**Polypropylene Surgical Mesh Coated with Extracellular Matrix Mitigates the Host Foreign Body Response**

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**Introduction:** Non-degradable, synthetic mesh materials, including knitted polypropylene, are routinely used for hernia repair and pelvic floor reinforcement. These mesh materials are mechanically robust and are quickly incorporated into the adjacent host tissue where they elicit a chronic pro-inflammatory response. Subsequently, dense fibrous tissue is deposited adjacent to the mesh that creates a compliance mismatch between the mesh and soft tissue; a phenomenon associated with pain and discomfort. Strategies investigated to minimize the fibrotic response include alterations in mesh composition, reduction of mesh surface area (referred to as a "light-weight" mesh), and application of bioactive coatings. Alternatively, non-synthetic surgical mesh materials composed of naturally occurring non-crosslinked extracellular matrix (ECM) do not elicit a foreign body response. In contrast, such ECM materials promote deposition of site appropriate soft tissue rather than dense fibrous tissue. However, ECM mesh materials typically lack the mechanical strength of polypropylene. Thus, development of an ECM- polypropylene hybrid could theoretically capitalize on both the mechanical properties of a polypropylene mesh and the favorable tissue remodeling properties of ECM.

**Methods:** Porcine dermal extracellular matrix was prepared via chemical decellularization with trypsin, Triton X-100, and peracetic acid. The dermal ECM was solubilized with acidic pepsin and brought to physiologic pH at 37°C to induce hydrogel formation. A 2 cm x 3 cm heavy-weight polypropylene surgical mesh, BARD™ Mesh (C.R. BARD-Davol Inc., Providence, RI), was coated with the dermal ECM hydrogel and compared to the light-weight meshes ULTRAPRO™ (Ethicon Inc., San Angelo, TX), and BARD™ Soft Mesh in a rat abdominal wall defect repair model. Scanning electron microscopy (SEM) assessed coating efficacy and mesh fiber architecture. The planar biaxial mechanical properties prior to and following implantation were determined under equibiaxial stresses up to 85 kPa (n = 8). The spatiotemporal host response was evaluated after 3, 7, 14, and 35 days of implantation (n = 4/group/time point) via quantitative histologic scoring of the inflammatory response around mesh fibers and the tissue remodeling in the areas between mesh fibers. Host response characteristics included giant cell formation, cellularity, vascularity, and connective tissue deposition. Significance was determined via one-way ANOVA and post-hoc Tukey's test ($p < 0.05$).

**Results:** The porcine dermal ECM hydrogel completely covered the polypropylene BARD™ Mesh fibers as shown macroscopically (Figure 1B) and via SEM (Figure 1D). All explanted meshes showed anisotropic mechanical behavior after 35 days, with greater strain in the longitudinal direction (Figure 1E). The strain was greatest for the light-weight ULTRAPRO™ mesh compared to the other meshes. Histologic evaluation showed that the ECM coated mesh attenuated the inflammatory response to individual mesh fibers (Figure 1F-I) with reduced giant cell formation up to 35 days compared to the uncoated mesh. The ECM coating also reduced the connective tissue density and cellularity between fibers over the time course.

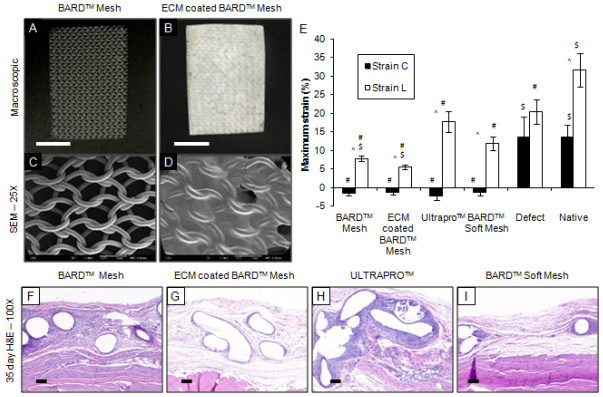


**Figure 1**. Macroscopic images (A,B, scale bar = 1 cm) and scanning electron micrographs (C,D) of uncoated and ECM coated BARD™ Mesh. The maximum equibiaxial strain (E) was found after 35 days in both the circmferential-C and longitudinal-L directions (perpendicular and parallel to the midline, respectively) for all devices, and unrepaired defect and native body wall controls. Significance is denoted with: (^) as different between circumferential and longitudinal axes, ($) as different from ULTRAPRO™, and (#) as different from the native tissue. H&E stained histologic cross sections of mesh devices after 35 days of implantation (F-G, scale bar = 100 μm).

**Conclusions:** A method to successfully coat a synthetic heavy-weight polypropylene hernia mesh with an ECM hydrogel is described. The ECM coating altered the default host response to the base polypropylene mesh by delaying and reducing the accumulation of pro-inflammatory foreign body giant cells. Though the base material was a heavy-weight mesh, after 35 days the tissue deposition was more similar to that which is typically seen with a light-weight mesh. However, the differences in remodeling of an ECM coated mesh did not translate to an altered biaxial mechanical response. An ECM coating can favorably alter short term tissue remodeling in response to an implanted polypropylene heavy-weight mesh without affecting mechanical strength. The long term response remains to be determined.