Yeast-Based Intein Platform for Drug Production

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing engineered inteins for improved production of fusion proteins in yeast.

OVERVIEW

The therapeutic and biochemical properties of proteins including antibodies can be enhanced by custom chemical functionalization that enables modifications, such as small molecule drug conjugation, PEGylation and conjugation to nanoparticles. Expressed protein ligation (EPL) is one common approach to chemically modify proteins in a site-specific manner. In EPL, the target protein is expressed as a fusion partner to a non-self-cleaving intein such as Mxe GyrA, which is able to excise itself and join the remaining portions.

These fusion proteins are most often expressed in E. coli bacteria. However, there are many disadvantages to using bacteria for fusion protein production. Drawbacks include protein refolding, instability and high loss (up to 90 percent) of the intein during expression.

Yeast provide a promising alternative to bacterial expression systems, given their eukaryotic nature and quality control mechanisms. To fully realize the advantages of a yeast-based platform, novel inteins must be developed to increase production.

THE INVENTION

UW–Madison researchers have engineered non-self-cleaving Mxe GyrA inteins shown to significantly improve the production of fusion proteins from Saccharomyces cerevisiae. The novel inteins were developed through directed evolution, and they enhance fusion protein display (up to 3x) and secretion levels (up to 30x) compared to the wild type intein. The new yeast-based platform provides a robust alternative to bacterial intein expression systems.
APPLICATIONS

- Target end users include pharmaceutical or biotech partners interested in developing protein biologic drug conjugates
- Kit for enhancing production of fusion proteins in yeast

KEY BENEFITS

- Significantly improves fusion protein display and secretion levels
- Competitive alternative to bacteria-based systems

STAGE OF DEVELOPMENT

Through directed evolution the researchers engineered Mxe GyrA intein to increase the amount of scFv-intein fusion proteins displayed on the yeast surface by ~1.5 to 3 fold, thus increasing the amount of chemically functionalized protein obtained via intein-linked yeast surface display. They demonstrated that the engineered intein improves secretion of scFv-intein fusion protein by ~3 to 30 fold over the wild-type intein. The secreted scFvs could be directly modified via EPL, immobilized onto surfaces and employed to bind to their respective antigens.

ADDITIONAL INFORMATION

Tech Fields
Drug Discovery - Drug production & design
Research Tools - Antibodies
Research Tools - Fermentation

CONTACT INFORMATION

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854.