Bioresponse of a Cell/Alginate Hydrogel Composite in Mammalian Kidney

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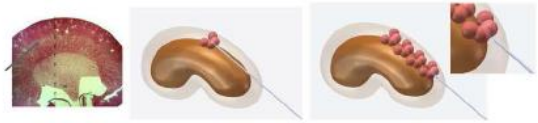
Introduction

Chronic Kidney Disease (CKD) results in a progression of decreased kidney function over time. There is a need to develop treatment that will reduce the need for dialysis or organ transplants. Regenerative medicine/tissue engineering is an alternative to address this need. Biomaterials are used in tissue engineering to support the biological and mechanical needs of the regenerating tissue. Previous work in our lab evaluated *in vivo* responses to biomaterial candidates combined with therapeutically relevant renal cell populations to form cell/biomaterial composites[1]. This study describes the evaluation of a low viscosity alginate hydrogel to support cell delivery for induction of a regenerative response in the kidney.

Materials and Methods:

Selected renal cell populations (SRC) used for *in vitro* assays and to produce NKA constructs (cells in alginate gel) were isolated from rodent kidneys[2-4]. Cell phenotype of the NKA constructs was evaluated *in vitro* by Live/Dead staining. A 1% low viscosity, ultrapure, sodium alginate in PBS was formulated with 2.5 x 10^6 cells and cross-linked with 4% $CaSO_4$ to form a gel. To evaluate the *in vivo* response to NKA construct implantation, 35 µl of the NKA construct was microinjected into the proximal and distal poles of the kidney parenchyma of healthy 3-month old female Lewis rats (Figure 1). Fixed kidney sections prepared at 1 and 4 weeks post-injection were evaluated for inflammation, fibrosis, foreign body reaction, neo-vascularization, biomaterials degradation, necrosis, and tissue infiltration.

Figure 1: NKA product delivery into the kidney cortex



Results

SRC in NKA constructs showed acceptable cell viability (Figure 2). Trichrome, Hemotoxylin and Eosin (H&E) staining of tissues harvested at 1 and 4 weeks post-injection showed that at 1 week post-injection, there was mild-moderate tissue/cellular in-growth and neo-vascularization. In addition, the alginate was present as an amorphous aggregate as shown in Figure 3 (representative boxed areas showing moderate chronic inflammation (macrophages and lymphocytes)). Degradation of the biomaterial was considered mild to moderate. By 4 weeks post-injection, the degradation of the alginate was considered moderate to marked and there was markedly dilated collecting ducts containing the biomaterial (Figure 4 - collecting ducts are highlighted by dashed circle and biomaterial indicated with an asterix). There was moderate tissue/cellular in-growth and neo-vascularization with mild chronic inflammation and occasional giant cells. There was also multifocal tubular regeneration at the injection sites indicated by double bracket as shown in Figure 4.

Figure 2: Live/Dead staining of cells in partially dissolved alginate gel

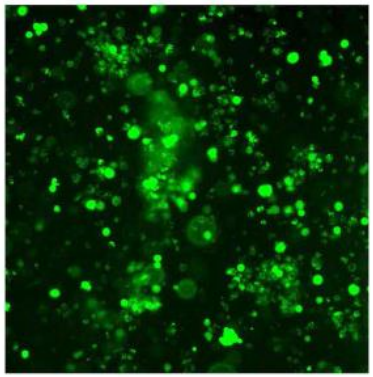


Figure 3: NKA Construct 1 week post-implantation

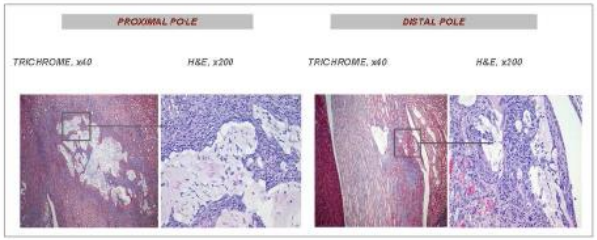
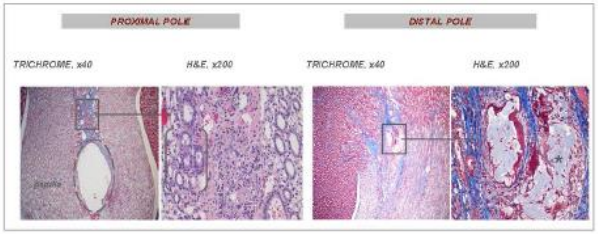


Figure 4: NKA construct 4 weeks post-implantation



Discussions and Conclusions

By 4 weeks post-implantation, preliminary evidence showed the cells in alginate gel to produce moderate tissue/cellular in-growth with mild inflammation. This study showed an encouraging *in vivo* response of healthy kidney tissue to the injection of an alginate and SRC composite. These results highlight the potential of the alginate/SRC composite to impact CKD and suggest further investigation of its effect in established animal models of chronic renal disease.

References

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