102a The Modular Antibody Targeting of Catalase Loaded Nanocarriers Provides Protection of Endothelial Cells from H2o2 Mediated Injury

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Vascular oxidative stress is a ubiquitous, difficult to treat pathological condition. Targeting of antioxidant enzymes (e.g., catalase) to the vascular endothelium affords protection against reactive oxygen species (e.g., H2O2) in acute settings. However, lysosomal degradation of targeted enzymes limits duration of therapy. We have loaded active catalase inside polymer biodegradable nanocarriers (PNC), which protects the cargo from rapid proteolytic degradation.

In this study, we employ a modular antibody docking scheme which allows for a catalase-loaded PNC formulation to be targeted using various antibodies. Poly(ethylene glycol)-block-Poly(lactic acid) (PEG-PLA) PNC were synthesized to contain 15 wt% Biotin terminated PEG-PLA, while antibody-streptavidin conjugates were prepared using NH3-to-SH conjugation. Incubation of biotin-PNC with antibody-streptavidin conjugates resulted in a high antibody PNC surface density (6000 antibodies/μm2 particle) without aggregation. Antibody-coated, catalase-loaded PNC specifically bound to endothelial cells (e.g., ~200 vs ~15 particles/cell, anti-PECAM/PNC vs IgG-PNC control) and significantly protected cells from H2O2(>60%, by 51Cr Release). This work provides proof of principle for targeting and uptake of degradable PNC loaded with an active antioxidant cargo, the first step toward the development of a long-acting targeted antioxidant delivery system.