489f Enhanced Adhesion of Anti-E-Selectin Biodegradable Nanoparticles to Tnf-A Activated Endothelium *in Vitro* and *in Vivo*

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The expression of certain endothelial cell adhesion molecules (ECAMs), e.g. E-selectin, has been shown to be up-regulated at sites of pathological inflammation. As demonstrated by our recent publications (Sakhalkar et al., PNAS, 2003 and FASEB J., 2005), this local upregulation of ECAMs can be exploited to target micron sized PEGylated biodegradable particles to inflamed tissue. We term these particles leukocyte – endothelial cell adhesive particles (LEAPs). Since micron sized particles cannot be endocytosed, our laboratories sought to develop smaller (<200 nm) particles that could be endocytosed to release their payload within endothelial cells. We thus conjugated a biotinylated ligand to E-selectin (□-E) to biodegradable nanoparticles to generate □-E nano LEAPs. □-E nano-LEAPs exhibit enhanced adhesion (~ 19 fold) to 4 hr. TNF-□ activated human umbilical vein endothelial cells (HUVEC) *in vitro* compared to unactivated HUVEC. Moreover, we found that □-E nano LEAPs exhibit 6-fold greater accumulation in the cremaster muscle vasculature of 4 hr. TNF-□ treated mice compared to control mice and exhibit augmented adhesion (~25 fold) to the vasculature of 4 hr. TNF-□ treated mice relative to particles bearing a control ligand. Thus, we have successfully generated □-E nano-LEAPs, which exhibit enhanced adhesion to TNF-□ activated endothelium *in vitro* and *in vivo*.