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Sensitive, specific, and dynamic biosensing using antibody-aptamer chimeras

Stanford University researchers have developed aptamer-antibody chimeras that achieve dynamic, sensitive, and specific biomolecule sensing beyond the capacity of antibodies or aptamers alone.

DNA aptamers are short sequences of engineered DNA that selectively bind to a target molecule and generate a reversible fluorescent or electrochemical signal in response, enabling continuous sensing in applications from diagnostics to environmental monitoring. However, aptamers are limited by poor sensitivity. Researchers therefore combined the signaling abilities of an aptamer with the high sensitivity and specificity of a monoclonal antibody by combining the two components with a short DNA linker.

This new sensor can detect target molecules at very low concentrations (Kd = \sim 100 pM) even in complex samples, enabling rapid, direct detection in biofluids or environmental samples without expensive and time-consuming sample preparation. Sensors can track changes in target concentration over time with high temporal resolution (\sim 10 minutes). Sensors are easy to engineer, as they can take advantage of existing antibodies and aptamers without any further engineering. Features like affinity, sensitivity, and temporal response can be rationally tuned by changing the length of the DNA linker or modifying the aptamer sequence.

Applications

- Fluorescent or electrochemical signal output
- Wearable or implantable biosensors
- Point-of-care and at-home diagnostics

- Personalized medicine
- Wastewater and agricultural monitoring

Advantages

- Sensitivity superior to traditional DNA aptamers (Kd = \sim 100 pM)
- No requirement for a secondary antibody
- Preparation-free, direct sensing in complex samples
- Continuous sensing of changes in target concentration over time
- Temporal resolution of ~10 minutes
- Highly modular and tunable

Publications

 Dehui Kong, Nicolo Maganzini, Ian A.P. Thompson, Michael Eisenstein, H. Tom Soh. <u>Aptamer-antibody chimera sensors for sensitive, rapid and reversible</u> <u>molecular detection in complex samples</u>. bioRxiv 2023.08.08.552518.

Patents

• Published Application: WO2025029630

Innovators

- H. Tom Soh
- Ian Thompson
- Nicolo Maganzini
- Dehui Kong

Licensing Contact

Eileen Lee

<u>Email</u>