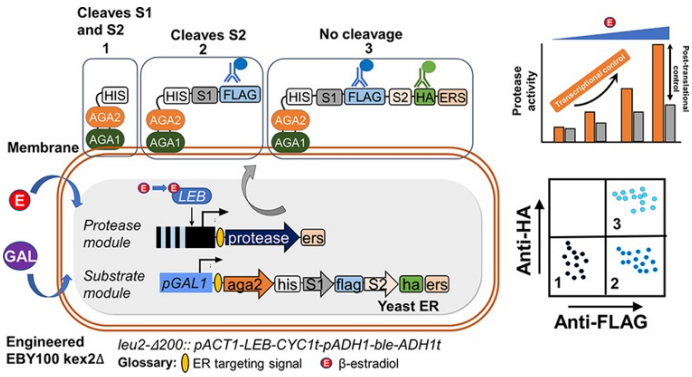
Biologic Therapeutic Discovery Tool

YESS

For discovery and engineering of enzymes

The transformation of monoclonal antibodies into effective therapeutics has coincided with the development of phage display technologies to screen and select for monoclonal antibodies with specific attributes. Proteases are another class of proteins that can be harnessed for a variety of applications due to the diversity and breadth of protease substrate preferences. Different approaches for enzyme engineering have been tested to date, and are illustrated in the figure on the right.

Based on similar characteristics to phage display, Dr. Iverson and colleagues have developed, YESS (**Y**east **E**ndoplasmic **S**equestration **S**ystem) a highly versatile system for screening, selecting, engineering and characterizing enzymes such as proteases with desired new activities. YESS 2.0, depicted in the figure below, is coupled with Next-Gen sequencing, circumventing the need to have purified proteins, and enabling access to a large sample of sequences (100 million), offering advantages over existing technologies.



Using YESS, our scientists have generated a superior TEV Protease, which has 8-fold higher catalytic efficiency compared to the industry benchmark, demonstrating that it's possible to alter an enzyme's substrate affinity and specificity while increasing its turnover rate.

YESS2.0

Work is ongoing to alter the specificity of other enzymes such as MMP7, kallikreins, neutrophil elastase, neprilysin, and catehpsin E. For example, to develop a treatment for SLE, the Iverson lab has repurposed the specificity of human matrilysin (hMMP7), a metalloprotease involved in the breakdown of extracellular matrix, to specifically cleave the IgG hinge region which leads to IgG deactivation. Using YESS, they have identified candidates that have altered substrate specificity and are now seeking to engineer enhanced stability to select a lead candidate for therapeutic development.

YESS is available for partnering

Patents and publications:

US8945855, US9546359, CA2,877,346, EP2864480, FR2864480, DE602013026157.1, CH2864480, UK2864480

US10900059, EP3207150, CA2,964,467

US16/178,991, AU2018358144, CA3079985, EP18874197.9

ACS Synth Biol. 2021 Jan 15;10(1):63-71.

ACS Chem Biol. 2019 Sep 20;14(9):1888-1895.

ACS Chem Biol. 2017 Feb 17;12(2):510-518

Methods Mol Biol. 2015;1319:81-93.

Proc Natl Acad Sci U S A. 2013 Apr 30;110(18):7229-34.

Clayton Biotechnologies Inc.
One Riverway, Suite 1520
Houston, TX 77056
+41-76-342-7147
arichardson@claytonbiotech.com

www.claytonbiotech.com