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ACUTE HOST RESPONSE AGAINST A NOVEL TISSUE ENGINEERED REPAIR MATERIAL FOR THE SURGICAL MANAGMENT OF STRESS URINARY INCONTINENCE AND PELVIC ORGAN PROLAPSE

Hypothesis / aims of study

Stress urinary incontinence (SUI) and pelvic organ prolapse (POP) are treated using a variety of materials to bolster and support surgical repairs. Synthetic non absorbable materials produce a vigorous inflammatory response followed by dense fibrosis, but the downside is the long term risk of erosion and pain associated with the non-absorbable material (1). Fast degradation of absorbable biological and synthetic alternatives will, on the other hand, lead to deterioration of biomechanical strength of such and consequent early failure (2). We have developed, *in vitro*, a novel tissue engineered material using a combination of adipose-derived stem cells (ADSC) and biodegradable poly-(L)-lactic acid (PLA) scaffolds (3). In this study we assess the acute host response to this material with the aim of evaluating the *in vivo* potential of a complication free long term repair of SUI and POP.

Study design, materials and methods

ADSC were isolated from human subcutaneous fat obtained with informed consent and ethical approval, using mechanical and enzymatic procedures. ADSC were characterized by fluorescence-activated cell sorting and differentiation assays. Thermoannealed PLA (Th PLA) scaffolds were constructed using electrospinning in a clean room. Following this, 200.000 cells were seeded and then cultured for 2 weeks on Th PLA scaffolds of 1 cm^2 size. Scaffolds with and without human ADSC were implanted, subcutaneously, on the abdominal wall of female rats (Sprague Dawley). After 3 and 7 days, 6 animals from each group were sacrificed. Sections from each sample were analyzed by Hematoxylin and Eosin staining, Sirius red staining and immunohistochemistry for macrophages, lymphocytes, collagen I and III.

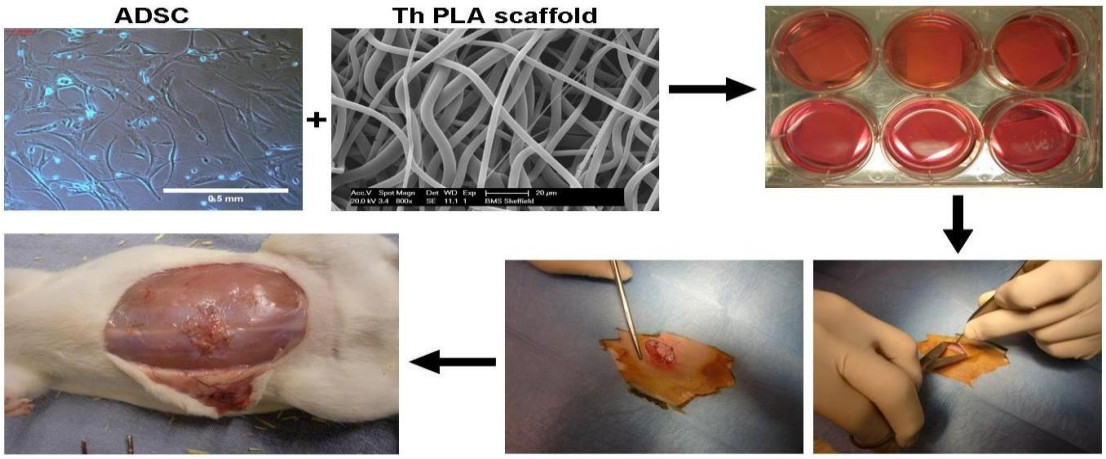

Figure 1. Info-graphics of materials and methods.

Results

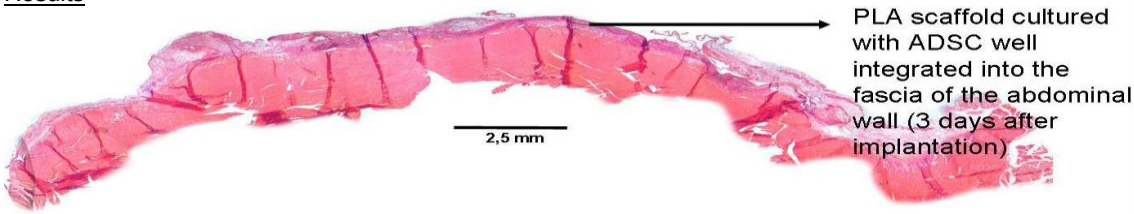

Figure 2. Panoramic image of a full cross section stained by H&E of the abdominal wall of a rat 3 days after tissue engineered implantation.

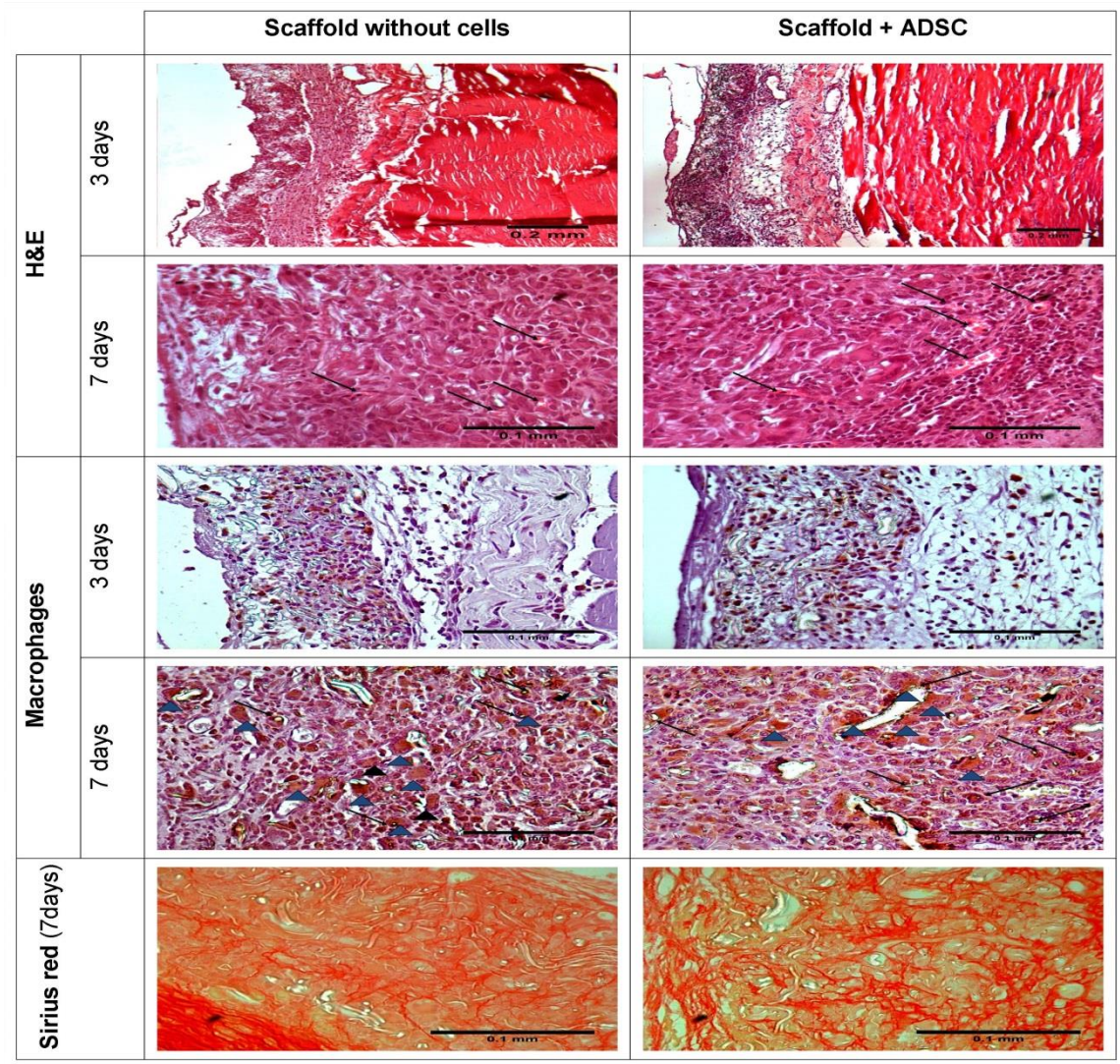

Figure 3. *In vivo* response to scaffolds implanted in rats both without cells and with ADSC (previously cultured for 2 weeks). H&E staining of histology sections is shown at 3 days and 7 days (first 4 panels); arrows indicate the presence of blood vessels at 7 days. Next 4 panels indicate the presence of macrophages stained by immunohistochemistry (here stained brown); arrows indicate macrophages surrounding PLA fibres and triangles indicate foreign giant cells. The final 9th and 10th panels show Sirius Red staining of total collagen at day 7.

Interpretation of results

In vivo studies have demonstrated good integration of our tissue engineered material composed of ADSC cultured with Th PLA scaffolds into native tissue. An acute macrophage response was evident specifically against the synthetic material. There was extensive host cell penetration and new collagen ingrowth, without evidence of encapsulation, throughout the full thickness of the scaffold after 7 days of implantation.

Concluding message

We have developed a novel tissue engineered to treat SUI and POP, which has *in vivo* potential to be integrated into host tissues with host cell infiltration being at same time, encouraging to avoid risk of infection. In addition, after an acute inflammatory response, new collagen ingrowth is developed being crucial for a long term retention. Future experiments will assess the outcome of longer term implantation of this material looking at the chronic immune response and the degradation rate and the biomechanical properties of the material post-explantation.

References

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3. (3) Roman Regueros S, Mangera A, Osman NI, Bullock AJ, Chapple CR, MacNeil S. Developing an autologous engineered connective tissue using a biodegradable scaffold for the treatment of stress urinary incontinence and pelvic organ prolapse. 42nd Annual Meeting of the International Continence Society (ICS), 15 – 19 October 2012, Beijing, China.

Disclosures

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