Unstructured non-repetitive polypeptides as a tool for imparting temperature-dependent physical properties to protein fusions

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Publication(s)

External Link(s)

- From the lab of Dr. Ashutosh Chilkoti

Value Proposition

Proteins can be useful therapeutic agents when engineered for specificity and selectivity for a clinical target. Their complexity, versatility, tolerability, and diversity often make them superior alternatives to small molecule drugs, and the long half-life, specificity, and selectivity can make them attractive for therapies. Although protein engineering allows for the development of potent therapeutics targeted toward a protein or receptor of interest, the body has many mechanisms with which to clear such protein therapies. Accordingly, there exists a need for reliable and broadly applicable protein delivery solutions.

Technology

Duke inventors have reported a tool for imparting temperature-dependent physical properties by fusion to proteins of interest. This is intended for application in a wide varety of biomedical applications, including therapeutics by fusion to drug partners, which upon administration to the subject will form a gel-like structure resulting in drug depots with sustained release. In addition, they can be used in diagnostics by fusion to a binding domain for a specific target. After administering to a subject, a sample obtained from the subject can be used to quantify the amount of target. This technology takes advantage of the lower critical solution temperature (LCST) phase transitions that polypeptides and synthetic polymers can exhibit. Unlike previous reports, this technology uses non-repetitive polypeptides that can be created by standard gene synthesis techniques. A variety of these non-repetitive polypeptides have been characterized in the lab to demonstrate LCST phase behavior similar to their repetitive polypeptide counterparts.

Advantages

- Can be fused to proteins of interest to impart useful temperature-responsive physical properties to help treat or diagnose a disease
- Can be created using standard gene synthesis techniques
- High diversity of polypeptide sequences with equivalent lower critical solution temperature phase transition behavior