



## Abstract **Piezoelectric PVDF-TrFE/Hydroxyapatite Nanofibers for Bone Tissue Engineering**<sup>†</sup>

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Bone-related diseases, particularly osteoporosis, have a growing prevalence among the adult population worldwide, being responsible for facilitating bone fractures. While in most cases, bone healing can be achieved as a result of the tissue's innate ability to repair itself, in some instances, non-union or delayed union fractures may occur (5–10%), for which current clinical practices have proven to be ineffective. As a result, bone tissue engineering (BTE) strategies are being studied as an alternative to developing scaffolds capable of temporarily replacing damaged bone tissue and promoting the tissue's regeneration. While the piezoelectric properties of bone have been extensively reported in different studies, they keep being neglected in the design of novel BTE scaffolds. In order to bridge this gap in the literature, we developed novel poly(vinylidene fluoride-co-tetrafluoroethylene)/hydroxyapatite (PVDF-TrFE/HAp)-based piezoelectric electrospun scaffolds capable of mimicking the piezoelectric nature of the tissue's fibrous extracellular matrix (ECM) and providing a potential platform for electrical and mechanical stimulation to promote the regeneration of damaged bone. While the addition of HAp was found not to drastically affect fiber morphology or the mechanical properties of the fibrous mats, slight improvements in the wettability and PVDF-TrFE  $\beta$ -phase content of the scaffolds were observed. Increases in  $\beta$ -phase content of the scaffolds were also detected through different heat treatments, albeit to the detriment of their mechanical properties. Further physicochemical characterization of the topography, composition and electrical properties of the fibers, via AFM, XRD and other techniques, was also conducted. The biological performance and osteogenic potential of the produced nanofibers was assessed after seeding the functionalized scaffolds with human bone-marrow-derived mesenchymal stem/stromal cells (hBM-MSCs). As expected, the addition of HAp was found to enhance the osteogenic potential of the scaffolds, which translated to augmented MSC proliferation, ALP activity and calcium production, respectively. The results obtained suggest that the generated PVDF-TrFE/HAp fibers have promising potential for BTE applications or as a biomimetic coating for metallic bone prosthesis, and as an in vitro platform for disease modeling.

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