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Office of Technology Management

PROTEIN-BASED DRUGS THAT TARGET CONDENSATE-DEPENDENT DISEASES

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Value Proposition: *Directed evolution of synthetic intrinsically disordered proteins for condensate editing.*

Technology Description

Researchers at Washington University in St. Louis have developed a directed evolution method and selection strategies to enable the evolution and selection of synthetic intrinsically disordered proteins for editing pathological condensates. Biomolecular condensates, which primarily form through the phase transitions of multivalent biomacromolecules, such as intrinsically disordered proteins (IDPs), play a pivotal role in nearly every aspect of cellular biochemistry, impacting processes like transcription, translation and stress responses. Unlike the conventional view of cellular functions governed by interlocking molecular interactions, where modifying a single molecule can impact its functional outcomes, condensate-mediated cellular functions depend on a cooperative process influenced by multiple interacting partners.

This invention utilizes protein-based drugs that can target condensates. This technique can be potentially delivered as mRNA specifically to different cell types, allowing for specific editor proteins to be selected to target native pathological condensates, such as viral condensates for SARS-CoV-2 and neuronal condensates for neurodegenerative disorders.

Stage of Research

Tested in mammalian cells

Publications

- Dai Y, Farag M, Lee D, Zeng X, Kim K, Son HI, Guo X, Su J, Peterson N, Mohammed J, Ney M, Shapiro DM, Pappu RV, Chilkoti A, You L. Programmable synthetic biomolecular condensates for cellular control. Nat Chem Biol. 2023 Apr;19(4):518-528. doi: 10.1038/s41589-022-01252-8. Epub 2023 Feb 6. PMID: 36747054; PMCID: PMC10786170.

- Dai Y, You L, Chilkoti A. Engineering synthetic biomolecular condensates. Nat Rev Bioeng. 2023 Apr 17:1-15. doi: 10.1038/s44222-023-00052-6. Epub ahead of print. PMID: 37359769; PMCID: PMC10107566.

Applications

- Treatment of condensate-dependent diseases

Key Advantages

- Can realize on-demand regulation of pathological condensates
- Specifically modulates phase transition propensity and the physical properties of target condensates

Patents

Patent pending

Related Web Links – Yifan Dai Profile; Dai Lab