EVOSELECT®

MACHINE LEARNING PLATFORM FOR
ENZYME ENGINEERING

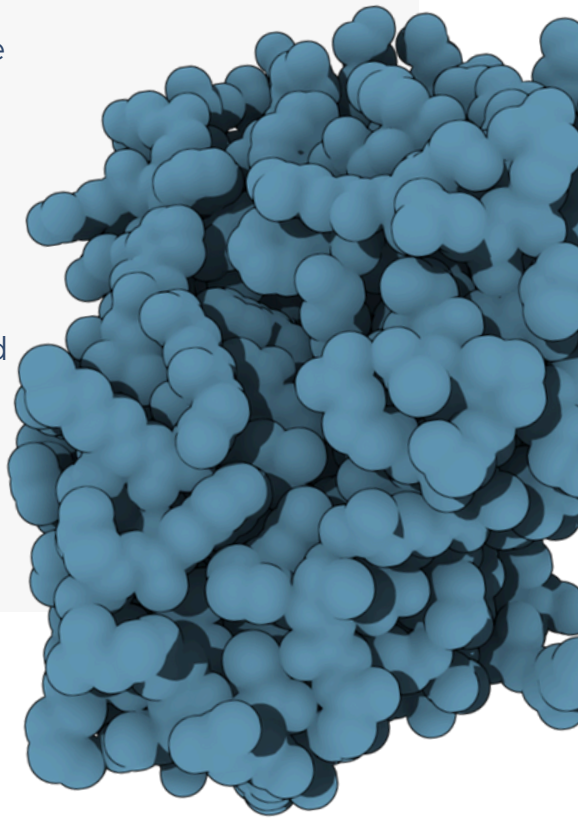
ISOMERASE

www.isomerase.com

EVOSELECT®

MACHINE LEARNING ENZYME ENGINEERING TOOL

EVOSELECT® is a machine learning-based enzyme engineering platform offering a revolutionary approach to protein design. It combines big data from proprietary and public protein sequence databases with evolutionary coupling analysis and *in silico* mutation simulations to predict beneficial enzyme mutations virtually. By simulating directed evolution *in silico*, EVOSELECT® drastically accelerates development – delivering optimized enzymes in as little as **6 weeks** – and produces variants tailored to specific properties.



ADDRESSING KEY INDUSTRIAL CHALLENGES IN ENZYME PERFORMANCE

Enzymes denature at high temperatures or lose activity in non-native conditions.
EVOSELECT® predicts beneficial mutations by leveraging proprietary sequences from extremophiles and mesophiles, enabling combination of valuable properties such as heat, solvent and pH stability with low-temperature activity, generating variants with robust industrial performance.

Requirement for patent protection or patent restrictions limit enzyme commercialisation.
EVOSELECT® can rapidly generate improved novel industrial enzymes with <80% identity to seed sequences, enabling patent protection and/or avoiding issues with competitor patent portfolios.

Biocatalysis costs are driven up by enzyme degradation over time and limited recyclability.
EVOSELECT® enhances enzyme stability through beneficial sequence modifications, improving resistance to inactivation, extending catalytic cycles and lower process costs.

Traditional enzyme development is slow and costly.
EVOSELECT® predicts beneficial mutations *in silico*, prioritising high-fitness variants for lab testing, reducing R&D time to 6-8 weeks and lowering costs, with typical projects costing <$100K with no additional milestones or downstream costs.

OUR SOLUTION TO PROTEIN ENGINEERING

Innovation
Generates **proprietary enzymes** with FTO

Speed
Ready-to-use enzymes in **<2 months**

Cost Efficiency
Screen **as few as 20-40** candidates, reducing costs

Improved Stability
Enhanced **thermal stability**, **solvent tolerance** and **enzyme recycling**

HOW IT WORKS

1. Input Sequence
Utilizes seed sequences provided by clients or sourced from literature as the foundation for optimisation.

2. Homology Analysis
Generates sequence alignments of homology families; drawn from public and proprietary sequence databases with a high prevalence of sequences from thermophilic genomes.

3. Predicting Evolutionary Couplings
Performs unsupervised learning to identify statistical patterns in the co-evolution of amino acid residues (inter-residue couplings).

4. Mutational Fitness Landscape
Uses machine learning-based probabilistic models to predict the impact of mutations. A priority matrix is constructed, ranking

mutations most likely to enhance enzyme fitness. This approach ensures greater accuracy compared to traditional single-site mutational methods.

CASE STUDY
KRED FAMILY

Objective

Develop novel ketoreductases with enhanced **thermal stability** using EVOSELECT®.

Approach

- Two well-studied enzymes were selected as seed sequences: YvgN (*B. subtilis*) and DkgA (*E. coli*).
- 5 EVOSELECT® variants were generated for each enzyme. YvgN and DkgA variants were ~80% and ~70% identical to parent sequence, respectively.
- Analytical monitoring for expression and activity was performed in-house.

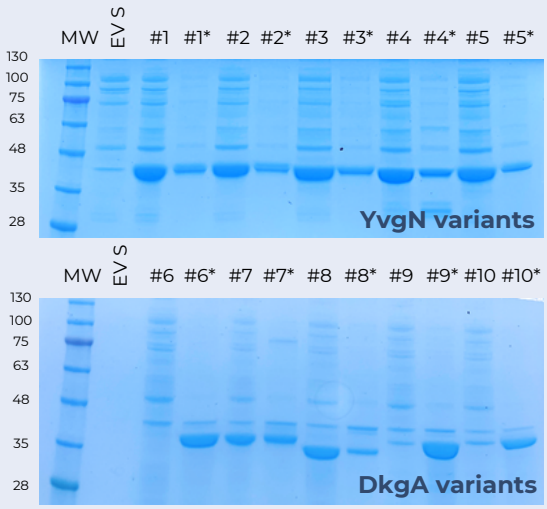


Figure 1. SDS-PAGE analysis of of YvgN and DkgA variants. Insoluble fractions are sindicated by (*).

5. Generation of Optimised Variants

Builds a generative probabilistic interpretation out of the model, from which we iteratively sample mutations, simulating evolution and generating new sequences with improved fitness.

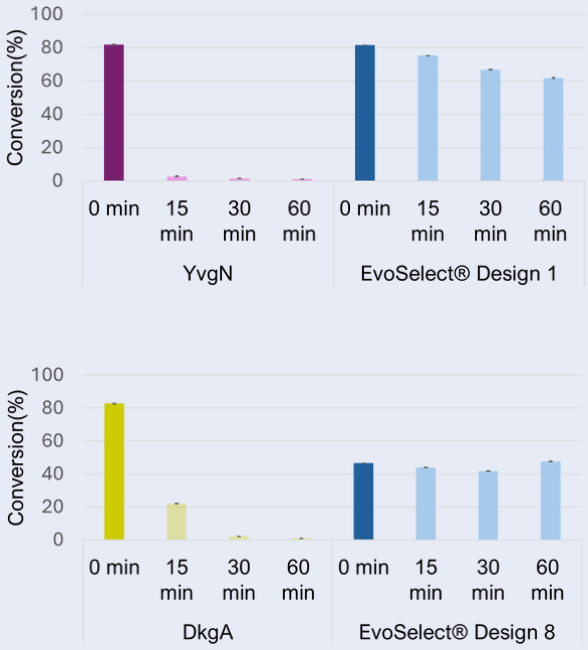


Figure 2. Enzymatic activity assessment for purified controls and of EvoSelect® variants. YvgN, DkgA and variants with higher activity of each set (Designs 1 and 8) were purified using His-tag affinity chromatography and assessed over extended periods to evaluate stability and performance.

Results

- Minimal set assessed (10 variants in total)
- 90% of variants exhibited soluble expression
- 60% of variants demonstrated higher thermal stability compared to the parent following stress test

END-TO-END SOLUTIONS FOR DISCOVERY & DEVELOPMENT

EVOSELECT® can be seamlessly integrated into the ISOZYM™ platform, which provides an **end-to-end solution for protein discovery and production**. By partnering with us, you gain access to a comprehensive suite of services, including expression using our proprietary industrial chassis or your preferred host, advanced analytics, process development, and scale-up. This ensures consistency, efficiency, and accelerated timelines across all stages of development. Each step can be executed as standalone work package based on the partner's current research or development stage, or combined into a cohesive workflow to support end-to-end enzyme production. In addition, using quality by design (QbD) tools we can define and characterise the product critical quality attributes (CQAs), perform extensive risk assessment and map all process parameters and materials to the quality specifications. We define what is critical to quality (CTQ) and generate bespoke control strategies to remove and reduce risk for our partner processes.

OUR DIFFERENTIATORS

Innovation

We combine deep expertise with proprietary tools for faster, more precise discovery and development.

Flexibility

We adapt and provide services across different sectors, technologies and client needs.

Integrated Solutions

Our in-house approach streamlines development by integrating most stages under one roof, eliminating complex tech transfers.

Ownership

Target and system developed belong to your organization – **no downstream costs**.

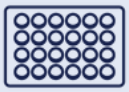
EXAMPLE PIPELINE

TYPICAL PROJECT TIMELINE: 8 WEEKS

Target enzyme /
Input seed sequence

EVOSELECT® iteratively mutates sequences to align with target criteria

Codon Optimisation
+ DNA synthesis



~40 Candidates overexpressed in ISOCHASSIS hosts and screened using SDS-PAGE and enzyme assay

~ 6 weeks turnaround

Select best enzyme candidate for material supply

~ 8 weeks turnaround

Stirred tank reactor trials and simple DSP to generate ~1-10g of selected enzyme for supply

DELIVERABLES

- Typical cost <$100K, ~8 weeks from sequence to material
- Report including recommendations, data on all enzymes tested and all enzyme sequences
- Supply of 1-10g of selected enzyme
- **No downstream costs or royalties required for commercial use**

CONTACT US

Discover how we can rapidly transform your enzyme needs into solutions ready for commercialisation

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