Docket #: S22-297

A unique protein engineering platform to co-evolve protein-protein pairs using combinatorial biology approaches

Engineering novel proteins through directed evolution have become a foundation of protein engineering in biotech. However, these techniques are incapable of simultaneous engineering of protein-protein pairs through library-on-library selections. An efficient synthetic system for bidirectional, simultaneous protein-protein coevolution could serve as a platform to simulate natural coevolution and for biotechnology applications

The Garcia Lab at Stanford has invented a unique protein engineering platform to co-evolve protein-protein pairs using combinatorial biology approaches. The method adopts Z domain-affibody pairs as a model system to generate co-evolved interfaces that were extensively characterized by 10 X-ray crystal structures, next-generation sequencing (NGS), isothermal titration calorimetry (ITC), and bioinformatics. The approach enabled efficient isolation of completely re-wired interfaces with a wide range of affinities and orthogonalities. Deep sequencing enabled the inventors to reconstruct evolutionary pathways of protein pairs and they have since sequenced thousands of protein-protein complexes with different degrees of specificity, cross-reactivity and orthogonality. These sequences could find applications in many types of synthetic biology methods. The integration of a synthetic coevolution platform with machine learning enables the interrogation of a protein-protein interaction with exceptional granularity.

Applications

- -T-cell engineering

- -Molecular biology research
- -Protein engineering

Advantages

- -Can co-involve protein-protein pairs
- -high degree of specificity
- -compatible with wide range of affinities and orthogonalities

Publications

- Yang, A., Jude, K. M., Lai, B., Minot, M., Kocyla, A. M., Glassman, C. R., ... & Garcia, K. C. (2023). " Deploying synthetic coevolution and machine learning to engineer protein-protein interactions."
- Science, 381(6656), eadh1720.

Innovators

- Kenan Christopher Garcia
- Kevin Jude
- Aerin Yang
- Aly Azeem Khan

Licensing Contact

Mona Wan

Senior Associate Director, Life Science

Email