Comparative Analysis of Xenograft ECM Particulates in Wound Management Applications

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INTRODUCTION

Biological scaffolds are derived from a native extracellular matrix (ECM) and used to supplement damaged or inadequate soft tissue. Ideally, these scaffolds demonstrate good biocompatibility and provide a structural framework that mimics the surrounding tissue by delivering the necessary biomechanical and biochemical cues to facilitate tissue regeneration processes including cell adhesion, chemotaxis and maturation. This study compared the in vivo biocompatibility and cellular response of xenograft ECM scaffolds from bovine[&,*] scaffolds, piscine[$], and porcine[#] sources.

MATERIALS AND METHODS

Hematoxylin & Eosin (H&E): Scaffold samples were paraffin-embedded and sections stained for H&E.

***In vivo* mouse model:** Female NU/J athymic nude mice were implanted with 50 mg of each product into a 1 cm x 1 cm surgical pocket. Mice were euthanized at 1-, 2-, and 4-weeks post implantation. Samples were fixed in 10% neutral buffered formalin for at least 12-24 hours, then transferred into 70% ethanol. Samples were paraffin-embedded and sections stained for H&E. H&E slides were reviewed and scored by an independent histopathologist at StageBio. Additional unstained slides were allocated for immunofluorescence and immunohistochemistry.

Immunofluorescence: Briefly, sections were deparaffinized, subjected to antigen retrieval followed by blocking in Serum-Free Protein Block (Agilent Dako) for 1 hour at room temperature. Incubation with primary antibodies was carried out overnight at 4°C followed by incubation with fluorescently labeled secondary antibodies to identify both implant material and new collagen synthesis. Images were acquired on a Leica microscope fitted with 10X objective using Leica Application Suite Advance Fluorescence software and the THUNDER Imager (Leica Microsystems).

Immunohistochemistry: Staining was performed by Inotiv (West Lafayette, Indiana). Briefly, sections were deparaffinized and stained with F4/80, a murine macrophage marker.

Scaffold Complexity

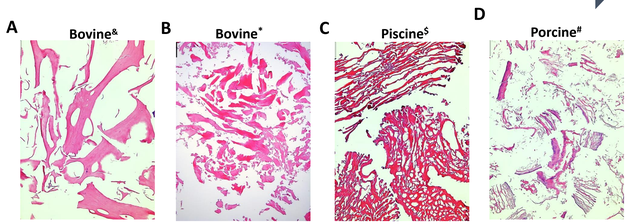

Figure 1. Tissue Scaffolds. H&E staining of (A) bovine collagen scaffold, (B) bovine collagen scaffold, (C) piscine collagen scaffold, and (D) porcine ECM scaffold.

CONCLUSION

The study demonstrates the *in vivo* biocompatibility of four xenograft scaffolds. The comparison of the resultant inflammatory response, cellular ingrowth, new collagen synthesis and implant degradation rates provided insight into the differences in source materials and processing methods. Increased early macrophage infiltration correlated with more rapid clearance as seen in the bovine[&] and piscine[$] groups. Whereas persistence of the bovine* and porcine[#] scaffold was attributed to a milder innate immune response, which facilitated cellular functions associated with remodeling and tissue regeneration out to four weeks.

ACKNOWLEDGEMENTS

The *in vivo* study was conducted at Veranex. Histological assessment of the *in vivo* study was conducted by StageBio. Staining for F4/80 was conducted by Inotiv.

[&]DermaCol™ 100, DermaRite, North Bergen, NJ
*HELIOGEN™, MIMEDX Group, Inc., Marietta, GA
[$]MariGen Micro™, Kerecis Limited, Ísafjörður, Iceland
[#]MicroMatrix®, Integra LifeSciences, Princeton, NJ

All authors are employees of MIMEDX Group, Inc.

RESULTS

In Vivo Response to Xenograft Scaffolds

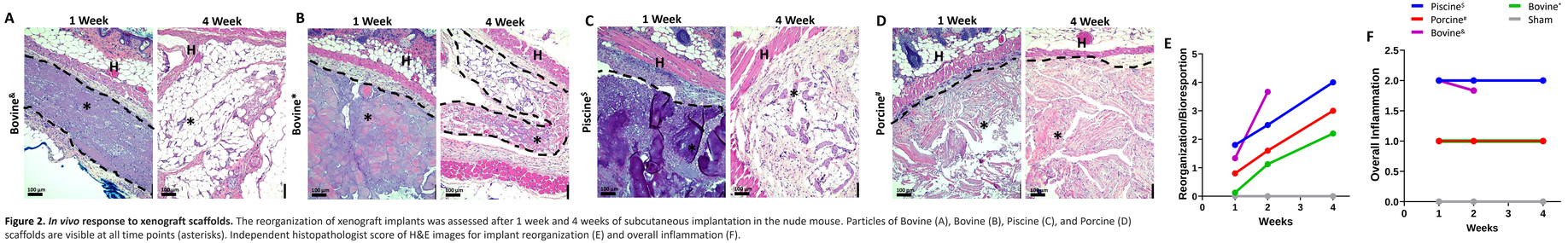

Figure 2. ***In vivo* response to xenograft scaffolds.** The reorganization of xenograft implants was assessed after 1 week and 4 weeks of subcutaneous implantation in the nude mouse. Particles of Bovine (A), Bovine (B), Piscine (C), and Porcine (D) scaffolds are visible at all time points (asterisks). Independent histopathologist score of H&E images for implant reorganization (E) and overall inflammation (F).

Elevated Macrophage Presence at Early Timepoints Results in Rapid Degradation of the Scaffold

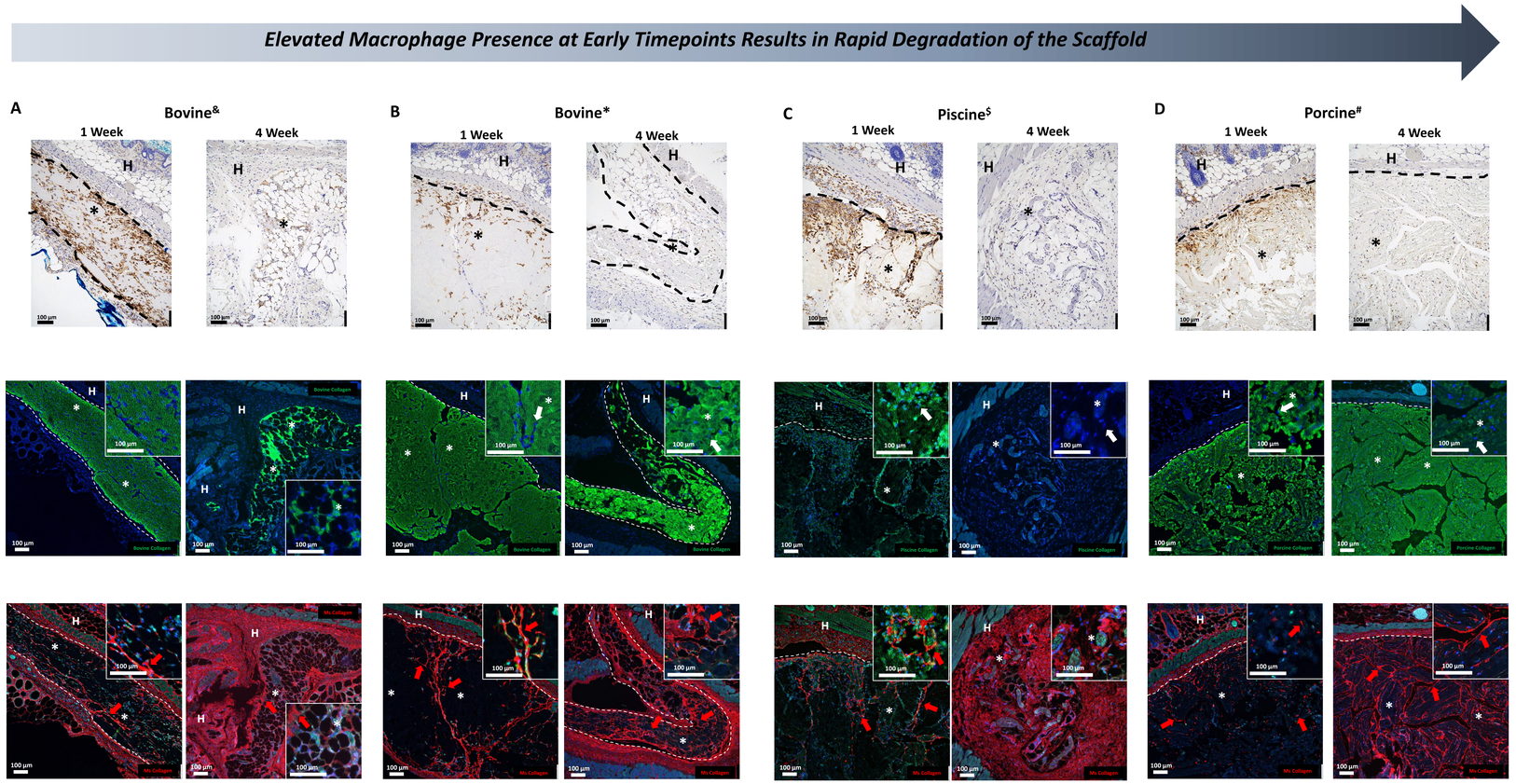

Figure 3. ***In vivo* macrophage response to xenograft scaffolds.** The macrophage infiltration (brown) of xenograft implants was assessed by F4/80 staining after 1 week and 4 weeks of subcutaneous implantation in the nude mouse. Immunofluorescence of new host collagen deposition (red) and xenograft implant (green) at 1 week and 4 weeks post subcutaneous implantation in the nude mouse: Bovine (A), Bovine (B), Piscine (C), and Porcine (D) scaffolds are visible at all time points (asterisks). Images taken at 10x magnification.