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Functionalized collagen conduit implantation in a paraplegic rat model

C Furne[1], G Clermont[1], Meh Begnier[1], A Letessier [1], C Correia[2], R A Sousa[2] and **R L Reis[2, 3, 4]**
[1]NAMSA Company, France
[2]Stemmatters, Biotecnologia e Medicina Regenerativa, Portugal
[3]University of Minho, Portugal
[4]ICVS/3B's, Portugal

Introduction: Limited regeneration occur spontaneously following spinal cord injury (SCI). Biomaterials hold great promising for the regeneration of many tissues including spinal cord (SC). The neurograft collaborative consortium proposed a novel micro-porous collagen conduit to restore SC functions. The conduit was designed to create a bridge across the lesion and provide a trophic support to the survival of neurons and axons outgrowth. The conduit was tested in a new paraplegic rat model that mimicked irreversible acquired paraplegia and in a rat transection model.

Methods: Paraplegia was induced in a rat model by a contusion at thoracic vertebra T9. Four weeks after contusion the injured portion of the SC was removed and replaced by the conduit (conduit), transected without implantation (transection control) or left untreated (contusion control). The motor functions were evaluated for 8 weeks after implantation using the Basso, Beattie and Bresnahan (BBB) rating scale. The inflammation and regeneration of the SC with/without conduits were investigated using histopathologic evaluation. The conduit was also combined with mesenchymal stem cells (MSC) and tested in single transection model. The transection was performed at T9 and the SC was implanted with the conduit (conduit), the conduit combined with neural/glial-differentiated MSC (conduit+MSC) or left empty (control transection). SCI regeneration was evaluated similarly over 12 weeks. The conduit was tested for its biocompatibility following ISO 10993 standard for irritation, cytotoxicity, acute systemic toxicity, degradation kinetic and genotoxicity.

Results: The conduit demonstrated its biocompatibility in all testing performed according to ISO 10993 standards. Its degradation kinetic was compatible with *in vitro* culture of MSC, allowing conduit functionalization before *in vivo* implantation. Its degradation kinetic was also compatible with the SC regeneration process, given that, after treatment period, the conduit was adherent to the surrounding spinal cord and restored the physical continuity of the spinal cord. Independent of the paraplegia model tested, BBB evaluation demonstrated no significant improvement of motor functions following implantation of the conduit, with or without MSC. The histopathologic evaluation is under process.

Discussion & Conclusion: To achieve cellular regeneration and functional recovery upon SCI has been a demanding challenge leading to the development of highly complex therapeutic systems including a biomaterial device with specific characteristics and bioactive agents (cells/ molecules). Such systems should ensure suitable mechanical properties, cell-adhesion, electrical activity and biodegradability. While these parameters have been seized within neurograft development, no motor function was restored after transection+conduit implantation; demonstrated by the BBB rating evaluation. Independent of the *in vivo* model used, outcomes were equivalent. Regeneration of the spinal cord is still being investigated by extensive histopathologic analysis for further understanding of the ongoing repair mechanisms and future fine-tuning of the therapeutic system. Nevertheless, the neurograft conduit has demonstrated its biocompatibility, becoming valuable as a scaffold to test other combination of active molecules and/or stem cells.

cfurne@namsa.com