Comparison of poly(ethylene glycol) and sulfobetaine chemical moieties for the suppression of biomaterial fouling

Daniel E. Heath[1], Stuart L. Cooper[1].
[1] Department of Chemical and Biomolecular Engineering, Ohio State University, Columbus, OH, 43210, USA,

Statement of Purpose: A promising technique for improving the biocompatibility of medical implants it through the incorporation of bioactive peptide sequences (ligands) to promote specific interactions between a desired cell population and the material surface. For instance, numerous researchers have incorporated the RGD tri-peptide unit into biomaterials which has resulted in up regulated cellular attachment, growth, and more natural cellular morphology of the target cell population. However, the bioactivity of these ligands can be masked through the adsorption of proteins and the attachment of undesired cell types. To prevent these non-specific interactions with the biological environment non-fouling chemical moieties have been developed. In this research we compare the efficacy of two powerful non-fouling chemical motifs.

Methods: In previous work, we have developed a biostable methacrylic terpolymer copolymerized from hexyl-methacrylate (HMA), methyl methacrylate (MMA), and methacrylic acid (MAA). The physical properties of the biomaterial system can be tailored by controlling the molar ratio of HMA to MMA incorporated into the polymer backbone. MAA was incorporated in small quantities (2 mole %) to allow post synthesis derivatizations. The biological properties of the polymer system were modified through the incorporation of topography using electrospinning and the covalent attachment of cell specific ligands. In this presentation we describe the incorporation non-fouling character into the polymer through copolymerization of methacrylate monomers which possess hydrophilic and electrically neutral pendant groups: poly(ethylene glycol) (PEGMA) and sulfobetaine (SBMA).

Results: Materials polymerized from 0 – 30 mol% of the PEGMA or the SBMA were prepared and characterized through ^{1}HNMR, GPC, water absorption studies, and static contact angle analysis. The polymer-biological interactions were probed through protein adsorption studies and platelet and HUVEC adhesion studies. Figure 1 shows results of fibrinogen adsorption to the PEG-containing polymer. From the figure, we see that suppression of protein adsorption occurs for materials synthesized from 5 mol% PEGMA and excellent resistance to fibrinogen adsorption is received from material polymerized from >15 mol % PEGMA.

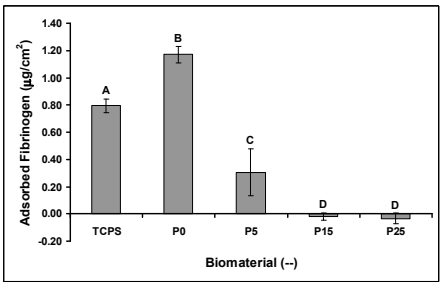

Figure 1. Fibrinogen adsorption to PEG-containing polymers

Figure 2 illustrates HUVEC attachment to SBMA-containing material after 4 days in static culture. From this data we see suppression of cellular attachment for materials polymerized from >15 mol% SBMA

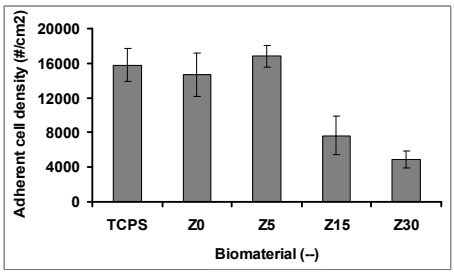

Figure 2. HUVEC adhesion to SBMA-containing polymers after 4 days in static culture

Furthermore, by copolymerizing the hydrophilic PEG and sulfobetaine monomers with relatively hydrophobic methyl and hexyl methacrylate, we can produce non-fouling thermoplstics, in comparison to most thermoset PEG gels. This enables the polymers to be processed using classic polymer fabrication techniques. For instance, each polymer has been electrospun into fibrous scaffolds and illustrated to retain its non-fouling character.

Future work will directly compare the efficacy of each chemical motif at the resistance to biofouling. Also, we will assess the stability of each chemical motif in both hydrolytic and oxidative environments since PEG has been illustrated to degrade *in vivo*.

Conclusions: A methacrylic terpolymer biomaterial containing either poly(ethylene glycol) or sulfobetaine functionality was polymerized through the incorporation of methacrylate monomers possessing the desired pendant groups. It was determined that each chemical species is capable of suppressing the non-specific interactions which often occur in the presence of dissolved proteins and suspended cells.