Surface stiffness modification by e-beam irradiation for stem cell growth control

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In tissue engineering, there is a need for highly selective and efficient methods for stem cell growth control to produce large populations of particular cell types. It has been observed that multi-potent stem cells might be driven in their differentiation by their tight or loose attachment depending upon the stiffness of the substrate. This discovery has evoked great attentions for looking for a method to achieve large range of stiffness on surface for stem cell growth with controllable manor. Although a variety of methods have been applied such as niche engineering, cell cycle regulation, direct cell contact and physic-chemical environmental signal manipulation, efficient control of stem cell growth is still far away from needed.

In this paper, we report, for the first time, a novel method of effectively modifying substrate stiffness while maintaining low surface roughness by electron beam irradiation in hydrogen silsesquioxane (HSQ) film. When HSQ is bombarded by e-beam, it is cured by forming a network and its stiffness is gradually built up. In our work, a fine electron beam of 100kV, generated by VB6 HR supplied by Vistec is used to produce a 10 by 10 matrix of squares in HSQ polymer with dosages ranging from 7.1 $\mu C/cm^2$ to 5000 $\mu C/cm^2$. Both Young's modulus for material stiffness and surface root-mean-square roughness are measured by a Veeco D-3000 AFM. Figure 1 shows that this technique is capable of achieving wide range material stiffness while still maintaining low and constant surface roughness on HSQ. On the created matrix with large range of stiffness, human mesenchymal stem cells are cultured on HSQ substrate coated with plasma polymerized allylamine and the result shows that stem cell fate is successfully controlled to grow into different cell types (figure 4).

In conclusion, we have successfully developed a reliable method to effectively control the stiffness of surface for differentiating stem cell growth. This technique has a number of advantages. It can precisely control the stiffness of HSQ surface. The e-beam direct write is able to generate elements with desired geometric shapes and size, offering a unique opportunity for further studying stem cell growth property. Moreover, it has great potential in bio-engineering for its high compatibility with organic materials.

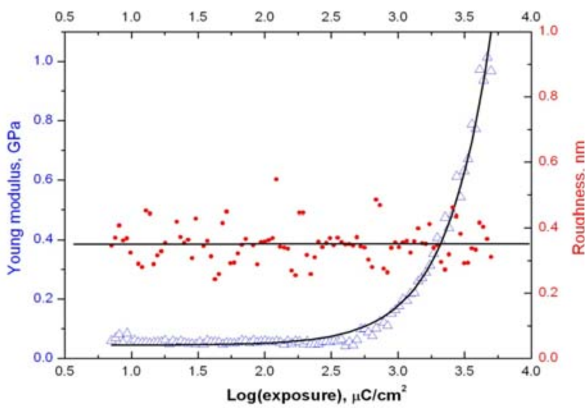

Figure 1. Young modulus and Root-mean-square roughness of the HSQ matrix as a function of electron beam exposure obtained by a Veeco D-3000 AFM.

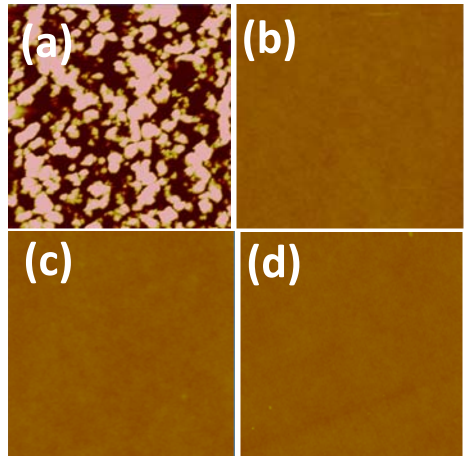

Figure 2. AFM images of 5 μm^2 of HSQ substrate after e-beam exposure at a lower dosage of 20 $\mu C/cm^2$ (a, c) and higher dosage of 2000 $\mu C/cm^2$ (b) and 5000 $\mu C/cm^2$ (d). The surface demonstrates roughness change between samples with development process (a, b) and without development (c, d)

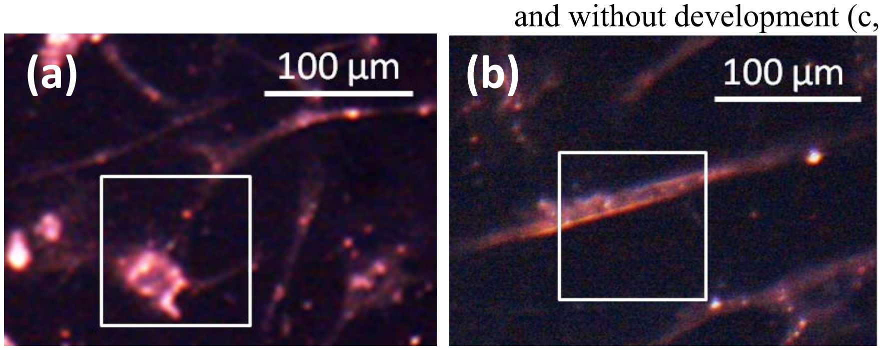

Figure 3. Human mesenchymal stem cells cultured on HSQ substrate coated with plasma polymerized allylamine with e-beam exposure dose at (a) 20.4 $\mu C/cm^2$ and (b) 1973$\mu C/cm^2$.