(SD2021-154) A new platform for the controlled entrapment and release of molecular cargo

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ABSTRACT

Researchers from UC San Diego have invented a new form of materials, polymer-integrated crystals (PIX), which combine the structural order of protein crystals with the dynamic, stimuli-responsive properties of synthetic polymers. The inventors have shown that the crystallinity, flexibility, and chemical tunability of PIX can be exploited to encapsulate guest proteins with high loading efficiencies. And, the electrostatic host-guest interactions enable reversible, pH-controlled uptake/release of guest proteins as well as the mutual stabilization of the host and the guest, thus creating a uniquely synergistic platform toward the development of functional biomaterials and the controlled delivery of biological macromolecules.

TECHNOLOGY DESCRIPTION

Background.

Current methods to entrap/release cargo (such as proteins) generally involve the use of either amorphous polymer systems or rigid, crystalline constructs like metal-organic frameworks (MOFs). Polymer systems can display dynamic properties by expanding and contracting. However, due to its intrinsically amorphous network, polymeric materials may suffer from unintentional passive leaching of the cargo, difficulty in controlled release, and maintaining structural integrity. On the other end of the spectrum, MOFs are examples of rigid materials with defined pore sizes. However, the required molecular interconnectivity thwarts MOFs from being dynamic (i.e., from expanding and contracting on demand or at all). The material's pore size dictates which biomolecules can be entrapped and limits the type of proteins available. Generally, this method requires passive diffusion of proteins into the material. Another approach involves de novo encapsulation where the protein is included in the MOF precursor mixture. Upon incubation, the MOF forms and the protein are trapped on the inside. However, this limits the types of MOFs available to use, due to the protein requiring compatible conditions – extreme conditions will denature the protein cargo.

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OTHER INFORMATION

KEYWORDS

Biocompatible Materials

CATEGORIZED AS

- **Medical**
  - Delivery Systems
- **Nanotechnology**
  - Materials

RELATED CASES

2021-Z08-1

biomaterials and the controlled delivery of biological macromolecules

APPLICATIONS

Controlled loading and release of pharmaceutical or diagnostic agents, stable/cold-chain-free preservation of biologics, sensing, biocatalysis, sequestration of toxic molecules.

ADVANTAGES

This approach utilizes PIX, which is a material that seamlessly combines the structural order and periodicity of crystals with the adaptive and tunable mechanical properties of polymeric networks, as a method to capture and release cargo. These materials have several unique properties:

1) The crystal's pore size is not a limitation of what size cargo it can capture because PIX can expand and contract.

2) Furthermore, this allows active/externally controllable/stimuli-responsive capture and release of molecules.

3) The polymeric network in a PIX can be changed/modified with specific functional groups, allowing more selective binding to molecules/proteins of interest.

4) The polymer component can be changed/modified to change the encapsulation/release efficiencies and kinetics.

5) In the first-generation PIX, the protein crystals are composed of human heavy chain ferritin. This is a non-immunogenic protein, which itself can be used for targeting of certain tissues or cancer cells and be used to store cargo in its interior.

6) Ferritin can be easily modified genetically/chemically to alter its interactions with the polymer matrix, thus providing an additional means to change the PIX encapsulation/release efficiencies and kinetics.

7) In addition, PIX can in principle be made using other protein crystals (besides those ferritin), which in turn would allow a) other protein-based functions to be exploited, b) the PIX encapsulation/release properties to be further modulated, and c) further increase the scope of guest/cargo molecules to be encapsulated.

STATE OF DEVELOPMENT

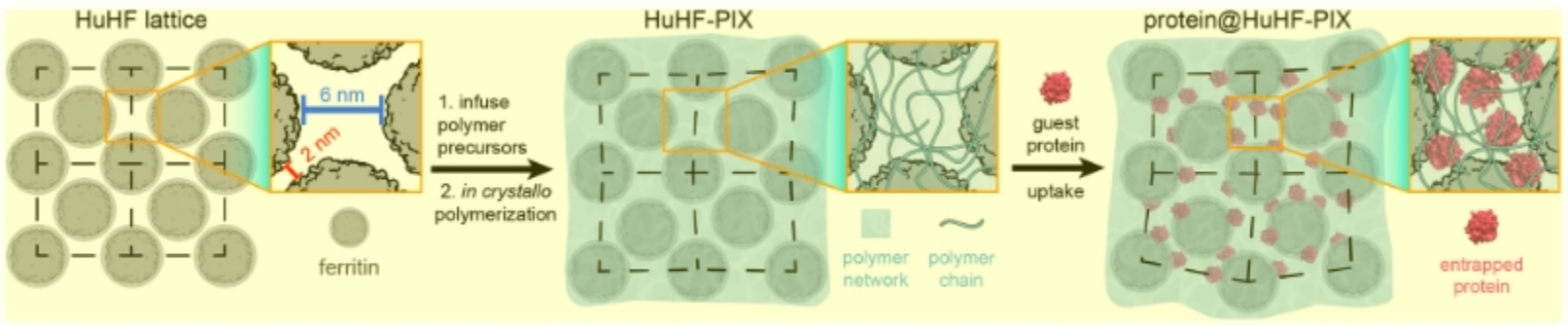

Figure 1. Schematic illustration for the uptake of guest proteins in HuHF-PIX.

INTELLECTUAL PROPERTY INFO

UC San Diego is a US patent pending and welcomes interest from companies interested in commercializing this technology.

RELATED MATERIALS

- Han K, Na Y, Zhang L, Tezcan FA. Dynamic, Polymer-Integrated Crystals for Efficient, Reversible Protein Encapsulation. J Am Chem Soc. 2022 Jun 15;144(23):10139-10144. doi: 10.1021/jacs.2c02584. Epub 2022 Jun 6. - 06/06/2022

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