594g Design of Novel Biomimetic Peptide-Amphiphiles for Functional Biomaterials

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Cell-matrix adhesion mediated by integrins regulates several aspects of cell behavior and is critical to cellular responses on biomaterial surfaces. While many integrins recognize a short Arg-Gly-Asp (RGD) motif present in several extracellular matrix proteins, integrin $\alpha_5\beta_1$ requires a synergy sequence, Pro-His-Ser-Arg-Asn (PHSRN), present in the 9th type III domain of fibronectin (FN), in addition to its primary recognition sequence Gly-Arg-Gly-Asp-Ser-Pro (GRGDSP), present in the 10th type III domain of FN, for enhanced specificity and higher affinity binding. The focus of this work was to engineer $\alpha_5\beta_1$ integrin-specific bioadhesive interfaces using supported bilayer membranes constructed from peptide-amphiphiles that mimic the adhesion domain of fibronectin. Novel peptide-amphiphiles were designed that contain both the GRGDSP and PHSRN sequences in a single peptide formulation, separated by a spacer. Cell adhesion, blocking assays, and confocal microscopy were used to evaluate human umbilical vein endothelial cell (HUVEC) response on biomimetic interfaces. Cell adhesion to the new peptides was found to be comparable to the one observed on the FN-coated surfaces both initially (1 and 4 hours of incubation) and at longer times, whereas surfaces with GRGDSP alone failed to sustain cell adhesion by 24 hours. The effect of the PHSRN, the spacer length between the GRGDSP and PHSRN in the new peptides, and incubation time on HUVEC adhesion to the new FN-mimetic peptide will be discussed.