Nano-Dimensional Bladder Tissue Replacement Constructs: An In Vivo Study

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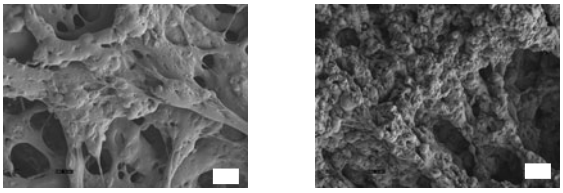
INTRODUCTION

Approximately 400 million people are affected by bladder disease; one of the most common forms is urinary bladder cancer[1-2]. Superficial cases of bladder cancer are often treated by removal of the cancerous portion of the bladder wall combined with adjuvant intravesical immuno-chemotherapy[2]. This therapy is limited because of local and systemic toxicity of the chemotherapy agents and the high possibility of recurrence and progression of the disease. Therefore, removal of the entire bladder wall is considered to be the most effective approach to stop the progression of this disease and to reduce mortality. In order to restore bladder functionality, this diagnosis and treatment brings an obvious need for bladder replacement implant designs with a high degree of efficacy. Since cells are accustomed to interacting with nanometer surfaces (i.e., like those present in native proteins), the present study hypothesized that bladder tissue should be more readily regenerated on and in nano-structured polymers.

MATERIALS AND METHODS

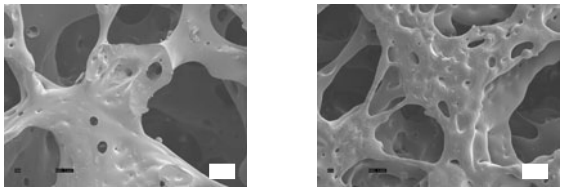
Tissue Engineering Scaffolds

Three-dimensional, biodegradable, porous poly-lactic-co-glycolic (PLGA) and polyurethane (PU) scaffolds were prepared according to methods well-established by the tissue engineering community[3]; when not further chemically treated, these scaffolds possessed conventional (micron-sized) surface features. Subsequently treating these conventional PLGA ands PU scaffolds for various periods of time and with various concentrations of NaOH or HNO_3, respectively, created nanometer surface roughness values. Surface properties of the PLGA and PU scaffolds were confirmed using SEM (to visualize scaffold properties; Figures 1 and 2).



(a) Untreated PLGA (b) Nanostructured PLGA

Figure 1: Untreated and Nanostructured (or treated) PLGA. Scale bar = 1 micron.



(a) Untreated PU (b) Nanostructured PU

Figure 2: Untreated and Nanostructured (or treated) PU. Scale bar = 1 micron.

In Vivo Experiments

Initial animal experiments utilized rats to study the feasibility and time course of nano-structured PLGA and PU patch incorporation into the bladder wall. Rats were augmented with a 1cm x 1cm patch of the respective biomaterial. The animals were then followed for evidence of anastomotic leak. Two control animals that underwent sham operations (midline laparotomy and closure) were used. In addition, a control material previously studied (AlloDerm) was included. The animals were sacrificed at 1, 3, 6 and 9 months. At this time, the bladder was tested for capacity and the patch tested for burst pressure. The tissue was also harvested and examined for urothelial and muscular ingrowth as well as neovascularization.

RESULTS AND DISCUSSION

The present study successfully created three-dimensional PLGA and PU scaffolds having nano-structured surface topographies and interconnected pores (as confirmed by SEM analysis). In vitro cellular experiments on these novel nano-dimensional polymeric scaffolds provided evidence that bladder smooth muscle cell attachment, growth, and elastin / collagen production (critical proteins indicative of bladder tissue regeneration) were increased as surface feature dimensions were reduced into the nanometer regime[4]. This finding makes sense since cells in the body are used to interacting with nano-dimensional proteins. In vivo results will also be discussed. Proof of material usefulness and technique would provide urologists with a readily accessible graft for a variety of bladder replacement applications.

ACKNOWLEDGEMENTS

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