Platform for the Continuous Directed Evolution of Antibodies in Yeast

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BRIEF DESCRIPTION

Researchers at UCI and Harvard have engineered a new platform for diversifying antibody genes in yeast, eliminating a crucial bottleneck in making effective antibodies. This technology enables the rapid continuous directed evolution of affinity reagents for applications ranging from structural and cellular biology to diagnostics and immunotherapy.

FULL DESCRIPTION

Antibodies are pervasive in life science research, diagnostics, and pharmaceutical therapeutics. The broad utility of antibodies comes from their ability to bind target molecules (antigens) tightly and specifically. Moreover, our rapidly expanding knowledge of biological and disease pathways creates a high demand for making new antibodies. Current methods for engineering antibodies (affinity maturation) include yeast display, where antibody fragment molecules are presented on the surface of a yeast cell and selected for a desired binding activity. While yeast is an excellent platform for displaying antibody fragments, preparing and delivering libraries of antibody variants into yeast cells in between binding selection steps is time-intensive and inefficient, limiting the number of binders that can be investigated. To address this, researchers at UCI and Harvard have engineered a new yeast display platform that eliminates the time-consuming recovery, mutagenesis, and re-delivery of DNA libraries to yeast during affinity maturation. Instead, antibody genes are continuously mutated within the yeast cell through an orthogonal DNA replication system developed by the inventors (OrthoRep). The resulting antibody variants are readily selected for one or more target binding activities, with the winning variants taken forward for further growth and passive re-diversification. This technology allows for the rapid continuous evolution of affinity reagents for applications ranging from structural biology to cancer immunotherapy.

SUGGESTED USES

- Making antibodies for diagnostics
- Developing immunotherapy reagents
- Creating custom antibodies for life sciences research
- Evolving binders to enable structural biology

ADVANTAGES

- Increased efficiency: mutations are added specifically to antibody DNA within the cell removing the need for time-consuming researcher intervention.
- More effective evolution: because mutations are added continuously, a low-binding starting library can explore multiple evolutionary paths to rapidly evolve into a high-affinity, mature antibody.
- Opportunity for parallelization: a range of binding selections (stringency, competition, different epitopes of the antigen) as well as stability selections can be explored at the same time from the same starting

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OTHER INFORMATION

CATEGORIZED AS

- **Materials & Chemicals**
  - Biological
- **Medical**
  - Diagnostics
  - Therapeutics
- **Research Tools**
  - Antibodies
  - Expression System
  - Protein Synthesis
  - Screening Assays
  - Vectors

RELATED CASES

2019-681-0

binder(s).

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,946,055	04/02/2024	2019-681

Additional Patent Pending

RELATED MATERIALS

» McMahon et al. “Yeast surface display platform for rapid discovery of conformationally selective nanobodies” Nature Structural & Molecular Biology 25, 289-296. 2018

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