral nerve regeneration is dependent on the survival of axotomized neurons, the efficacy of axonal outgrowth from those neurons, and the specificity of reinnervation of peripheral targets by those neurons. Experimental evidence indicates that following peripheral nerve injury, primary sensory (DRG) neurons and in some cases, motoneurons are lost. This cell death, which can involve one third or more of the axotomized neurons, suggests that some neurons in the adult are dependent on nerve or target-derived neurotrophic factors. One of these factors, NGF, when supplied to the cut proximal stump of the sciatic nerve, can save 100% of the DRG neurons that would normally succumb to axonal injury. But not all neurons are NGF-dependent, and other factors, including gonadal hormones, may be important to their survival following axotomy. Axonal elongation following peripheral nerve injury is dependent upon molecules in the extracellular matrix as well as secreted molecules from nonneuronal cells within the distal stump of the nerve. Extracellular matrix molecules such as laminin provide an adhesive substrate for axonal growth; but Schwann cells in the

distal stump, which have been shown to synthesize increased amounts of NGF following peripheral nerve injury, appear to be essential for axonal elongation. Although neuronal survival and the efficacy of axonal elongation are important to peripheral nerve regeneration, the most important determinant of the success of peripheral nerve regeneration is the specificity of reinnervation. There remains some debate over whether regenerating axons are physically guided to the appropriate targets by mechanical guides in the form of basal laminar tubes, or whether they are lured by neurotropic factors derived from the distal nerve stump and targets. There is evidence that both factors are operative in the adult PNS. However, although recent data suggest that neurotropic factors within the adult nerve can influence the sorting of regenerating axons, clinical and experimental data indicate that physical constraints of nerve cytoarchitecture can override those tropic factors. Finally, although some degree of specificity of reinnervation of peripheral targets has been demonstrated, particularly for sensory receptors in skin and muscle, there are typically perturbations of sensation and movement due to axonal misrouting and aberrant reinnervation. Further laboratory research is needed to understand how neuron-target specificity is established during development of the PNS and to determine how the developmental mechanisms can be exploited to reestablish that specificity following peripheral nerve injury [3].

Tyrosine-Derived Polycarbonate Nerve Guidance Tube

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