A nanoparticle drug delivery system for small molecule cancer drugs that binds endogenous albumin

Unmet Need

Small molecule cancer drugs often suffer from poor systemic exposure, resulting from their low water solubility and short plasma half-life. Additionally, the off-target toxicity is the main challenge that undermines efficacy. Nanoparticle drug delivery systems, such as self-assembling micelles, can solve these problems when carrying chemotherapeutic agents by improving the drug pharmacokinetics and tissue distribution. However, micelles are often unstable and quickly removed from systematic circulation because they’re preferentially taken up by macrophages. Therefore, there remains a need for new nanoparticulate drug delivery systems that can overcome these disadvantages yet provide efficacy for delivery of poorly water-soluble anti-cancer agents.

Technology

Duke inventors have reported a nanoparticle drug delivery system intended to improve the uptake of poorly water-soluble small molecule cancer drugs by tumors. These nanoparticles encapsulate small molecule cancer drugs and bind endogenous albumin upon intravenous injection. Albumin is present in millimole concentrations in blood, making this a simple and attractive strategy for improving circulation. The synthesis of the nanoparticles was achieved by fusing the gene encoding a protein-G derived albumin binding domain to that of a chimeric polypeptide, and the ABD-CP fusion was recombinantly synthesized by bacterial expression of the gene. The polypeptides exhibit lower critical solution temperature phase behavior, enabling them to form gel-like depots that increase the half-life of their cargo. Animal studies have demonstrated

increased plasma stability and tumor uptake of nanoparticles carrying doxorubicin, a common chemotherapeutic agent.

Advantages

- A simple, attractive method for improving the efficacy of poorly soluble cancer drugs by taking advantage of endogenous blood albumin
- Canine studies show 6-fold increase in blood plasma exposure
- Increased uptake of doxorubicin by tumors demonstrated in mouse models
- Unlike other methods for coating nanoparticles with albumin, this strategy avoids the extra processing steps during nanoparticle synthesis that can cause conformational changes in the structure of albumin that can lead to immunogenicity

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Department

Biomedical Engineering (BME)

Publication(s)

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External Link(s)

• From the lab of Dr. Ashutosh Chilkoti