Polymer Systems Tuned to Endothelial Progenitor Cell Adhesion

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Statement of Purpose: The function of many blood contacting biomedical devices is compromised by thrombus development at the biomaterial/blood interface. No surface except a healthy endothelium is fully blood compatible. However, a confluent and functioning endothelial cell layer on a biomaterial surface has not yet been successfully achieved in humans. In this research we attempt to design a surface tuned to the selective adhesion of endothelial progenitor cells (EPCs) in hopes that when such a surface is exposed to blood it will scavenge circulating EPCs and the adult stem cells will spread, divide, differentiate, and eventually lead to a confluent and functioning endothelial cell layer.

Methods: The polymer system used in this research is a random acrylic terpolymer polymerized from hexyl methacrylate (HMA), methyl methacrylate (MMA), and methacrylic acid (MAA). Acrylic polymers were chosen for their cost effectiveness, ease of synthesis, and proven biocompatibility. By controlling the molar ratio of HMA, MMA, and MAA we can tailor the physical properties of the polymer to a specific application. Selective adhesion of the EPCs is achieved through the covalent incorporation of EPC specific ligands. These ligands were determined by screening a phage library (~2 billion dodecapeptide clones). The library was prescreened against other common blood cell types to ensure specific EPC adhesion, and the binding study was repeated twice starting with the tightest binders to ensure identification of high affinity ligands. The ligands were covalently immobilized to the biomaterial through chain transfer chemistry: a novel approach for biofunctionalization. To maximize the cellular response the polymer material was electrospun into a fibrous structure with high porosity. The EPCs used in this study are obtained by density centrifugation from human whole blood.

Results/Discussion: The first step in this research was a study of EPC adhesion to unfunctionalized polymer surfaces (solution cast, random electrospun mats, and aligned electrospun mats). The results from this study are shown in Figure 1 and serve as baseline data to which we can compare EPC adhesion to the ligand-derivitized material.

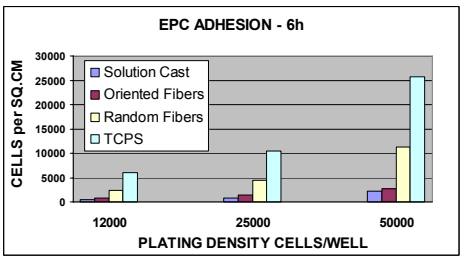

Figure 1: EPC Adhesion to Unfuctionalized Surfaces

From the phage display study, three ligands were chosen for further exploration (one is a negative control). The twelve peptide sequence found through the phage display experiment was terminated by a GGGSC spacer group whereby the cysteine residue, containing a mercaptan functional group, enables the novel incorporation method. All three of the EPC ligands have been successfully immobilized to the polymer material, and each of the biofunctional polymers has been successfully electrospun. An electron micrograph of electrospun functionalized polymer is shown below in Figure 2. Data on the EPC adhesion and proliferation on ligand containing films and electrospun surfaces will be presented.

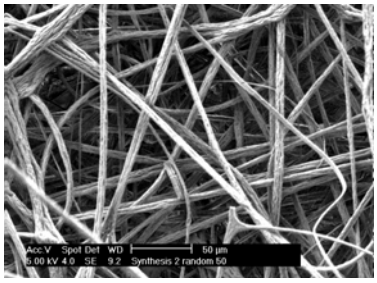

Figure 2: Electrospun biofunctional polymer

Conclusions: As seen in Figure 1, the unfunctionalized terpolymer material does not adhere EPCs as well as TCPS. One of the goals of this research is to create a surface which is (1) selective to EPC adhesion, and (2) better at EPC adhesion than TCPS. In this research we have discovered novel ligands for the specific adhesion of EPCs and successfully immobilized them to a synthetic polymer which can be electrospun into a highly porous matrix.

References:

Fussell, GW, et al, Biomaterials. 2004; 25: 2971 – 2978.

Veleva, AN, et al, JBMR. 2005; 74A: 117 – 123.