594e Biodegradable Covalently-Linked Laminin Peptide Gradients for Promotion and Assay of Cell Migration

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The migration of cells that are involved in the early (inflammation) stage of wound healing, such as neutrophils, macrophages, and T lymphocytes has been extensively studied. However, the migration of slower migrating cells, such as fibroblasts and endothelial cells, which are involved in the later stages (proliferation and remodeling) of wound healing, is more difficult to study. Techniques such as Boyden chamber assays, in which the cells are allowed to migrate across a membrane or filter may be good models for processes such as metastasis or extravasation, but may not be relevant models for connective tissue cells migrating across a wound. Cells migrate to a wound in response to concentration gradients of soluble chemotactic factors by a process known as chemotaxis. Because these gradients are inherently unstable, it is difficult to use them to study the migration of slower moving endothelial cells and fibroblasts. Endothelial cells and fibroblasts can also respond to bound (rather than soluble) peptide gradients in a process known as haptotaxis. This process may be exploited in novel tissue engineering scaffolds to recruit cells to a wound site and promote the migration of cells into a tissue engineering construct. A technique for preparing surfaces and three-dimensional scaffolds with covalently bound peptide gradients is presented. Six peptides from the alpha and beta chains of Laminin-1, a basement membrane protein, that are known to promote adhesion or migration of endothelial cells or fibroblasts are used to develop surfaces, based on poly(L-lysine) and chitosan, and three-dimensional scaffolds, based on chitosan and fibrin, with covalent peptide gradients. Time-lapse video microscopy of cell culture is used to monitor the behavior of cells with respect to the gradients. This approach offers a new technique for screening the haptotactic potential of peptides. It also permits the study of haptotaxis for slowly migrating cells that are difficult to characterize by other techniques. Finally, these materials are readily adaptable to clinical applications of tissue engineering as they do not contain unstable gradients and are based on materials with well-established biocompatibility for a variety of in vivo applications.