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Abstract

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Grant Number:	1R01GM060692-01
PI Name:	CHEN, CHRISTOPHER S.
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PI Title:	ASSISTANT PROFESSOR
Project Title:	REGULATION OF ANGIOGENESIS BY MICROENVIRONMENTAL CUES

Abstract: DESCRIPTION: (Description adapted from applicant's abstract): While current understanding of growth factor biology has been incorporated into the design of tissue-engineered products, little is known about how the architecture and composition of the adhesive matrix regulates angiogenesis. It is proposed that changes in cell shape, as governed by the architecture of the extracellular matrix (ECM), act as a distinct signal to regulate capillary endothelial cell proliferation, apoptosis and differentiation in angiogenesis. To test this hypothesis, we will probe how cells respond to changes in cell shape and structure as controlled by the geometry of microfabricated islands of ECM. Preliminary findings suggest that the degree of cell spreading regulates a switch between cell proliferation and apoptosis. In Specific Aim 1, geometric parameters controlling this switch will be identified by using multiple series of geometric islands to specifically vary projected cell area, perimeter, length, aspect ratio, cell height, membrane surface area or volume. The P.I. will determine whether an island size exists where cells neither grow nor die, and therefore can be effectively maintained for long periods in vitro without passage to a new substrate. In Aim 2, he will explore the ability of integrins and growth factors to modulate the degree to which changes in cell shape regulate cell proliferation and apoptosis. In Aim 3, he will determine the geometric requirements for ECM-induced capillary differentiation and tube formation. In this manner, he will seek to determine the ability of matrix architecture to regulate capillary cell behavior and, thus, provide a rational basis for the design of the engineered matrices to promote tissue vascularization.

Thesaurus Terms:
angiogenesis, capillary, cell growth regulation, cell proliferation, extracellular matrix, programmed cell death, vascular endothelium
cell differentiation, epidermal growth factor, fibroblast growth factor, integrin, vascular endothelial growth factor
immunocytochemistry, tissue /cell culture, western blotting

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