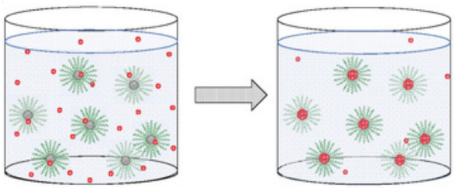
A novel class of nanoparticles that can be recombinantly synthesized for drug delivery and other applications

Unmet Need

Recombinant biopolymers are used for a diverse array of applications including drug delivery, tissue engineering, and clinical diagnostics. Peptide polymers are particularly attractive candidates for biomedical applications because of their biocompatibility, biodegradability, and precisely specified, genetically encoded sequence. However, compared to their synthetic counterparts, recombinant peptide polymers are made up of a limited number of building blocks - the twenty standard amino acids - which severely restricts their potential design space. Nature itself has evolved numerous strategies to diversify the proteome through post-translational modifications (PTMs), but these are inaccessible with commonly used prokaryote systems. There is a need to diversify the peptide polymers available for creating biopolymers that still maintain a simple recombinant synthesis workflow. This technology is valuable for recombinant synthesis of protein nanoparticles with a lipid core.

Technology

Duke inventors have reported a nanoparticle drug delivery system that would be particularly useful for hydrophobic small molecules without a handle for conjugation. This is a self-assembled micelle comprising a fatty acid conjugated to an unstructured polypeptide. Inspired by biohybrid molecules that are synthesized in nature through post?translational modifications (PTM), the inventors have exploited a eukaryotic PTM to recombinantly synthesize lipid–polypeptide hybrid materials. By co?expressing yeast N?myristoyltransferase with an elastin?like polypeptide (ELP) fused to a short recognition sequence in E. coli,



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Patent Information

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Department

Biomedical Engineering (BME)

Publication(s)

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External Link(s)

• From the lab of Dr. Ashutosh Chilkoti

they show robust and high?yield modification of the ELP with myristic acid. ELPs exhibit lower critical solution temperature phase behavior, enabling them to form gel-like depots that increase the half-life of their cargo. The ELP's reversible phase behavior is retained upon myristoylation and can be tuned to span a 30–60 °C. Myristoylated ELPs provide a versatile platform for genetically pre?programming self?assembly into micelles of varied size and shape. Their lipid cores can be loaded with hydrophobic small molecules by passive diffusion. Cellular studies and mouse models demonstrated improved efficacy and antitumor effects.

Other Applications

While the inventors have completed studies related to drug delivery applications, this technology could be used to encapsulate other hydrophobic molecules such as imaging agents. The invention can also be expanded to polypeptides other than ELPs.

Advantages

- Offers a novel class of hybrid material that can encapsulate any hydrophobic small molecule, including those without a chemical handle for conjugation
- Longer plasma circulation than free drug upon intravenous injection demonstrated in mice
- ELPs are thermally responsive biopolymers that undergo an inverse phase transition, which results in thermal targeting of tumors
- Physically encapsulated doxorubicin and paclitaxel exhibit cytotoxic effects on 4T1 and PC3?luc cells