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Micromechanical Compatibility Between Cells and Scaffold Mediates the Efficacy of Regenerative Medicine

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Abstract : Objective: To experimentally substantiate the micromechanical compatibility between cell and scaffold, in the regenerative medicine approach for restoring bone volume, is essential for phenotypic transitions Methods: Through nanotechnology and electrospinning process, nanofibrous scaffolds were fabricated to host dental follicle stem cells (DFSCs). Blends (50:50) of polycaprolactone (PCL) and silk fibroin (SF), mixed with various content of cellulose nanocrystals (CNC, up to 5% in weight), were electrospun to prepare nanofibrous scaffolds with heterogeneous microstructure in terms of fiber size. Colloidal probe atomic force microscopy (AFM) and conventional uniaxial tensile tests measured the scaffold stiffness at the micro-and macro-scale, respectively. The cell elastic modulus and cell-scaffold adhesive interaction (i.e., a chemical function) were examined through single-cell force spectroscopy using AFM. The quantitative reverse transcription-polymerase chain reaction (qRT-PCR) was used to determine if the mechanotransduction signal (i.e., Yap1, Wwr2, Rac1, MAPK8, Ptk2 and Wnt5a) is upregulated by the scaffold stiffness at the micro-scale (cellular scale). Results: The presence of CNC produces fibrous scaffolds with a bimodal distribution of fiber diameter. This structural heterogeneity, which is CNC-composition dependent, remarkably modulates the mechanical functionality of scaffolds at microscale and macroscale simultaneously, but not the chemical functionality (i.e., only a single material property is varied). In in vitro tests, the osteogenic differentiation and gene expression associated with mechano-sensitive cell markers correlate to the degree of micromechanical compatibility between DFSCs and the scaffold. Conclusion: Cells require compliant scaffolds to encourage energetically favorable interactions for mechanotransduction, which are converted into changes in cellular biochemistry to direct the phenotypic evolution. The micromechanical compatibility is indeed important to the efficacy of regenerative medicine.

Keywords : phenotype transition, scaffold stiffness, electrospinning, cellulose nanocrystals, single-cell force spectroscopy
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