Influence of Acellular Dermal Matrices on the Expression of Mediators Involved in Wound Healing and Tissue Remodeling

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Abstract

Background: Biologic meshes for reconstructive procedures have been introduced recently in an effort to create a graft that demonstrates improved integration into host tissue and resistance to infection compared to synthetics. However, no currently available biologic mesh has demonstrated optimal biocompatibility. (1) Molecular mechanisms that direct the extent of the foreign body reaction to implanted biologics and their subsequent incorporation are poorly understood. We therefore compared the influence of two commonly used biologic meshes on the expression of genes critical for wound healing and tissue remodeling in a rat ventral hernia model.

Methods: Full thickness abdominal wall defects were repaired using non-cross-linked human dermis (Alloderm, LifeCell Inc.; n=10), cross-linked porcine dermis (Permacol, Covidien; n=10), or suture repair (no mesh; n=10). Explants were harvested 90 days after repair and divided for histological, immunohistochemical, and mRNA analyses. Real-time quantitative PCR arrays were used to profile the expression of 84 wound healing-associated genes at the tissue-mesh interface.

Results: Both meshes induced the differential expression ($\geq$3-fold change relative to suture repair, $p \leq 0.01$) of extracellular matrix components, remodeling enzymes, and inflammatory cytokines (Permacol, 16 genes; Alloderm, 3 genes). Genes most markedly upregulated included matrix metalloproteinase (MMP) 9 (Permacol, 66-fold, p=0.02; Alloderm, 19-fold, p=0.01) and the monocyte and fibrocyte chemoattractant CCL12 (Permacol 24-fold, p<0.001; Alloderm 71-fold, p=0.06). Histologically Alloderm demonstrated overall better remodeling characteristics than Permacol. Immunohistochemistry using antibodies against MMP9 (Figures 1 and 2) confirmed differential expression at the protein level, with significantly increased expression in Permacol samples compared to Alloderm (p<0.001).

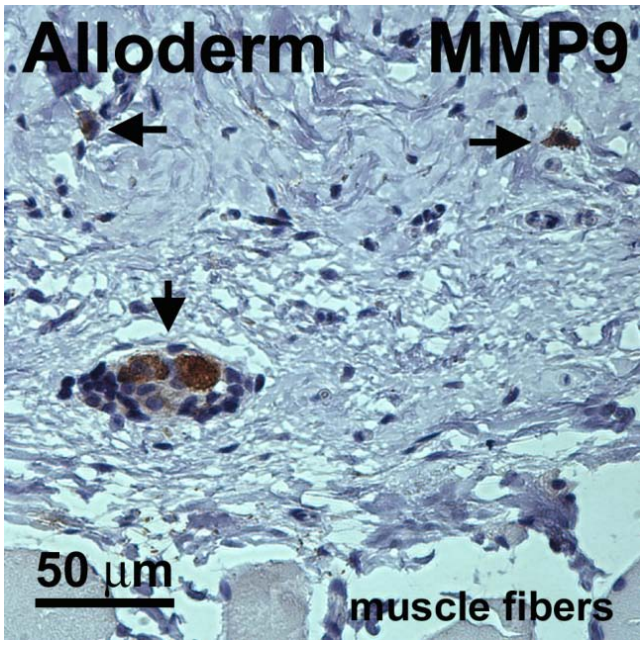

Figure 1. MMP9 expression in Alloderm explant.

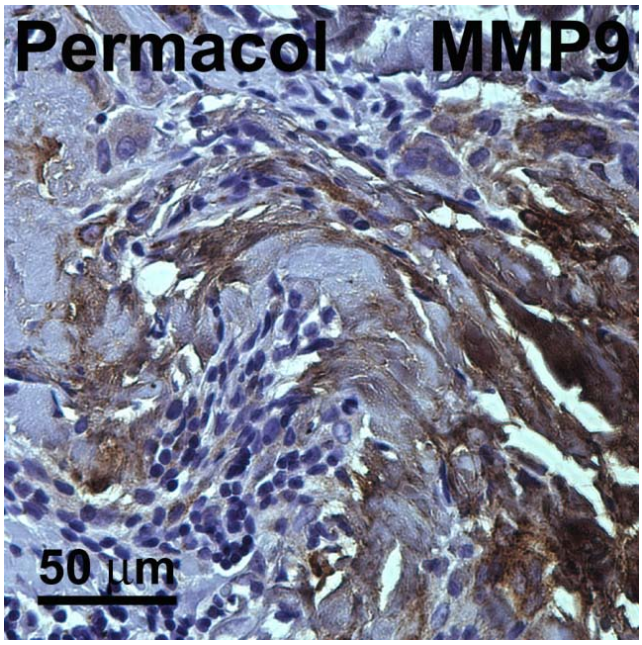

Figure 2. MMP9 expression in Permacol explant.

Conclusions: Permacol elicits increased protease expression and reduced cellular and vascular infiltration compared to Alloderm 90 days after implantation, indicative of delayed remodeling induced by cross-linking. Increased understanding of the host response to implanted materials ultimately will enable the development of improved meshes with enhanced wound healing properties and fewer graft-related complications.

References

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