Endothelial Cell Response to Artificial Extracellular Matrix Proteins

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Introduction

Endothelialization has been shown to reduce the high rates of vascular graft failure due to thrombosis and intimal hyperplasia.[1] Consequently, various coatings, including fibronectin, collagen, and peptides, have been used to promote the retention of endothelial cells on synthetic grafts.[2] Our laboratory has developed a family of materials that mimic the properties of extracellular matrix (ECM) proteins. These artificial ECM proteins are comprised of elastin-based repeats (VPGIG) to confer the needed mechanical properties and a cell-binding domain to support the growth of an endothelial monolayer. It has been demonstrated that by varying the extent of crosslinking within a free-standing artificial ECM film, it is possible to tune the modulus within the range characteristic of elastins (0.3-0.6 MPa).[3] This study focuses on the endothelial response to proteins containing the RGD and CS5 sequences derived from fibronectin.

Results and Discussion

Using peptide inhibition studies and sequence-scrambled negative controls, we have shown that human umbilical vein endothelial cells (HUVECs) adhere specifically to the cell-binding sequences in the artificial ECM proteins. Furthermore, the identity of the cell-binding domain has a significant effect on the cellular response. When subjected to a normal detachment force, more cells remain adherent to proteins containing the RGD sequence than to those containing the CS5 sequence (see Figure 1). The RGD cell-binding sequence also elicited rapid cell spreading whereas the CS5 cell-binding sequence did not encourage robust spreading at short times. These results indicate that cell-binding domain choice can be used to alter the cell response to artificial ECM proteins. Further studies are being done to assess the effect of an RGD synergy domain (PHSRN) and the effect of cell-binding sequence on cell migration rates.

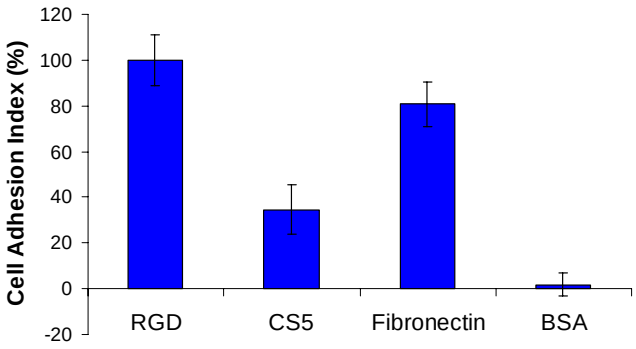

Figure 1. HUVEC resistance to detachment forces. Cells were incubated on fibronectin, BSA, and artificial ECM proteins containing the RGD and CS5 sequences for 30 minutes. The cells were then subjected to a normal detachment force of 780 pN.

References

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[3]Di Zio K.; Tirrell, D.A. *Macromolecules* **2003**, *36*, 1553-1558.