Abstract Submitted
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Cooperative assembly in targeted drug delivery DEBRA AUGUSTE, Harvard University — Described as cell analogues, liposomes are self-assembled lipid bilayer spheres that encapsulate aqueous volumes. Liposomes offer several drug delivery advantages due to their structural versatility related to size, composition, bilayer fluidity, and ability to encapsulate a large variety of compounds non-covalently. However, liposomes lack the structural information embedded within cell membranes. Partitioning of unsaturated and saturated lipids into liquid crystalline (Lα) and gel phase (Lβ) domains, respectively, affects local molecular diffusion and elasticity. Liposome microdomains may be used to pattern molecules, such as antibodies, on the liposome surface to create concentrated, segregated binding regions. We have synthesized, characterized, and evaluated a series of homogeneous and heterogeneous liposomal vehicles that target inflamed endothelium. These drug delivery vehicles are designed to complement the heterogeneous presentation of lipids and receptors on endothelial cells (ECs). EC surfaces are dynamic; they segregate receptors within saturated lipid microdomains on the cell surface to regulate binding and signaling events. We have demonstrated that cooperative binding of two antibodies enhances targeting by multiple fold. Further, we have shown that organization of these antibodies on the surface can further enhance cell uptake. The data suggest that EC targeting may be enhanced by designing liposomes that mirror the segregated structure of lipid and receptor molecules involved in neutrophil-EC adhesion. This strategy is employed in an atherosclerotic mouse model in vivo.

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