ML 07-20 (14/02/2020)

Acta Biomater. 2020 Feb 5. pii: S1742-7061(20)30066-0. doi: 10.1016/j.actbio.2020.01.048. [Epub ahead of print]

Acceleration of Chondrogenic Differentiation of Human Mesenchymal Stem Cells by Sustained Growth Factor Release in 3D Graphene Oxide Incorporated Hydrogels.

Shen H[1], Lin H[2], Sun AX[3], Song S[4], Wang B[2], Yang Y[5], Dai J[6], Tuan RS[7].
Author information

Abstract

Damaged articular cartilage has limited self-healing capabilities, leading to degeneration that affects millions of people. Although cartilage tissue engineering is considered a promising approach for treatment, robust and long-term chondrogenesis within a 3-dimensional (3D) scaffold remains a major challenge for complete regeneration. Most current approaches involve incorporation of transforming growth factor-β (TGF-β) into the scaffold, but have limited utility owing to the short functional half-life and/or rapid clearance of TGF-β. In this study, we have tested the incorporation of graphene oxide nanosheets (GO) within a photopolymerizable poly-D, L-lactic acid/polyethylene glycol (PDLLA) hydrogel, for its applicability in sustained release of the chondroinductive growth factor TGF-β3. We found that with GO incorporation, the hydrogel scaffold (GO/PDLLA) exhibited enhanced initial mechanical strength, i.e., increased compressive modulus, and supported long-term, sustained release of TGF-β3 for up to 4 weeks. In addition, human bone marrow-derived mesenchymal stem cells (hBMSCs) seeded within TGF-β3 loaded GO/PDLLA hydrogels displayed high cell viability and improved chondrogenesis in a TGF-β3 concentration-dependent manner. hBMSCs cultured in GO/PDLLA also demonstrated significantly higher chondrogenic gene expression, including aggrecan, collagen type II and SOX9, and cartilage matrix production when compared to cultures maintained in GO-free scaffolds containing equivalent amounts of TGF-β3. Upon subcutaneous implantation in vivo, hBMSC-seeded TGF-β3-GO/PDLLA hydrogel constructs displayed considerably greater cartilage matrix than their TGF-β3/PDLLA counterparts without GO. Taken together, these findings support the potential application of GO in optimizing TGF-β3 induced hBMSC chondrogenesis for cartilage tissue engineering. Statement of Significance In this work, we have developed a graphene oxide (GO) incorporated, photocrosslinked PDLLA hybrid hydrogel for localized delivery and sustained release of loaded TGF-β3 to seeded cells. The incorporation of GO in PDLLA hydrogel suppressed the burst release of TGF-β3, and significantly prolonged the retention time of the TGF-β3 initially loaded in the hydrogel. Additionally, the GO improved the initial compressive strength of the hydrogel. Both in vitro analyses and in vivo implantation results showed that the GO/PDLLA constructs seeded with human mesenchymal stem cells (hMSCs) showed significantly higher cartilage formation, compared to GO-free scaffolds containing equivalent amount of TGF-β3. Findings from this work suggest the

potential application of the GO-TGF/PDLLA hydrogel as a functional scaffold for hMSC-based cartilage tissue engineering.

Nanomaterials (Basel). 2020 Jan 29;10(2). pii: E243. doi: 10.3390/nano10020243.

Vascular Wall-Mesenchymal Stem Cells Differentiation on 3D Biodegradable Highly Porous CaSi-DCPD Doped Poly (α-hydroxy) Acids Scaffolds for Bone Regeneration.

Forni M[1], Bernardini C[1], Zamparini F[2], Zannoni A[1], Salaroli R[1], Ventrella D[1], Parchi G[2], Degli Esposti M[3], Polimeni A[4], Fabbri P[3], Fava F[3], Prati C[5], Gandolfi MG[2].
Author information

Abstract

Vascularization is a crucial factor when approaching any engineered tissue. Vascular wall-mesenchymal stem cells are an excellent in vitro model to study vascular remodeling due to their strong angiogenic attitude. This study aimed to demonstrate the angiogenic potential of experimental highly porous scaffolds based on polylactic acid (PLA) or poly-e-caprolactone (PCL) doped with calcium silicates (CaSi) and dicalcium phosphate dihydrate (DCPD), namely PLA-10CaSi-10DCPD and PCL-10CaSi-10DCPD, designed for the regeneration of bone defects. Vascular wall-mesenchymal stem cells (VW-MSCs) derived from pig thoracic aorta were seeded on the scaffolds and the expression of angiogenic markers, i.e. CD90 (mesenchymal stem/stromal cell surface marker), pericyte genes α-SMA (alpha smooth muscle actin), PDGFR-β (platelet-derived growth factor receptor-β), and NG2 (neuron-glial antigen 2) was evaluated. Pure PLA and pure PCL scaffolds and cell culture plastic were used as controls (3D in vitro model vs. 2D in vitro model). The results clearly demonstrated that the vascular wall mesenchymal cells colonized the scaffolds and were metabolically active. Cells, grown in these 3D systems, showed the typical gene expression profile they have in control 2D culture, although with some main quantitative differences. DNA staining and immunofluorescence assay for alpha-tubulin confirmed a cellular presence on both scaffolds. However, VW-MSCs cultured on PLA-10CaSi-10DCPD showed an individual cells growth, whilst on PCL-10CaSi-10DCPD scaffolds VW-MSCs grew in spherical clusters. In conclusion, vascular wall mesenchymal stem cells demonstrated the ability to colonize PLA and PCL scaffolds doped with CaSi-DCPD for new vessels formation and a potential for tissue regeneration.

Biomacromolecules. 2020 Feb 3. doi: 10.1021/acs.biomac.9b01550. [Epub ahead of print]

Combining Biologically Active β-Lactams Integrin Agonists with Poly(L-lactic acid) Nanofibers: Enhancement of Human Mesenchymal Stem Cell Adhesion.

Martelli G, Bloise N, Merlettini A, Bruni G, Visai L, Focarete ML, Giacomini D.

Abstract

Regulating stem cell adhesion and growth onto functionalized biomaterial scaffolds is an important issue in the field of tissue engineering and regenerative medicine. In this study, new electrospun scaffolds of poly(L-lactic acid) (PLLA) as bioresorbable polymer, and β-lactam compounds agonists of

selected integrins, as functional components with cell adhesive properties, are designed. The new β-lactam-PLLA scaffolds contribute significantly in guiding proteins translation involved in human bone marrow mesenchymal stem cells (hBM-MSC) adhesion and integrin gene expression. Scanning electron microscopy, confocal laser scanning microscopy, and Western Blot analyses reveal that GM18-PLLA shows the best results, promoting cell adhesion by driving significantly changes in focal adhesion proteins distribution (β1 integrin and vinculin) and activation (pFAK), with a notable increase of GM18-targets subunits integrin gene expression, α4 and β1. These novel functionalized sub-micrometric fibrous scaffolds demonstrate, for the first time, the powerful combination of selective β-lactams agonists of integrins with biomimetic scaffolds, suggesting a designed rule that could be suitably applied to tissue repair and regeneration.