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Superior Osteo-Inductive and Osteo-Conductive Properties of Trabecular Titanium vs. PEEK Scaffolds on Human Mesenchymal Stem Cells: A Proof of Concept for the Use of Fusion Cages

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Free article

Abstract

Fusion cages composed of titanium and its alloys are emerging as valuable alternative to standard polyetheretherketone (PEEK) ones routinely used in cervical and lumbar spine surgery. Aim of this study was to evaluate osteo-inductive and osteo-conductive ability of an innovative trabecular titanium (T-Ti) scaffold on human mesenchymal stem cells (hMSCs), in both absence and presence of biochemical osteogenic stimuli. Same abilities were assessed on PEEK and standard 2D plastic surface, the latter meant as gold-standard for in vitro differentiation studies. hMSCs adhered and colonized both T-Ti and PEEK scaffolds. In absence of osteogenic factors, T-Ti triggered osteogenic induction of MSCs, as demonstrated by alkaline phosphatase activity and calcium deposition increments, while PEEK and standard 2D did not. Addition of osteogenic stimuli reinforced osteogenic differentiation of hMSCs cultured on T-Ti in a significantly higher manner with respect to standard 2D plastic culture surfaces, whereas PEEK almost completely abolished the

process. T-Ti driven differentiation towards osteoblasts was confirmed by gene and marker expression analyses, even in absence of osteogenic stimuli. These results clearly indicate superior in vitro osteo-inductive and osteo-conductive capacity of T-Ti compared to PEEK, and make ground for further studies supporting the use of T-Ti cages to improve bone fusion.

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Pore geometry influences growth and cell adhesion of infrapatellar mesenchymal stem cells in biofabricated 3D thermoplastic scaffolds useful for cartilage tissue engineering

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Abstract

The most pressing need in cartilage tissue engineering (CTE) is the creation of a biomaterial capable to tailor the complex extracellular matrix of the tissue. Despite the standardized used of polycaprolactone (PCL) for osteochondral scaffolds, the pronounced stiffness mismatch between PCL scaffold and the tissue it replaces remarks the biomechanical incompatibility as main limitation. To overcome it, the present work was focused in the design and analysis of several geometries and pore sizes and how they affect cell adhesion and proliferation of infrapatellar fat pad-derived mesenchymal stem cells (IPFP-MSCs) loaded in biofabricated 3D thermoplastic scaffolds. A novel biomaterial for CTE, the 1,4-butanediol thermoplastic polyurethane (b-TPUe) together PCL were

studied to compare their mechanical properties. Three different geometrical patterns were included: hexagonal (H), square (S), and, triangular (T); each one was printed with three different pore sizes (PS): 1, 1.5 and 2 mm. Results showed differences in cell adhesion, cell proliferation and mechanical properties depending on the geometry, porosity and type of biomaterial used. Finally, the microstructure of the two optimal geometries (T1.5 and T2) was deeply analyzed using multiaxial mechanical tests, with and without perimeters, µCT for microstructure analysis, DNA quantification and degradation assays. In conclusion, our results evidenced that IPFP-MSCs-loaded b-TPUe scaffolds had higher similarity with cartilage mechanics and T1.5 was the best adapted morphology for CTE

Sci Rep

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Adipose-derived mesenchymal stem cells differentiate into heterogeneous cancer-associated fibroblasts in a stroma-rich xenograft model

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Free PMC article

Abstract

Cancer-associated fibroblasts (CAFs) are the key components of the densely proliferated stroma in pancreatic ductal adenocarcinoma (PDAC) and contribute to tumor progression and drug resistance. CAFs comprise heterogeneous subpopulations playing unique and

vital roles. However, the commonly used mouse models have not been able to fully reproduce the histological and functional characteristics of clinical human CAF. Here, we generated a human cell-derived stroma-rich CDX (Sr-CDX) model, to reproduce the clinical tumor microenvironment. By co-transplanting human adipose-derived mesenchymal stem cells (AD-MSCs) and a human PDAC cell line (Capan-1) into mice, the Sr-CDX model recapitulated the characteristics of clinical pancreatic cancer, such as accelerated tumor growth, abundant stromal proliferation, chemoresistance, and dense stroma formed from the heterogeneous CAFs. Global RNA sequencing, single-cell based RNA sequencing, and histological analysis of CAFs in the Sr-CDX model revealed that the CAFs of the Sr-CDX mice were derived from the transplanted AD-MSCs and composed of heterogeneous subpopulations of CAF, including known and unknown subtypes. These lines of evidences suggest that our new tumor-bearing mouse model has the potential to address an open question in CAF research, that is the mechanism of CAF differentiation.

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Enhancing the Therapeutic Potential of Mesenchymal Stem Cells with Light-Emitting Diode: Implications and Molecular Mechanisms

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Free PMC article

Abstract

This study evaluated the effects of light-emitting diode (LED) on mesenchymal stem cells (MSCs). An electronic search was conducted in PubMed/MEDLINE, Scopus, and Web of Science database for articles published from 1980 to February 2020. Ten articles met the search criteria and were included in this review. The risk of bias was evaluated to report quality, safety, and environmental standards. MSCs were derived from adipose tissue, bone marrow, dental pulp, gingiva, and umbilical cord. Protocols for cellular irradiation used red and blue light spectrum with variations of the parameters. The LED has been shown to induce greater cellular viability, proliferation, differentiation, and secretion of growth factors. The set of information available leads to proposing a complex signaling cascade for the action of photobiomodulation, including angiogenic factors, singlet oxygen, mitogen-activated protein kinase/extracellular signal-regulated protein kinase, Janus kinase/signal transducer, and reactive oxygen species. In conclusion, although our results suggest that LED can boost MSCs, a nonuniformity in the experimental protocol, bias, and the limited number of studies reduces the power of systematic review. Further research is essential to find the optimal LED irradiation parameters to boost MSCs function and evaluate its impact in the clinical setting.

Nat Commun

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Janus 3D printed dynamic scaffolds for nanovibration-driven bone regeneration

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Abstract

The application of physical stimuli to cell cultures has shown potential to modulate multiple cellular functions including migration, differentiation and survival. However, the relevance of these in vitro models to future potential extrapolation in vivo depends on whether stimuli can be applied "externally", without invasive procedures. Here, we report on the fabrication and exploitation of dynamic additive-manufactured Janus scaffolds that are activated on-command via external application of ultrasounds, resulting in a mechanical nanovibration that is transmitted to the surrounding cells. Janus scaffolds were spontaneously formed via phase-segregation of biodegradable polycaprolactone (PCL) and polylactide (PLA) blends during the manufacturing process and behave as ultrasound transducers (acoustic to mechanical) where the PLA and PCL phases represent the active and backing materials, respectively. Remote stimulation of Janus scaffolds led to enhanced cell proliferation, matrix deposition and osteogenic differentiation of seeded human bone marrow derived stromal cells (hBMSCs) via formation and activation of voltage-gated calcium ion channels.