BOTM: July 2009

Porous & Reticulated Polycarbonate-Polyurethane-Urea (PCPU) Scaffold For Soft Tissue Repair

Dr. Balakrishna Haridas, Ph.D. Chief Technology Officer, Biomerix Corporation

The Biomaterial of the Month is a three-dimensional macroporous elastomeric, reticulated PolyCarbonate-Polyurethane-Urea (PCPU) scaffold for soft tissue repair and wound healing applications. Urethanes based on PC (polycarbonate) soft segments and aromatic isocyanate based hard segments have been shown to provide superior biostability, i.e., resistance to hydrolytic, oxidative, and enzymatic degradation in vivo [1-3]. These desirable characteristics of the solid forms of this class of polymers led Biomerix towards the development of a macroporous PCPU biomaterial [4,5], a reticulated, elastomeric, and resilient scaffold for soft tissue repair (Figure 1).

Histological Response of Porous Reticulated PCPU in a Rat Abdominal Wall Defect Model

Early Phase of Wound Healing – By 2-4 weeks following implantation, macrophages and foreign body giant cells surround the small white unstained filaments of the PCPU scaffold (Fig 2). This foreign body response is localized to a boundary layer around the PCPU filaments. There is evidence of early collagen synthesis (blue staining) indicating fibroblast activity, likely driven by growth factors and other cytokines released as a result of platelet activation and inflammatory response to the PCPU scaffold.

Intermediate Phase of Wound Healing: By 8 Weeks, the PCPU scaffold shows fibroblast infiltration and angiogenesis (Fig 3). Neoangiogenesis of a robust capillary bed is critical for delivery of nutrients to the cells recruited into the scaffold/matrix. Staining is positive for fibrillar collagen (Type I) with early evidence of organization into fiber bundles (Fig 3). Also seen are several groups of blood vessels indicative of active angiogeneic and cellular activity in the interstices of the biomaterial. Classic multinucleate giant cell morphology is observed as a boundary layer of cells surrounding the PCPU biomaterial filaments (white).

Late Stage Healing and Remodeling: By 26 weeks, the PCPU scaffold demonstrates biointegration with a 3-fold increase in total connective tissue collagen relative to the early healing phase (Fig 5). A well developed capillary bed (2X increase compared to early healing phase) and cellular (fibroblast) morphology is evident. At this time point, the chronic inflammatory and macrophage activity appears to have stabilized and is present as a thin boundary layer surrounding all the microfilaments of the PCPU biomaterial.

Role of Histopathological Investigations in Scaffold Evaluation

Histopathological investigations in preclinical models are critical to determine the safety as well as the efficacy profile of tissue engineering scaffolds. These studies allow to assess the ability of scaffold materials to recruit and maintain the organization of cells drawn into the scaffold early in the healing process, assess angiogeneic activity, and track the time course of evolution of the foreign body response.

Role of Scaffold design, Material chemistry, and Structure

Macroporous scaffolds like the PCPU based Biomerix Biomaterial with appropriately sized pores and interconnected pore structure are critical for the induction of appropriate soft tissue healing and repair. Cell migration, proliferation, and attachment into the high surface area presented by a macroporous scaffold material is dependent on the surface chemistry and hydrophobicity. These characteristics determine the adsorption sequence and specificity of various plasma and extracellular matrix proteins and subsequent cell adhesion to the adsorbed proteins. By leveraging these features, material chemistry, and maximizing interconnected porosity in a biostable elastomeric scaffold, it is possible to produce desirable clinical outcomes, i.e., stable tissue ingrowth, while at the same time limiting the extent of the foreign body response to prevent encapsulation/scar formation.

For more information about the Biomerix PCPU Biomaterial Scaffold, contact.
Dr. Balakrishna Haridas, Ph.D., Chief Technology Officer, Biomerix Corporation, 47757 Fremont Boulevard, Fremont, CA 94538

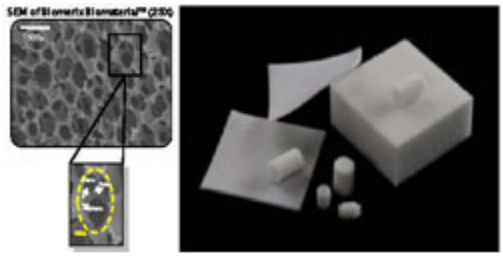

Figure 1: The Biomerix Biomaterialâ„¢ – Fully Reticulated and Crosslinked PCPU Scaffold

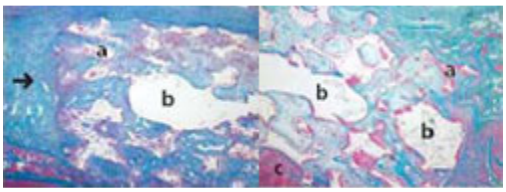

Figure 2: Rat Body Wall Repair at 2wks (left) and 4 Weeks (right) (Trichrome Stain 4X) PCPU Scaffold (a), and Polypropylene Mesh (b). Muscle fibers (c) are also seen

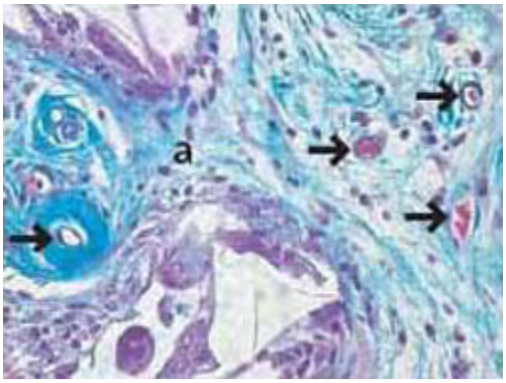

Figure 3: Rat Body Wall Repair at 8 Weeks (Trichrome Stain 4X), showing fibroblast activity, angiogenesis (black arrows-blood vessels), and multinucleate cells surrounding the white unstained regions of the PCPU Scaffold material

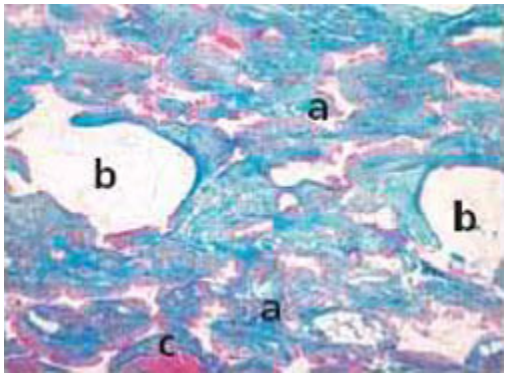

Figure 4: Rat Body Wall Repair at 26 Weeks (Trichrome Stain 4X) (a) Biomerix Biomaterialâ„¢ - PCPU scaffold, (b) Polypropylene Mesh, (c) Muscle Fibers.

References

1. Lamba N, Woodhouse K, Cooper S. Polyurethanes in Biomedical Applications, CRC Press, 1997.
2. Santerre P, Woodhouse K, Laroche G, Labow RS. Understanding the biodegradation of polyurethanes: From classical implants to tissue engineering materials, Biomaterials, 26 (2005), 7457 – 7470
3. Christenson EM, Dadsetan M, Wiggins M, Anderson JM, Hiltner A. Poly(carbonate urethane) and poly(ether urethane) biodegradation: In vivo studies, Journal of Biomedical Materials Research, 69A: 407–416, 2004

4. Friedman C, Song Y, Datta A, Lavelle L, Majmumdar R. “Biodurable Reticulated Elastomeric Matrix as Scaffolds for Tissue Engineering”. American Inst of Chemical Engineers, Nov 2008.
5. Datta A, Friedman C, Jordan MA, Gupta K, Jena A. “Novel characterization techniques for prediction of tissue in-growth in reticulated porous materials”. Soc. Of Biomaterials, May 2005.

Submitted by Implant Pathology Special Interest Group