Skysong Innovations
Advancing the Arizona State University Knowledge Enterprise

1475 N. Scottsdale Road, Suite 200
Scottsdale, AZ 85287-3538
Phone: 480 884 1996 Fax: 480 884 1984

Case ID:M16-030L^
Published: 2/26/2020

Inventors

John Chaput
Andrew Larsen
Matthew Dunn

Contact

Jovan Heusser
jovan.heusser@skysonginnovations.com

Highly Sensitive Optical Sensor for Polymerase Screening

The field of synthetic genetics is generating a lot of excitement in the synthetic biology community, especially with the advent of xeno-nucleic acid polymers (XNAs) that can be replicated by standard molecular biology techniques. DNA and RNA have had limited utility in diagnostics and therapeutics because of their rapid degradation by nucleases. XNA polymers have the potential to overcome this shortcoming and offer new chemical properties with therapeutic value. Polymerases that allow for the synthesis of unnatural genetic polymers hold great promise, however, engineering natural polymerases to replicate unnatural genetic polymers is a challenge.

Researchers at Arizona State University have developed a highly efficient system for evolving polymerases for new and improved activities. Using their DrOPS technology, genes encoding active polymerases are identified by the optical signal of their microcomparment on a microfluidic device. This method has been applied to evolve a manganese-independent α-L-threofuranosyl nucleic acid (TNA) polymerase that functions with >99% template-copying fidelity.

This in vitro polymerase selection strategy combines microfluidic control with optical reporting to create a versatile tool that could be used to evolve any polymerase function.

Potential Applications

- Improve the activity of existing polymerases by screening large variant libraries
- Generate new polymerases that utilize templates and substrates with natural or modified components
  - XNA templates
  - Natural DNA templates

Benefits and Advantages

- Signal-to-noise-ratio is ~200-fold over background – this is greater than

existing systems which report STNRs of about 10-20-fold

- Because the STNR is so high, solution based monitoring of polymerase activity is enabled
- Solves the problem of evolving polymerases with activity to non-natural DNA templates
- Holds record for highest enrichment of functional proteins from libraries of ~1,200 fold per round of selection

For more information about the inventor(s) and their research, please see Dr. Chaput's laboratory webpage