Docket #: S19-310

Rational Design of Ultratight RNA Aptamers against Protein Targets

Stanford researchers have developed a computational approach for designing RNA modules with ultratight and ultraspecific recognition of any protein. These modules may be incorporated into future RNA therapeutics and can potentially displace monoclonal antibodies for some, or all, disease treatments. While the pharmaceutical industry is investing heavily in RNA vaccines and therapeutics for diseases ranging from cancer to HIV to COVID-19, these new RNA therapeutics cannot currently be turned *on* or *off* through recognition of proteins in target cell types or on target pathogens. Furthermore, these drugs do not yet have the ability to bind proteins with nanomolar affinity. The new approach, with its precision targeting and structural control, overcomes critical limitations for developing protein-binding RNA aptamers.

This invention has four key elements: (i) **Computational identification** of likely binding sites on the target protein for RNA fragments (ii) **Computational design** of 3D RNA nanostructure to connect those fragments (iii) **Computational design of a library of sequences** that form the designed 3D RNA nanostructures, and (iv) **Experimental selection** of sequences that bind the target protein.

This technology is part of a portfolio of innovations aimed at fighting the COVID-19 pandemic.

Related technologies for optimizing RNA-based therapeutics and vaccine design:

Stanford docket S20-205 - Repurposing the SARS-CoV2 5'-UTR for RNA Based Therapeutics
Stanford docket S20-176 - Software for Rapid Mapping of RNA Structure
Stanford docket S20-135 - Translation Enhancer for Gene Regulation
Stanford docket S19-143 - Primerize: Software for Designing Primers for Rapid RNA Synthesis

Stanford docket S19-174 - Optimized Synthesis and Translation of RNA Therapeutics

Applications

- Rational design of RNA aptamers for increased stability and/or function
- Targeting proteins to alter or disrupt their function for therapeutic applications
- Imaging in cells
- Detecting proteins for diagnostic applications
- Scaffolding several proteins together to create RNA-protein nanomachine

Advantages

- Libraries of RNA sequences are biased to bind tightly to the protein target, rather than starting from a pool of random sequences
- Targets multiple distinct sites on a target protein, enabling ultratight and ultraspecific RNA aptamers
- Enables specific control over the structure of an RNA aptamer and protein-binding sites

Publications

- Miao, Z. et al. RNA-Puzzles Round IV: 3D structure predictions of four ribozymes and two aptamers. *RNA* 2020.Published in Advance May 5, 2020, doi: 10.1261/rna.075341.120

Innovators

- Rhiju Das
- Kalli Kappel
- Joseph Yesselman

Licensing Contact

Sam Rubin

Licensing Associate, Life Science

Email