

Endothelial Cell-Cell Cohesion

Background

Prosthetic bypass grafts placed in circulation in human beings, unlike in animals and primates, do not attach endothelial cells to heal the graft. Endothelial cells produce factors that inhibit blood clotting and the lack of endothelial healing could be problematic for successful engraftment. Attempts to populate grafts prior to transplantation have been unsuccessful. Furthermore, human endothelial cells derived from arteries are more prone to shear induced detachment. Previous studies at UMDNJ have revealed that a family of proteins known as cadherins is reduced in human endothelial cells when compared with bovine cells. Cadherins are glycosylated transmembrane polypeptides responsible for cell-cell interactions. Some examples include Ncadherins, E-cadherins, P-cadherins and VE-cadherins. Thus, restoring the function of human vascular endothelial cells by modulating the levels of these factors on the surface of vascular endothelial cells could greatly improve the cell-cell cohesion thereby facilitating the endothelial cells to populate the grafts.

The present invention discloses methods for coating graft surfaces with cells or inducing cells to populate implanted devices or grafts.

Description of the Technology

Based on the hypothesis that endothelial cell-cell cohesion is significantly reduced in human endothelial cells, UMDNJ researchers measured the cohesive binding energies of human and bovine aortic endothelial cells by tissue surface tensiometry. The human aortic endothelial cells cohered too weakly compared to smooth muscle cells of both species. An aggregation assay whereby the formation of cellular aggregates over time was measured for bovine aortic, human aortic and umbilical vein endothelial cells revealed reduced aggregation for human aortic endothelial cells. Taken together, the results of these two studies reveal that human aortic endothelial cells and bovine aortic endothelial cells differ substantially in cohesivity. Next, the cause for the reduced cohesivity of human endothelial aortic cells was evaluated by examining the levels of cadherins in bovine and human aortic, and human umbilical vein endothelial cells. Both bovine aortic and human umbilical vein endothelial cells expressed similar levels of cadherin while human aortic endothelial cells expressed significantly less. Other components of adherins such as catenins were also examined to evaluate the cause of decreased cohesivity. These studies reveal that the failure of human aortic endothelial cells to endothelialize grafts is largely due to the downregulation of cadherin expression, and thus, restoration of its expression levels could restore the migration, and consequently, cell-cell adhesion of endothelial cells.

Advantages

- Broadly applicable to any cell such as epithelial, endothelial, muscle, fibroblasts or nerve cells.

Applications

- To populate grafts, stents, catheters, pumps, or artificial organs with cells to increase the success of transplantation

File RWJ 00-18/Nackman

Patent Status

- . •United States patent application filed
- . •Application published on 06/12/2003 (Publication No.: US-2003-0108529-A1)

Licensing Opportunity

- This technology is available for exclusive license.

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