Human endothelial cell growth and gene expression on three dimensional poly(lactic acid-*co*-glycolic acid) sintered microsphere scaffolds for bone tissue engineering

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Abstract

Bone tissue engineering offers promising alternatives to repair and restore orthopaedic disorders. Our laboratory has employed poly(lactic acid-co-glycolic acid) (PLAGA) microspheres to develop a three dimensional (3-D) porous bioresorbable scaffold with a pore structure similar to the structure of human trabecular bone. The success of osseous healing and integration of the engineered implants with the surrounding host tissue depends on the feasibility of new blood vessel formation within the porous structure. Since endothelial cells play a key role in angiogenesis (formation of new blood vessels from preexisting vasculature), we examined human endothelial cell attachment, viability, growth and phenotypic expression on sintered PLAGA microsphere scaffolds. In addition, we investigated the effects of scaffold pore size on the proliferation and gene expression of the endothelial cells by varying microsphere diameter. Scanning electron microscopy (SEM) images of cells cultured on the scaffolds demonstrated the ability of the scaffolds to support cellular attachment as cells covered the surface of microspheres and bridged the pores. Cell proliferation studies up to 21 days indicated that cell number increased during early stages and reached a plateau between days 10-14. Immunofluorescent staining for actin showed that cells were proliferating three-dimensionally through the scaffolds and staining for platelet endothelial cell adhesion molecule-1 (PECAM-1) displayed typical localization at cell-cell contacts. Finally, gene expression analysis showed that endothelial cells grown on PLAGA scaffolds maintained their normal characteristic phenotype. Nevertheless, the comparison between scaffolds fabricated with different microsphere diameter ranges showed that the changes in pore architecture do not yield significantly different endothelial cell growth behavior. This allows for scaffold pore diameter variation with no effect on cell function and proliferation. These results demonstrate that PLAGA sintered microsphere scaffolds can support the growth and biological functions of human endothelial cells and is not limited by scaffold pore architecture. The insights from this study will aid in future studies to direct and enhance the blood vessel formation into 3-D tissue engineered scaffolds.

Key words: Tissue Engineering; Endothelial cell; Poly(lactic acid-co-glycolic acid); Bone; Scaffold