

Docket #: S22-130

Antibody Compositions and Optimization Methods

Researchers at Stanford have invented a method using directed evolution for predicting antibody improved antibody variants.

Evolution searches across an immense space of possible sequences for rare mutations that improve fitness. In nature, this search is based on random mutation and recombination, but using this same approach for directed evolution of proteins in the laboratory imposes a considerable experimental burden. Indeed, current approaches are limited as high-throughput evolutionary screens, that rely on random guessing or brute-force search, often devote substantial effort to interrogating weakly active or nonfunctional proteins. There is therefore a need for more efficient and effective methods of generating protein variants using directed evolution.

Stage of Development

Research -

in vitro

Stage of Research

The inventors have developed methods for predicting improved antibody variants. Such variants can be used (or selected) to improve properties of known therapeutic antibodies in methods described herein. The present disclosure is also based, in part, on antibody variants designed using the provided methods that are able to specifically bind to viral antigens.

Technology Reference Nos.

Biohub ref. no. CZB-245S-PC

Stanford ref. no. S22-130

Applications

- Predicting a small, manageable set (~10) of high-likelihood protein variants from a single antibody sequence using the predictive capabilities of protein language models.
- Additional characterization of evolved antibodies to find variants with higher binding affinity and higher thermostability.

Advantages

- Exploring a mutational space which is multiple orders of magnitude larger than is possible with in vivo evolutionary trajectories.
- The computational portion of this approach takes seconds, whereas traditional methods employed by the state-of-the-art (rounds of cell culture and sorting) takes weeks

Publications

- Brian L. Hie, Varun R. Shanker, Duo Xu, Theodora U. J. Bruun, Payton A. Weidenbacher, Shaogeng Tang, Wesley Wu, John E. Pak, Peter S. Kim. "[Efficient evolution of human antibodies from general protein language models](#)." Nature Biotechnology (2023).

Patents

- Published Application: [WO2023196658](#)

Innovators

- Brian Hie
- Peter Kim
- Varun Shanker

Licensing Contact

Sunita Rajdev

Senior Director, Licensing and Strategic Alliances

[Email](#)