Docket #: S18-351

COMPOSITIONS AND METHODS INVOLVING NON-NATURAL APTAMER LIBRARIES

Researchers at Stanford, funded in part by the Chan Zuckerberg Biohub, have developed Click-PD, a framework for the customizable generation of non-natural, base-modified aptamer libraries with diverse chemical modifications. These libraries are used in a high-throughput particle display screening strategy to measure the affinity and specificity of the aptamer libraries to target molecules.

Interactions between glycans and carbohydrate-binding proteins underlie many key biological processes, such as red blood cell agglutination. The generation of synthetic affinity reagents that can faithfully mimic elements of a glycan's protein-binding properties is critically important for modulating these interactions. However, there has not been an efficient or generalizable strategy to generate or characterize these so-called glycomimetic reagents.

Stage of Research

The inventors have developed PCR-based methods for the direct incorporation of non-natural nucleotides into particle-conjugated DNA aptamers. Non-natural nucleotides can be subsequently chemically modified using click conjugation to introduce additional binding agents with diverse arrays of functional groups. Each particle contains multiple copies of a unique base-modified aptamer. Particle-conjugated aptamer libraries can be screened, and subsequently isolated, for target binding. The inventors demonstrated the utility of Click-PD in generating glycomimetic aptamer reagents through the identification and characterization of mannose base-modified aptamers with high affinity and specificity for the lectin, concanavalin A (ConA).

Applications

- Platform for the efficient generation and screening of customizable aptamer libraries for a wide range of biological and biomedical applications.

Advantages

- Facile generation of non-natural DNA aptamers with commercially-available reagents.
- Click-chemistry-generated aptamer libraries with diverse functional groups.
- Particle display to determine both affinity and specificity of every base-modified aptamer for desired target molecule.

Publications

- Gordon CKL, Wu D, Pusuluri A, Feagin T, Csordas AT, Eisenstein M, Hawker CJ, Niu J, Soh HT. Click-Particle Display for Base-Modified Aptamer Discovery. ACS Chemical Biology 14 (12):2652-2662 (2019).

Patents

- Published Application: WO2019236571
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