Polydopamine-Coated PDMS-PCL Shape Memory Polymer Foams for Bone Regeneration

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Statement of Purpose: Scaffolds employed in bone regeneration must meet stringent requirements for osteoconductivity and osteoinductivity. It is also critical that these scaffolds form a strong physical interface with adjacent bone tissue to promote osteointegration. In the proposed work, a "self-fitting" scaffold with osteo-conductive and osteoinductive potency will be prepared using a highly porous, shape memory polymer (SMP) scaffold coated with bioactive polydopamine. This new SMP foam is comprised of polydimethylsiloxane (PDMS) segments and poly(ε-caprolactone) (PCL) segments. When treated with warm saline, the compressed foam not only expands but is in a softened state ($T > T_m$ of PCL) which permits its manipulation and conformability along irregular bone defect "boundaries". In this way, the PDMS-PCL foam scaffold is "self-fitting". Importantly, recent studies demonstrate that these SMP scaffolds achieve moduli similar or superior to other porous polymer scaffolds commonly studied in bone tissue engineering [e.g. PCL and poly(L-lactic acid) PLLA] while avoiding the brittleness associated with injectable "all ceramic" and ceramic/biostable polymer composite fillers.[1] To enhance the osteoinductivity of PDMS-PCL scaffolds, we propose to coat the foams with polydopamine, a molecule recently found to promote osteoblast adhesion and matrix mineralization.[2] Importantly, the polydopamine coating has been shown not to disrupt the "self-fitting" properties of the foam (in contrast to calcium phosphate coatings). Thus, the polydopamine coating is envisioned to increase PDMS-PCL foam osteoinductivity while maintaining or enhancing its capacity for osteointegration. It is the goal of the present study to determine the extent to which the polydopamine-coated PDMS-PCL foams support mesenchymal stem cell (MSC) osteogenesis.

Methods:

Fabrication of PDMS-PCL foams. Photosensitive PCL_{40}-*block*-$PDMS_{37}$-*block*-PCL_{40} macromers were formed into open porous foams via a "salt-fusion/salt leaching" technique which increases pore interconnectivity versus traditional salt-leaching.[3] Salt crystals (460 μm) were used to achieve a foam of ~80% porosity and an open porous network was confirmed using SEM (**Fig. 1A**). Following salt leaching, a subset of foams were coated with an aqueous dopamine chloride solution for 16 h to allow spontaneous oxidative polymerization of dopamine on pore walls.

Construct Culture and Analysis. Coated and uncoated PDMS-PCL foams were seeded with human MSCs (Lonza) at $1x10^6$ per cm^3. The resulting constructs were cultured for 2 weeks in DMEM supplemented with 10% MSC-qualified FBS, 0.1 μM dexamethasone, 50 μg/ml L-ascorbic acid-2-phosphate, 10 mM β-glycerolphosphate. Gene expression was then analyzed relative to β-actin using qRT-PCR. Total calcium deposition was quantified using the CPC liquid color kit (Stanbio).

Results and Discussion: The capacity of polydopamine-coated foams to support MSC osteogenesis was analyzed following 2 weeks of culture. Although collagen I expression was not altered by polydopamine presence, expression of the osteogenic transcription factor runx2 was increased 2.1-fold in polydopamine-coated scaffolds relative to uncoated controls ($p = 0.035$) (**Fig. 1Bs**). In addition, the bone extracellular matrix molecule osteopontin (SPP1) was upregulated 1.9-fold in the presence of polydopamine ($p = 0.04$). Further assessment of matrix mineralization indicated a 3-fold increase in calcium deposition in polydopamine-coated scaffolds relative to uncoated controls ($p = 0.04$) (**Fig. 1C**). Cumulatively, these results support the osteogenic potential of polydopamine-coated PDMS-PCL foams.

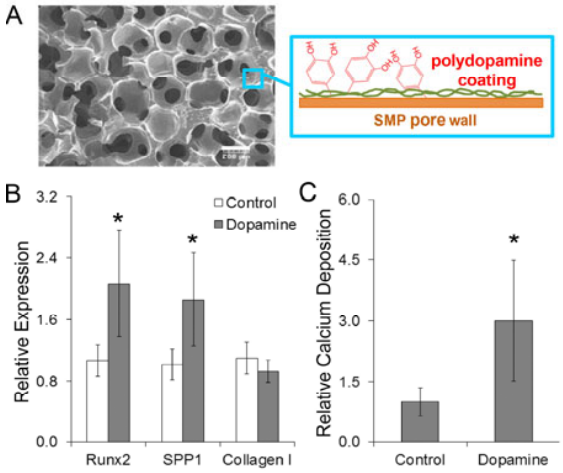

Fig 1. (A) SEM of PDMS-PCL foam and schematic of associated coating; (B) Relative gene expression of osteogenic markers runx2, osteopontin (SSP1) and collagen I; (B) Relative calcium deposition. *, significantly different from uncoated control, $p < 0.05$, $n = 5$.

Conclusions: PDMS-PCL SMP foams have significant potential as bone regeneration scaffolds due to their high porosity, elastomeric (non-brittle) nature, and capacity to be inserted in conformal contact with bone defect boundaries (promoting osteointegration). The present studies indicate that coating these SMP foams with polydopamine increases the osteoinductive capacity of these novel scaffolds.

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