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A bionic multichannel nanofiber conduit carrying Tubastatin A for repairing injured spinal cord

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ABSTRACT

Spinal cord injury is a kind of nerve injury disease with high disability rate. The bioscaffold, which presents a biomimetic structure, can be used as "bridge" to fill the cavity formed by the liquefaction and necrosis of spinal nerve cells, and connects the two ends of the fracture to promote the effective recovery of nerve function. Tubasatin A (TUBA) is a potent selective histone deacetylase 6 (HDAC6) inhibitor, which can inhibit the overexpression of HDAC6 after spinal cord injury. However, TUBA is limited by high efflux ratios, low brain penetration and uptake in the treatment of spinal cord injury. Therefore, an effective carrier with efficient load rate, sustained drug release profile, and prominent repair effect is urgent to be developed. In this study, we have prepared a bionic multichannel Tubasatin A loaded nanofiber conduit (SC-TUBA(+)) through random electrospinning and post-triple network bond crosslinking for inhibiting HDAC6 as well as promoting axonal regeneration during spinal cord injury treatment. The Tubasatin A-loaded nanofibers were shown to be successfully contained in poly(glycolide-co-ε-caprolactone) (PGCL)/silk fibroin (SF) matrix, and the formed PGCL/SF-TUBA nanofibers exhibited an uniform and smooth morphology and appropriate surface wettability. Importantly, the TUBA loaded nanofibers showed a sustained-release profile, and still maintains activity and promoted the extension of axonal. In addition, the total transection large span model of rat back and immunofluorescent labeling, histological, and neurobehavioral analysis were performed for inducing spinal cord injury at T9-10, evaluating therapeutic efficiency of SC-TUBA(+), and elucidating the mechanism of TUBA release system *in vivo*. All the results demonstrated the significantly reduced glial scar formation, increased nerve fiber number, inhibited inflammation, reduced demyelination and protected bladder tissue of TUBA-loaded nanofibers for spinal cord injury compared to SC-TUBA, SC and Control groups, indicating their great potential for injured spinal cord healing clinically.

1. Introduction

Spinal cord injury (SCI) results in partial or complete loss of motor and sensory function of the limbs below the plane of neurological injury, which imposes a huge economic burden on the patient and society [1]. The ineffective regeneration for axons is a major obstacle to the functional recovery of central nervous system (CNS) in mammals [2–4]. Insufficient intrinsic growth capacity of damaged neurons, glial scarring,

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