Heteromultivalent Approaches to Clot-Targeted Nanomedicine: Combination Targeting of Drug Delivery Systems to Active Platelets and Fibrin

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Occlusive thrombus (blood clot) formation is a major pathological event in cardiovascular diseases. Therefore, removing the clot is critical to restore blood flow to vital organs. One way to remove clots is by administering clot-busting drugs. Side effects, including off-target drug action and hemorrhagic risks, can be minimized by localizing the drug to the clot. Thus, a nanoparticle technology that can bind to the clot and stay retained for site-localized drug-delivery can be of significant benefit. The project explores targeting of nanoparticles to clots by decorating the surface of liposomes with combinations of peptides that bind to active platelets and fibrin, two prominent components of clots. The central hypothesis of the project is: combining the targeted binding of active platelets and fibrin on a single nanoparticle platform can lead to a unique nanovehicle design with superior abilities of clot-specific binding and retention. To test this hypothesis, peptides binding to active platelet integrin GPIIb-IIIa and fibrin were attached onto the liposome surface. Resultant nanoconstructs were studied for binding efficacy on platelet-rich and/or fibrin-rich clots in microfluidic chambers in vitro. Studies show that combination targeting enhances clot-specific binding and retention of the nanoconstructs, compared to those with a single targeting mechanism.

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