A Comparative Study of Decellularized Extracellular Matrix Biomaterials from Different Sources

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Statement of Purpose: Advanced biomaterials prepared from decellularized extracellular matrix (ECM) have been increasingly used in regenerative medicine. Numerous clinical studies reported improved outcomes with newly designed ECM scaffold applications, but the biological mechanism, especially regarding interaction between host tissue and biomaterials during different stages of wound healing, has received relatively less attention. The goal of this study was to identify effective methods to systematically evaluate decellularized ECM scaffolds from different sources or manufacturers, and compare their intrinsic biological properties that modulate cell metabolism and recruitment both *in vitro* and *in vivo*.

Methods: Six commercial products (Table 1) were received in their original package and handled according to manufacturers' instructions.

Table 1: Competitive biomaterials

Material	Company	City & State	Source
Meso Biomatrix	Kensey Nash	Exton, PA	Porcine Peritoneum
Veritas	Synovis	Deerfield, IL	Bovine Pericardium
SurgiSIS	Cook Biotech	West Lafayette, IN	Porcine small intestinal submucosa (SIS), 4 layers
Oasis	Cook Biotech	West Lafayette, IN	Porcine small intestinal submucosa (SIS), 1 layer
Alloderm	LifeCell	Branchburg, NJ	Human Dermis
Gelfoam	Pfizer	New York, NY	Porcine Dermis

Material-conditioned cell culture medium was prepared by incubating finely chopped biomaterials in serum-free medium for 24 hours and centrifuging to obtain the supernatant. Proliferation and migration of NIH 3T3 fibroblasts in material-conditioned medium incubation were determined after 24 hours and 12 hours. Apoptosis reversal was evaluated in Human Umbilical Vein Endothelial Cells recovering from starvation stress by caspase 3/7 assay. Chemotaxis was assessed by migrated MDA-MB-231 cell number through the Boyden chamber membrane (Neuro Probe, Gaithersburg, MD). Cell adhesion was determined by human foreskin fibroblasts attachment to biomaterial in 3 hours of agitated culture. Biocompatibility *in vivo* was assessed by implanting punched biomaterial mesh directly on the Chicken Chorioallantoic Membrane (CAM) for 7 days, then removing the implanted material with surrounding tissue, sectioning and staining with H&E and DAPI for histological analysis.

Results: The result of the material-conditioned media study demonstrated Meso Biomatrix, Oasis and Gelfoam supported cell proliferation (Figure 1 A). Meso Biomatrix provided the greatest migration and chemotaxis signaling, followed by Veritas and Oasis (Figure 1B and C). Oasis had the best suppression of cell apoptosis. The direct adhesion assay suggested Meso Biomatrix, Veritas and Alloderm had sidedness. In the CAM assay, Gelfoam had the greatest infiltrated cell number ($2062 \pm 576/cm^2$), followed by Meso BioMatrix ($1565 \pm 473/ cm^2$) and Oasis ($1986 \pm 165/ cm^2$). Alloderm and SurgiSIS had the least cell infiltration (Figure 2B).

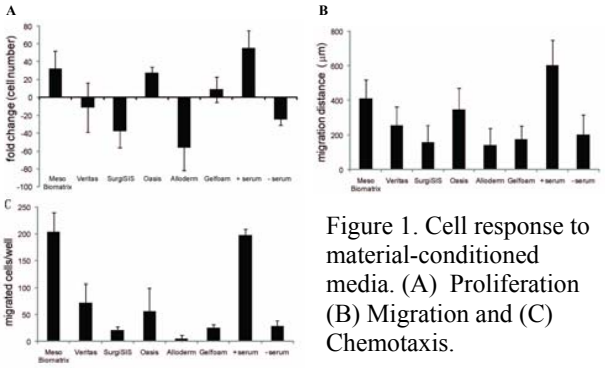

Figure 1. Cell response to material-conditioned media. (A) Proliferation (B) Migration and (C) Chemotaxis.

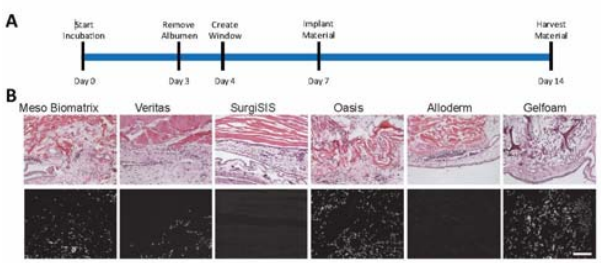

Figure 2. CAM assay. (A) Time line (B) Day 14 H&E staining showing the interface structure, DAPI staining identifying infiltrated cells. Scale bar =100 μ m

Conclusions: The panel of assays we designed provided a comprehensive assessment on decellularized ECM scaffolds effects on cells. The innate biological properties of biomaterials are not only defined by their original sources, but also include manufacturer processing techniques. Surface composition as well as pore size and thickness are major factors influencing cell infiltration and migration in the early stage of wound healing. Among tested ECM materials, Meso Biomatrix and Oasis have unique characteristics that facilitate scaffold incorporation, making them promising choices for a variety of clinical applications. Additional investigation into the long-term response of host tissue to biological materials will help develop guiding principles for biomaterial design.

References:

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