Self-Assembling Protein Fibers and Hydrogels as Theranostic Agents

Biocompatible theranostic agents for simultaneous diagnostic imaging and drug delivery.

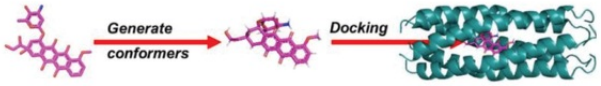

Figure: Schematic showing doxorubicin encapsulation within the coiled-coil pore of the Q8•Dox) protein fiber (Q8•Dox)

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Technology

The Montclare Lab has engineered a collection of innovative self-assembling proteins that form into coiled-coil fibers and hydrogel, with the option to replace one or more leucine residues with trifluoroleucine residues, presenting a tunable modality for improved diagnostic imaging and localized drug delivery. The trifluoroleucine residues of these proteins provide a highly specific spectroscopic signal without interference from biological tissues, enabling enhanced visualization by MRI (^{1}H MR spectroscopy, ^{19}F MR spectroscopy) and ultrasound. One self-assembling protein, termed Q8, shows particular promise as a drug delivery hydrogel due to its high gelation rate and mechanical strength. In published proof of concept studies (*Britton et al., Biomacromolecules 2024*), the researchers used Q8 to encapsulate doxorubicin (Dox) within the pore of the coiled-coil protein, termed Q8•Dox (See Figure). Ultrasound was then employed to precisely deliver the chemotherapeutic hydrogel to triple negative breast cancer (TNBC) tumors in an in vivo mouse model. A single subcutaneous injection of Q8•Dox showed significant tumor suppression in just one week (36%) compared to control treatments of Q8 and doxorubicin alone (58% and 30% tumor growth, respectively). Unlike current TNBC treatments, which suffer from off-target toxicity and limited efficacy due to poor targeting, Q8 offers localized delivery of chemotherapeutic cargo via subcutaneous injections, thereby minimizing dosage levels and reducing systemic toxicity. In all, the Montclare Lab has developed innovative protein-based hydrogels that enable sustained drug delivery and real-time monitoring of treatment progression, marking a significant advancement in the field of theranostics.

Background

Theranostics, the integration of diagnostics and therapeutics into a single approach, has emerged as a promising solution to meet the urgent demand for more precise and effective treatments. Traditional imaging, like MRI, relies on hydrogen-based signals (^{1}H), which are naturally abundant in the human body. For this reason, this imaging method suffers from signal interference and poor specificity, making it challenging to monitor therapeutic progress accurately. Contrast agents for enhanced imaging, such as quantum dots (QDs) and radiolabeling, augment MRI resolution, but suffer drawbacks due to poor stability and cytotoxicity. Current chemotherapeutic drug delivery systems for metastatic breast cancer (MBC), such as pegylated liposomal doxorubicin (PLD) and nanoparticle albumin-bound paclitaxel (NP), attempt to improve drug solubility and pharmacokinetics, yet they encounter significant challenges in precisely targeting tumor cells, leading to systemic off-target effects and toxicity. Therefore, when taken together, there is a critical unmet need for new theranostic agents that can safely deliver chemotherapeutics with a controlled and localized release while minimizing drug load and systemic toxicity, particularly for treatment of chronic illnesses.

Development Status

The research team is exploring the delivery of other therapeutics and controlling the gelation behavior for other disease applications.

Proof of Concept Studies

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11094684/Intellectual property

Applications

- **Drug delivery platform:** For hydrophobic small molecule therapeutics in a variety of disease contexts where localized drug delivery is important (e.g., solid tumor cancers).
- **Diagnostic use:** Real-time disease treatment monitoring via MRI (^{1}H MRS, ^{19}F MRS) and ultrasound.

Advantages

- **Improved theranostic capabilities:** Enables simultaneous diagnosis and treatment for real-time disease.
- **Enhances imaging specificity:** Trifluoroleucine residues provide a robust autofluorescence signal.
- **Minimal systemic toxicity:** Localized delivery systems are expected to reduce adverse off-target effects.
- **Minimizes immune response and enhances biocompatibility:** Protein-based hydrogels are less likely to trigger immune reactions compared to synthetic polymers.
- **Maximizes chemotherapy efficacy:** Encapsulation of chemotherapeutic agents within hydrogels ensures higher drug retention at tumor sites.
- **Highly tunable proteins:** Gelation properties and electrostatic potential of hydrogel can be customized.

Intellectual Property

NYU holds a pending U.S. non-provisional patent covering the composition of the fluorinated fibers, their method of use for imaging and drug delivery in specific disease contexts, and the method of constructing a self-assembled protein fiber.

References

1. Britton, Dustin et al. , https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11094684/