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CONTROLLED RELEASE OF FGF-2 IN CORE–SHELL PLGA MICROFIBERS FOR USE IN TISSUE ENGINEERING

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Introduction: Coaxial electrospinning is a robust technique for the encapsulation of fragile, water-soluble bioactive agents such as fibroblast growth factor 2 (FGF-2), an important growth factor involved in tissue repair. Aim: To develop scaffolds made of core-shell fibers encapsulating FGF-2 and analyze their biological potential. Methods: The core of the fibers consisted of 100μg/ml FGF-2 , 10% polyethylene glycol and 2% bovine serum albumin diluted in water; the shell solution consisted of 18% poly(lactic-co-glycolic acid) (PLGA 75:25) in hexafluoro-2-propanol. The core solution was injected at a controlled flow rate of 0.2 ml/h and the shell solution at 2 ml/h. The applied voltage was 16 kV and the spinneret tip/collector distance was 15 cm. The electrospinning processes were performed at 22 °C with 45% humidity. The biological potential of the microfiber scaffold was evaluated using the rat pheochromocytoma PC-12 cell line. For this, scaffolds were placed in 24-well plates and seeded with PC-12 cells in DMEM high glucose media supplemented with 5% horse serum and 10% fetal bovine serum (FBS) and 1% penicillin/streptomycin (P/S) in a humid incubator at 37°C with 5% CO_2. The morphology of the PLGA/FGF-2 microfibers was analyzed by scanning electron microscopy (SEM) and their diameter was calculated using ImageJ software. Verification of the core–shell structure was performed by transmission electron microscopy (TEM) and laser confocal scanning microscopy (CLSM). For the release study, the samples were placed in 7 ml PBS at 37°C and 1 ml of the sample was collected at 1 hr, 8 hr, 24 hr, 5, 10, 15, 20, 25 and 30 days. Cell viability was evaluated by MTT assay; cell proliferation and morphology was analyzed using images from SEM and CLSM. Results: Coaxial electrospinning resulted in a uniform fiber morphology without any beads with a hydrophobic surface. Through TEM

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analysis, it was possible to visualize the core–shell structure of the microfibers. Additionally, by using fluorescein in the core, it was possible to confirm the presence of fluorescence inside the fibers by CLSM. The average diameter of the fibers was of 2.18 ± 0.74 µm. Preliminary results by the ELISA technique demonstrated an FGF-2 release for at least 30 days with an initial burst in the first 24 hours. *In vitro*, the coaxial fiber scaffold supported the PC12 cell attachment and proliferation, demonstrating the cytocompatibility of the material. Conclusion: These results indicate that coaxial polymeric microfibers provide for local and sustained growth factor delivery and have great potential in tissue engineering. Financial support: CNPq, CAPES, FAPERGS and Stem Cell Research Institute.

Keywords: Coaxial electrospinning. FGF-2. Tissue engineering.