A Highly Error-Prone Orthogonal Replication System For Targeted Continuous Evolution In Vivo

Tech ID: 29021 / UC Case 2017-816-0

BRIEF DESCRIPTION

Inventors at UC Irvine have engineered an orthogonal DNA replication system capable of rapid, accelerated continuous evolution. This system enables the directed evolution of specific biomolecules towards user-defined functions and is applicable to problems of protein, enzyme, and metabolic pathway engineering.

FULL DESCRIPTION

The dominant technology for directing the evolution of specific biomolecules involves rounds of in vitro PCR mutagenesis, cloning, transformation, and selection. This technique is disadvantageous because there are numerous steps and iterations, and the number of adaptive paths a biomolecule can take is limited. Further, this current approach cannot be scaled up to accommodate multiple, parallel experiments for comparative analysis. Researchers at UC Irvine have addressed these shortcomings by designing a replication system that is specific, continuous, and parallelizable. This invention enables researchers to evolve a gene or a collection of genes toward novel functions that require long mutational paths and large-scale replication of parallel, directed evolution experiments. This system is orthogonal, meaning that the error-prone DNA replication system does not increase the mutation rate of genomic DNA, it enables targeted mutagenesis of the genes of interest. Additionally, the method is entirely in vivo, which allows for continuous mutagenesis. Unlike other systems, this technique may be conducted in highly parallel format, owning to the small volumes required.

SUGGESTED USES

» Protein engineering: Develop novel proteins for medical purposes such as therapeutic antibodies or agricultural uses such as proteins for improving crop yields

» Metabolic pathway engineering: Evolve enzymes and metabolic pathways for superior production of commodity chemicals and biofuels

» Drug development: Utilize platform to understand the emergence of target-based drug resistance and drug screen for alternative lead drug candidates

ADVANTAGES

» In vivo: Invention enables for manipulation of DNA replication inside a cell as opposed to in vitro

» Versatile: User can define selection for even whole-cell or systems-level behaviors

» Targeted: Orthogonal system will limit non-specificity and allow for mutations specifically in the genes of interest

» Parallelizable/High-throughput: Platform is readily amenable to massively parallel evolution experiments

» Continuous/Rapid: Direct evolution of genes that require long mutational paths with >100,000-fold higher than host genomic mutation rates

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OTHER INFORMATION

CATEGORIZED AS

» **Agriculture & Animal Science**
  » Other
» **Biotechnology**
  » Health
  » Industrial/ Energy
  » Other
» **Energy**
  » Bioenergy
  » Other
» **Materials & Chemicals**
  » Agricultural
  » Biological
  » Chemicals
  » Other
» **Medical**

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20230242902	08/03/2023	2017-816

STATE OF DEVELOPMENT

Inventors have developed and tested several working prototypes.

RELATED CASES

2017-816-0

RELATED MATERIALS

» An orthogonal DNA replication system in yeast - 02/02/2014

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