

Integrated Enzyme Technologies

- Integrated biology facility providing expertise from discovery through to commercially viable enzymes
- Rapid enzyme library generation and supply
- Enzyme engineering
- Enzyme formulation development & immobilisation
- Strain and synthetic pathway engineering
- Fermentation development & scale-up
- Commercial enzyme supply
- **selectAZyme™**



Integrated Enzyme Technologies

At Almac we have the expertise and capabilities to deliver enzyme technologies from their discovery through to commercial enzyme supply

Enzyme discovery

- Access to large novel INSIGHT databases of gene and protein sequences
- A wide range of DNA, genomic and protein sequence analytical tools, as well as evolutionary biology computational tools
- Expertise in building, annotating, and querying biological pathways
- Expertise in the study of the protein structure using computational chemistry methods and bioinformatics tools
- Highly experienced bioinformaticians who provide inclusive analysis on DNA, protein and protein modelling

These capabilities enable us to provide unique panels of enzymes built around your specific transformation within weeks.

Enzyme engineering

Enzyme performance can be increased through both computational and directed evolution expertise. We have evolved enzymes for increased selectivity, activity, solvent tolerance and thermostability.

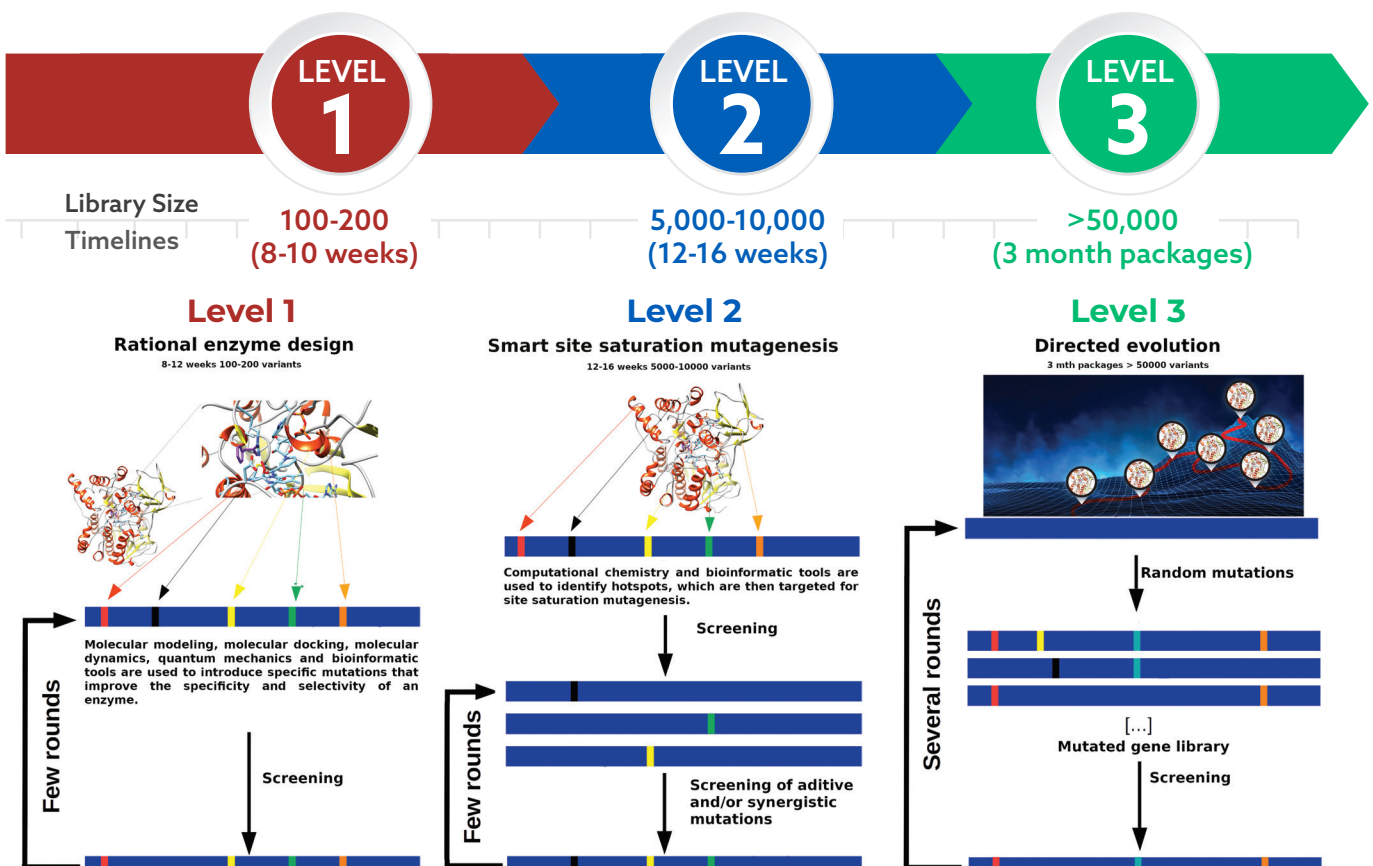
- Directed evolution by both site-specific and random mutagenesis
- Specialists in expression systems such as *E.coli*, *P.pastoris*, *Streptomyces* & *saccharomyces cerevisiae*
- Computational physics based and machine learning methods that allow rational and focussed site saturation mutagenesis
- Rapid screening of libraries using parallel UPLC systems
- High throughput assay development and screening

Enzyme manufacture

With extensive experience in fermentation, we can optimise the fermentation protocol for your specific process to obtain kilograms to tonnes of enzyme. Our enzymes can be tailored for your process by our dedicated team.

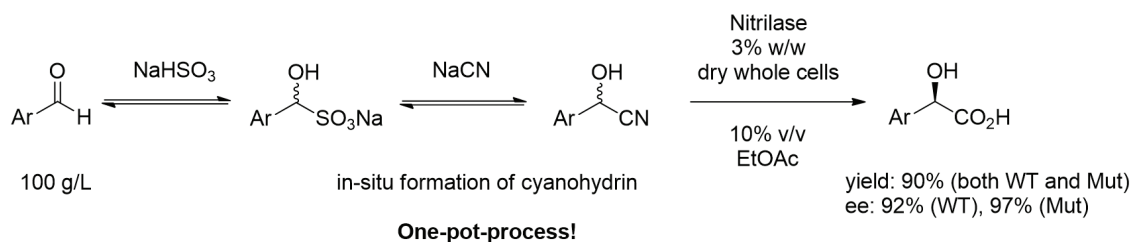
- Fermentation development from shake flask scale to batch fermentation in weeks
- High level of expertise in optimisation of fermentation and downstream processing
- Fermentation capabilities from 1 L to 15 m³
- Formulation in multiple physical forms

Our approach to engineering



Case studies

Case study 1 - Process development and Nitrilase screening



Our client required an enzyme mediated synthesis of (R)-2-methoxy mandelic acid.

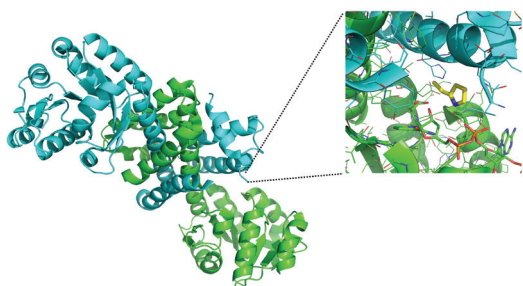
Almac's solution involved screening of the selectAZyme™ Nitrilase library followed by rational enzyme design and process development to improve selectivity and activity. A one-pot process was implemented without need for

cyanohydrin intermediate handling. A yield of 90% and ee. of 97% for the best variant was achieved.

Value for client:

Purpose built one-pot process without need for handling with a highly toxic intermediate. Access to an active and highly selective Nitrilase enzyme.

Case study 2 - Recombinant enzyme panel building and screening



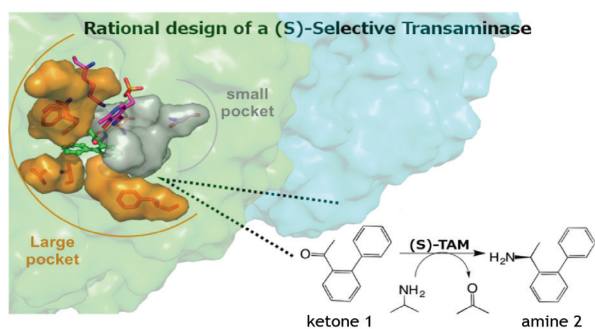
Our client required access to cyanide manipulating enzymes.

Almac's solution was to create a panel of cyanide dihydratase enzymes using our computational and bioinformatics expertise combined with expertise in micro- and molecular biology.

Value for client:

Purpose built enzyme panel for their specific process.

Case study 3 - Transaminase enzyme molecular modelling and engineering



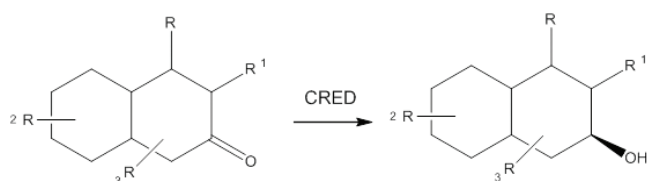
Our client had previously screened our transaminase selectAZyme™ panel against their substrate and achieved a successful hit. They required the enzyme to be more active and selective for their product.

Almac performed molecular modelling with substrate docking studies to identify key residues for mutations. These new enzymes were tested for activity. We were able to increase the activity more than 1716 fold.

Value for client:

Access to active and selective transaminase enzyme for production of a chiral amine.

Case study 4 - CRED enzyme supply



Our client required 60 kg of carbonyl reductase (CRED) enzyme for a bioreduction step in their process.

Almac utilised their experience in fermentation to develop and optimise the fermentation procedure leading to rapid scale-up and enzyme supply.

Value for client:

Access to cost-effective spray dried enzyme for bioreductive process.

Supporting Capabilities

Almac's integrated enzyme technologies can be applied throughout the product lifecycle to guide your synthesis projects from conception to scale-up

Research and development

- Enzyme screening
- Access to selectAZyme™ libraries
- Smart enzyme discovery and engineering
- INSIGHT metagenomics enzyme discovery
- Machine learning assisted enzyme discovery and engineering
- Directed evolution enzyme engineering
- Strain and pathway engineering
- Biotransformation process development
- Enzyme immobilisation development

Process intensification and manufacture

- Ultrasound assisted biotransformation technology
- Integrated chemical manufacture of intermediates
- Immobilised enzyme supply
- Intermediate and active ingredient supply

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