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Carbon nanotubes-reinforced cell-derived matrix-silk fibroin scaffolds for bone tissue engineering applications

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SUMMARY

Musculoskeletal diseases are one of the principal causes of disability, especially in elderly patients. Since such conditions dramatically affect the quality of life of those patients and represent a burden for health systems, new and effective strategies are highly required. With this in mind, bone tissue engineering researchers have been focusing their efforts on emulating bone tissue's highly complex and hierarchical structure, envisioning an effective strategy. For so, the present work's main goal was to produce a scaffold capable of mimicking some bone tissue features, like structure, mechanical properties, and composition. For that, silk fibroin was mixed with decellularized cell-derived extracellular matrix and reinforced with carbon nanotubes to mimic the collagen structure with nanocrystals of hydroxyapatite typical of bone tissue. The previous mixture was subjected to enzymatic cross-linking and freeze-modeling to obtain these complex scaffolds, resulting in carbon nanotubes-reinforced cell-derived matrix-silk fibroin scaffolds. The scaffolds' mechanical properties and structure were assessed, showing that

they were elastic with a stiffness of ≈ 5 kPa, pore sizes of ≈ 112 ± 22 μm, and total porosity of ≈ 75 ± 3%. Then, carbon nanotubes-reinforced cell-derived matrix-silk fibroin scaffolds were biologically evaluated *in vitro* using human adipose derived-stem cells (hASCs). The results revealed that scaffolds supported the adhesion, spreading, proliferation, and ultimately, the differentiation of hASCs along the osteoblastic lineage without the need for an osteogenic supplemented medium. Such effect was further confirmed by analysis of collagen secretion, ALP activity, and expression of osteogenic-related genes (e.g., ALP, Runx-2, Col Iα, and OPN). Finally, scaffolds' *in vitro* bioactivity and hemocompatibility were evaluated, showing the formation of mineral deposits and no hemolytic effect, foreseeing its positive behavior upon in vivo implantation. Overall, these promising results demonstrated that the developed carbon nanotubes-strengthened cell-derived matrix-silk fibroin scaffolds hold an excellent promise for bone tissue engineering scaffolding applications.

Keywords:

Bone tissue engineering, hierarchical scaffolds, decellularized cell-derived matrix, carbon nanotubes, silk fibroin.

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