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INDEPENDENT CONTROL OF THE THERMODYNAMIC AND KINETIC PROPERTIES OF APTAMER SWITCHES

Researchers at Stanford and the Chan Zuckerberg Biohub have developed methods for independent tuning of aptamer switching binding affinities and kinetics.

Aptamers are useful molecular switches with excellent binding properties that can reversibly change their confirmation upon target binding. Unfortunately, the thermodynamic and kinetic properties of aptamer switches developed to date are intrinsically coupled, hampering control and tuning efforts to match intended function. There is considerable interest in engineering molecular switches that can achieve a selective and sensitive output in response to target binding.

Stage of Research
The inventors have developed methods for independent control of the thermodynamic and kinetic properties of aptamer switches. The authors describe an intramolecular strand displacement (ISD)-based design strategy that decouples effective binding affinity and temporal resolution. Their ISD design is a single molecule switch in which the aptamer is attached to a partially complementary displacement strand by a flexible linker. They use a model aptamer and vary displacement strand length, linker length or introduce displacement mismatches to create an array of aptamer switches with effective dissociation constants ranging from 10 ?M to 40 mM and binding kinetics ranging from 170 ms to 3 s.

Applications

- Generation and screening of aptamer switch libraries for diverse applications, including imaging, biosensing and drug delivery.

Advantages

- Tunable binding kinetics and dissociation constants, suitable for a diverse range of biotechnology applications
- Aptamer switches are easily synthesized and readily adaptable to chemical modification

Publications

- Wilson BD, Hariri AA, Thompson IAP, Eisenstein M and Soh HT. Independent control of the thermodynamic and kinetic properties of aptamer switches. Nat Commun. 2019. 10, 5079. Doi: 10.1038/s41467-019-13137
- WO-2020/086762-A1

Patents

- Published Application: WO2020086762

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