Biosynthetic Tissue Scaffold Recruits Progenitor Cells in Muscle Tissue Healing Model

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BACKGROUND

Bioabsorbable mesh, both biological and biosynthetic, are widely used in hernia repair surgeries for their ability to provide tissue reinforcement and to be later absorbed and replaced by native tissue. The clinical success of bioabsorbable mesh depends largely on their ability to facilitate the regeneration of high quality tissue. The open porosity of a bioabsorable mesh device has shown to be an important attribute in facilitating tissue generation and healing via cell movement into the device structure. Many types of cells are recruited to the site of surgical injury to facilitate tissue generation and healing. The recruitment of muscle satellite/ progenitor cells (Pax7+) to healing sites has recently been proposed as a critical event in muscle tissue regeneration because of their capability to migrate, proliferate and differentiate into muscle cells.[1,2]

This study demonstrates that the open, porous structure of the GORE® BIO-A® Tissue Reinforcement is able to recruit the Pax7+ cells residing in host muscle, a critical step in muscle regeneration.

PURPOSE

The objective of this in vivo study was to evaluate progenitor cell (Pax7+) recruitment in bioabsorbable meshes in a muscle tissue regeneration model.

METHODS

- Two bioabsorbable meshes were used: biologic mesh (collagen matrix) and biosynthetic non-woven mesh (GORE® BIO-A® Tissue Reinforcement)
- Devices were intramuscularly implanted in the hind leg biceps femoris muscle of Sprague Dawley rats.
- The test devices were retrieved at 7 and 14 days. Tissue responses to the implanted devices were characterized by standard hemotoxylin and eosin and Milligan's trichrome staining.
- The infiltrating cells that were recruited from host tissue were characterized by immunohistochemistry of Pax7, CD146 and smooth muscle actin.

RESULTS

Local Tissue Responses

Compared to biosynthetic mesh, collagen matrix had greater inflammatory responses at both 7 and 14 days, which were characterized by extensive inflammatory encapsulation (Figure 1A & 1C). The biosynthetic mesh had minimal inflammatory response at the interface, and the infiltration of host cells within the biosynthetic mesh was greater than collagen matrix and increased over time (Figure 1B & 1D).

Blood Vessel Formation

At both 7 and 14 days, more blood vessels were found in biosynthetic mesh comparing to collagen matrix (Fig. 2).

Pax7+ Cell Recruitment

At 7 days, Pax7 positive cells were not observed in or around any of the 4 implanted collagen matrices, but were found in 2 of 4 biosynthetic meshes at the material/tissue interfaces. At 14 days (Fig. 3), Pax7 positive cells were present at 2 of 4 collagen matrix devices, however those cells were separated from the device by a thick layer of inflammatory cells. Interestingly, Pax7 positive cells were found to infiltrate 3 of 4 biosynthetic meshes at 14 days.

Histological evaluation of local tissue responses and angiogenesis

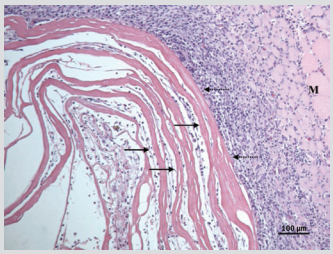

Figure 1A. Collagen Matrix Day 7 - The device (solid arrows) is delaminated. Within the device an inflammatory infiltrate is evident. The interface (dashed arrows) demonstrates extensive histiocytic and lymphocytic infiltrate. Some normal muscle (M) is present separated from the device by inflammatory cells.*

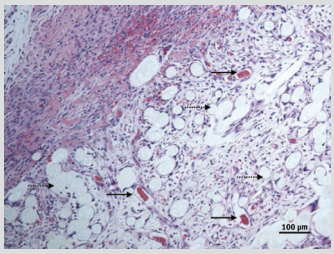

Figure 1B. GORE® BIO-A® Tissue Reinforcement Day 7 - Numerous large and small blood vessels (solid arrows) are present within the device. The device fibers (dashed arrows) are surrounded by granulation tissue. The interface is composed predominantly of granulation tissue.*

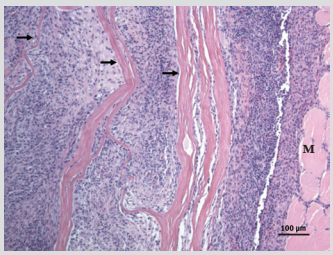

Figure 1C. Collagen Matrix Day 14 - The device (arrows) is delaminated. Within the device a persistent inflammatory infiltrate is evident. The interface demonstrates extensive histiocytic and lymphocytic infiltrate with occasional neutrophils. Normal muscle tissue (M) is present separated from the device by inflammatory cells.*

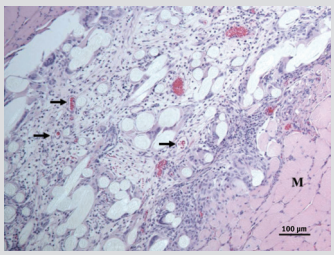

Figure 1D. GORE® BIO-A® Tissue Reinforcement Day 14 - Numerous large and small blood vessels (arrows) are present within the device. By this time, much of the device is infiltrated with cellular components and collagen deposition. There is minimal interface inflammation.*

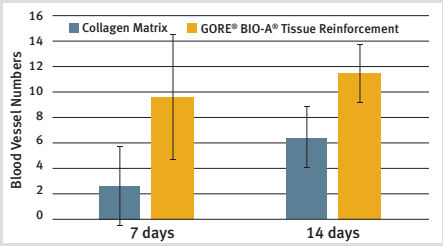

Figure 2. Blood Vessel Formation at 7 and 14 days

Immunohistochemistry evaluation of Pax7+ cell recruitment

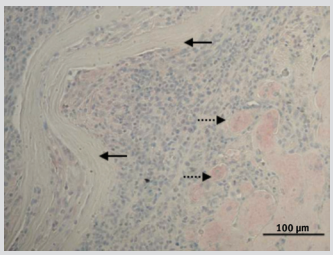

Figure 3A. Collagen Matrix Day 14 - Persistent inflammation covers the device (solid arrows). A few positively stained cells (dashed arrows) are present at the interface.*

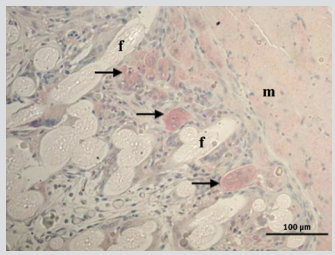

Figure. 3B. GORE® BIO-A® Tissue Reinforcement Day 14 - The arrows indicate positively stained cells within the device (f). Native muscle cells (m) appear unremarkable.*

CONCLUSIONS

We demonstrated that open, porous bioabsorbable meshes can recruit Pax7+ progenitor cells from host tissue for muscle healing. While progenitor cells were only present in the surrounding tissue of collagen matrix, they were recruited and able to fully infiltrate the implanted biosynthetic mesh.

* Data on File – Internal Study

[1] Péault B, Rudnicki M, Torrente Y, *et al.* Stem and progenitor cells in skeletal muscle development, maintenance, and therapy. *Molecular Therapy* 2007;15(5):867-877.

[2] Sambasivan R, Yao R, Kissenpfennig A, *et al.* Pax7-expressing satellite cells are indispensable for adult skeletal muscle regeneration. *Development* 2011;138(17):3647-3656.