Biological Scaffolds: Molecular Surface Characterization and Host-Tissue Response

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INTRODUCTION

Abdominal wall defects cover a broad spectrum of conditions[1]. Tension-free mesh placement is the gold standard. Polymeric materials are prone to complications, and new biological meshes are developed. These devices, composed of animal extracellular matrices (ECMs), are degradable and provide constructive cues and modulation of the micro-environmental *niche* to favor tissue repair and regeneration[2]. Experience with these prostheses is still miniscule. The goals of this study were twofold: (1) To determine the surface characteristics of the ECM-scaffolds (ECMS) available in our domestic market; (2) To evaluate the relationship between these properties and the host response and downstream tissue remodeling outcome in an experimental rat abdominal wall defect model.

EXPERIMENTAL METHODS

Flight secondary ion mass spectroscopy (ToF-SIMS) was used to examine the molecular surface characteristics of the ECMS (ION-TOF IV; Bi_3 source). Multivariate and Principal Component Analyses (PCA) were performed. Full-thickness defects (2x2 cm) were created in the abdominal wall of Sprague-Dawley rats (n=240; 8 groups), and repaired with one of the following ECMS: *Bovine pericardium* non-crosslinked (ncl, n=2); *Porcine dermis* (ncl, n=2; cl, n=2); *Intestinal submucosa* (nc; n=2). A polypropylene (PP) mesh was used as control. Animals were euthanized (7, 15, 30, 90, 180d), and tissue explants were evaluated by histological, gene expression (qRT-PCR), and zymographic methods. The explant tensile properties were analyzed by uni-axial mechanical testing (DY34; Adamel Lhomargy; 100N static load cell). (M)ANOVA and correlation procedures were performed.

RESULTS AND DISCUSSION

ECMS significantly differed in their ultraperipherical molecular composition. Specifically, they varied in the apparent fibronectin and collagen content, as well as in PChead group and DAG (fatty acids). *Ex vivo*, histological analyses revealed ECMS-related ongoing remodeling processes all during the study. ECMS containing fewer surface fibronectin displayed a specific gene expression pattern characterized by a significant downregulation in *Arg1*, *Mmp9*, *Mmp3*, *Mmp2* and *Gusb*, up to day 30, which was followed by a significant upregulation of the same genes as well as of *Hpse* during the last 5mo ($P<0.001$; $r\geq0.60$, $P<0.05$). Interestingly, *Hyal2* was upregulated in DAG-enriched ECMS ($P<0.05$). Stiffness was linked to *Mmp*2 and *Mmp*3 downregulation during the last 5m ($P<0.01$); PP exhibited a similar profile ($P<0.05$). Finally, zymographic analyses revealed additional specific mesh-dependent post-translational regulation of the degradative enzymes.

CONCLUSION

ECMS have unique properties which are dependent not only on the tissue from which they are harvested or on the manufacture procedure, but also on the intrinsic molecular surface composition of the devices. These properties trigger specific differential (cellular, molecular and biomechanical) host-tissue responses, which could have a clinical potential in material-based soft-tissue repair.

REFERENCES

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