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Targeted Artificial DNA Replisome (TADR) a Tool for Targeted Mutagenesis

TADR is a protein-complex designed to target and mutate specific genes on plasmid in vivo

Technology No. 2021-073

IP Status: Provisional Patent Application Filed

Applications

- Optimization of biologic based drugs
- Optimization of industrial enzymes
- Evolution studies in laboratory settings

Key Benefits & Differentiators

- **Specific targeting:** Able to target any gene-sized (or larger) regions of DNA with low off-target mutation rate
- **Enhanced mutagenesis** high mutation rates which can be switched on-off and include all types of nucleotide substitutions
- **Easy to use:** designed as a protein-complex as opposed to phage-bacteria interaction or complex CRISPR-based tools

In-vivo Direct Evolution Research Tool for Protein Engineering

Protein engineering is the process of modifying existing protein structures to develop new proteins that have desirable properties and enhanced performance when compared to the original unmodified version.Typically, the process of engineering proteins starts with choosing the necessary changes, producing these changes through mutagenesis and evaluating if the modifications indeed resulted in improved properties (screening or selection). To obtain proteins with desirable properties typically millions of mutants need to be generated through the mutagenesis step. Mutagenesis can be performed through several techniques, but recently direct evolution has become the standard approach in protein engineering. However, several improvements are still needed to increase the quantity and quality of mutations generated

through currently available research tools.

To address this gap, researchers at the University of Minnesota have developed the Targeted Artificial DNA Replisome (TADR) research tool. TADR is a protein complex that operates in live cells to processively replicate one strand of a plasmid with errors.This novel tool enhanced mutagenesis of target genes up to 2.3×105-fold with only a 40-fold increase in off-target mutagenesis. TADR was used to evolve itself to increase error rate and increase the efficiency of an efflux pump while simultaneously expanding the substrate repertoire. In addition, TADR is capable of (i) targeting a region no less than a gene and show low off-target mutagenesis, (ii) has a high mutation rate that can be turned on and off and include all types of nucleotide substitutions, and (iii) it is easy to use and does not limit the type of trait that can be evolved. Currently available in vivo mutagenesis tools lack one or more of these features. Therefore, this novel research tool can be a critical asset to discover new proteins for biologic drugs and industrial applications.

Phase of Development

TRL: 3-5
Proof of concept has been demonstrated.

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

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Researchers

- **Romas Kazlauskas, PhD** Professor, Department of Biochemistry, Molecular Biology, and Biophysics
- **Michael Travisano, PhD** Professor, Department of Ecology, Evolution and Behavior

References

Yi, X., Khey, J., Kazlauskas, R.J. and Travisano, M., https://doi.org/10.1126/sciadv.abg8712, Science Advances

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