Ferritin caged molecules for photodynamic therapy and drug delivery

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Technology description

Technology Summary

Nanoparticle-based drugs are emerging as an important class of therapeutics. Nine nanoparticle drugs have received regulatory approval for the treatment of various cancers. These include Doxil and ABI-007 that have entered mainstream of cancer management in the clinic. Unlike conventional small-molecule chemotherapeutics, nanoparticle- or macromolecule-based drugs can selectively egress at leaky tumor vasculatures and remain in the tumor interstitium for an extended period of time. Despite relative leakiness compared to normal vessels, endothelial lining can remain a barrier to the delivery of nanoparticles to tumors. This underscores the need for a therapy that enhances tumor endothelium leakiness. Using a clinically approved photodynamic therapy (PDT)-based method, we selectively permeabilize tumor vasculatures to boost therapeutic effect. Current PDT methods lack selectivity acting on both endothelial and luminal targets (e.g. red blood cells/platelets), causing massive destruction that includes vessel collapse and thrombus formation. We have generated an RGD modified ferritin (RFRT) as a targeted carrier to deliver the photosensitizer $ZnF_{16}Pc$ site-specifically to enhance tumor therapeutic uptake by as much as 17.8-fold, while causing no adverse effects to normal tissues. Increased tumor uptake was observed with a wide range of nanoparticles. Using Doxil as a representative nanoparticle drug, we also studied the impact of the increased tumor vasculature permeabilization on cancer treatment. While inducing little cytotoxicity by itself, the PDT significantly improved the treatment efficacy of Doxil, improving the tumor growth inhibition by 75.3%. These observations indicate this composition as a safe, selective, and effective means to enhance the therapeutic treatment of tumors.

Application area

Targeted therapeutics for cancer treatment utilizing ferritin caged drugs and photosensitizers for enhanced and specific delivery.

Advantages

Selective tumor vascular permeabilization using photodynamic therapy

Enhanced tumor uptake of therapeutic

Prevents vessel collapse and thrombosis typically associated with photodynamic therapy

Increased therapy efficacy up to 75%

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