Capturing tissue microenvironment on a click-chemistry based biodegradable polymer membrane

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Statement of Purpose: Tissue engineering is an emerging field that combining material science and cell biology with the purpose of modulating tissue regeneration. Our overarching objective is to recuperate the tissue formation process by integrating cells into biodegradable scaffold that mimics the native tissue microenvironment(TME). To study how the interaction between cell and TME regulate behaviors of cells, our previous research[1] has developed an experimental model through a technique of bioimprinting by using a non-degradable material Polydimethylsiloxane(PDMS). However, due to the lack of hydrophilicity and manipulativeness of this material, these intrinsic problems hindered the translation of the finding to clinical use. In this study, we explored the use of a recently developed click-chemistry based biodegradable polymer poly(1,8-octanediol citrate)[2] in bioimprinting. Here, we tested the mechanical properties of this material and its suitability of replicating tendon microenvironment.

Methods: Membrane made of click-chemistry modified degradable polymer poly(1,8-octanediol citrate) was fabricated through the established technique[1] in which it is able to replicate the surface pattern and mechanical property of tissue (i.e. longitudinal alignment of bovine tendon fibers in this case). Biochemical component was incorporated onto the polymer to serve as the extracellular matrix(ECM) in the TME we established. The surface topography of the membrane was characterized through SEM and AFM respectively. Mysenchymal stem cell(MSC) was cultured on the polymer membrane and tendon section respectively to investigate the similarity of these two TME in regulating the cell behavior.

Results: Figure 1 illustrates the use of our click-chemistry modified poly(1,8-octanediol citrate) with replicated surface topography from bovine tendon through bioimprinting. The SEM image(Fig 1**B**) indicates that, through our bioimprinting technique, the overall topographical information of closely packed collagen fibrils in bovine tendon section was successfully replicated into the polymer membrane. AFM results in Figure 2 and 3 further demonstrate that the topography of the polymer membrane after bioimprinting is similar to the submicron details of the original tendon section template. These results demonstrate that we can successfully fabricate the polymer membrane which accurately duplicate the surface topography and physical dimension of the tendon section at sub-micron levels. Figure 4 illustrates the TME we established on the polymer membrane(Fig 4**B**) can effectively induce the elongation, alignment and tenogenic behavior of MSC cultured on it similar to the MSC cultured on the bovine tendon section(Fig 4**A**).

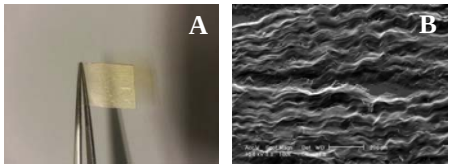

Figure 1 Normal size of click-chemistry modified poly (1,8-octanediol citrate) membrane with replicated surface topography of tendon section(**A**) and SEM image(**B**).

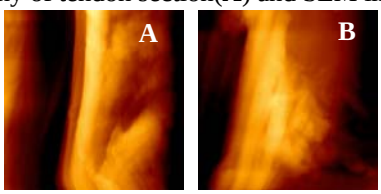

Figure 2 Surface topography of tendon section(**A**) and click-chemistry modified poly(1,8-octanediolcitrate) membrane(**B**) as measured by AFM.

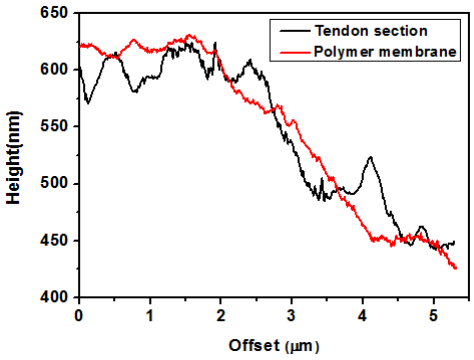

Figure 3 Relative height of tendon section and click-chemistry modified poly(1,8-octanediolcitrate) membrane as measured by AFM.

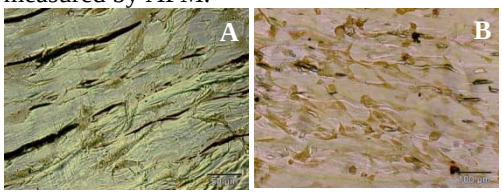

Figure 4 Tenomodulin expression of MSC in tendon section(**A**) and click-chemistry modified poly(1,8-octanediolcitrate) membrane(**B**).

Conclusions: In summary, we have proved that the biodegradable polymer used in our study can faithfully replicate topographical and physical information from the bovine tendon section. The MSC behavior on the TME we established through bioimprinting on the polymer is similar as the cell cultured on the tendon section. This combined results may increase the feasibility of our further in vivo study.

References:

[1] Tong WY. Biomaterials.2012;33:7686-7698
[2] Guo JS. Adv. Mater. 2014;26:1906-1911