Industrial Applications of Marine Enzymes

Innovative screening and expression platforms to discover and use the functional protein diversity from the sea

www.inmare-h2020.eu

The INMARE project brings together facilities, biotechnology tools, genetic resources and scientific experts from more than 20 academic and industrial partners across 12 countries, to mine for and use newly-discovered marine microbial enzymes and metabolites for the targeted production of fine chemicals, environmental clean-up technologies and anti-cancer drugs.

The main objectives of INMARE are:

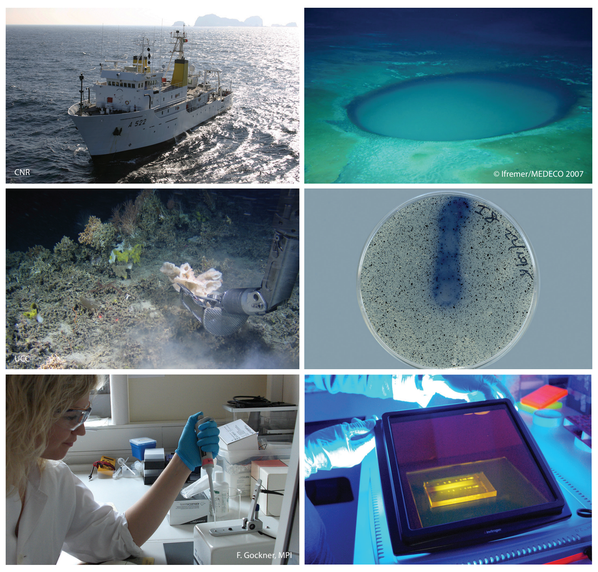
1. **Streamline and significantly shorten the pipelines of marine enzyme and bioactive compound discovery for industrial applications;**
2. **Develop marine enzyme collections with a high proportion of promising enzyme-allrounders;**
3. **Identify new lead products and deliver prototypes for new biocatalytic processes based on marine microbial enzyme resources for targeted production of fine chemicals, drugs and materials for use in environmental clean-up applications.**

Marine enzymes for industrial applications

With a growing global population our societies are facing important challenges in food and energy security, sustainable economic development, maintaining the health of ageing populations and protecting the environment from over-exploitation, degradation and pollution. While terrestrial resources are being depleted, our seas and oceans offer a sustainable source of materials, food and energy, as well as potential for the development of new drugs and biotechnological applications.

Marine bio-resources hold particular promise for innovation in industrial biotechnology - a growing sector developing "greener" bio-based alternatives to current chemical production processes that use environmentally damaging bulk organic solvents and energy-demanding processes.

Most industrial biotechnology processes are derived from micro-organisms. It is anticipated that new processes and applications will emerge from research on as-yet unknown microbial biodiversity: "microbial dark matter". An area that remains largely untapped as a source of microbiological organisms is our ocean: the marine environment could provide new resources from which to produce safer, cheaper and greener products and industrial processes.

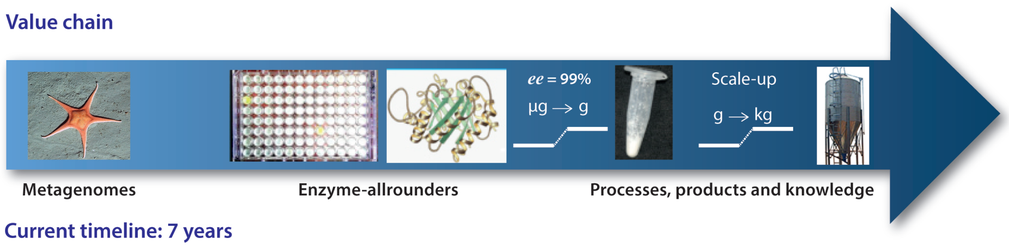


Life began in the ocean and 3.5 billion years of evolution has given rise to a wealth of untapped genes, enzymes and natural products that could have industrial application. Marine microbes are of special interest because they dominate our planet in terms of cell numbers, numbers of species, total biomass and the range of environmental conditions in which they can grow.

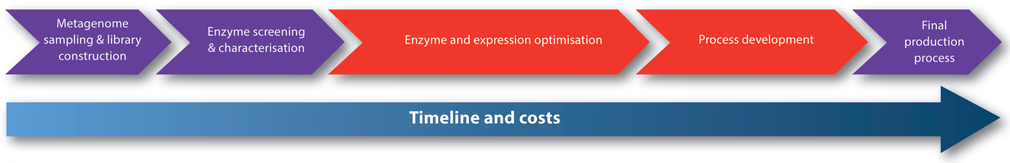
The marine environment hosts some of the most challenging conditions on Earth, from high pressures in the deepest parts of the ocean, to temperatures of more than 300° C at hydrothermal vents and extreme chemical conditions in hypersaline brine pools and at cold seeps. The metabolic diversity of microorganisms adapted to survive in these conditions could provide a source of enzymes uniquely able to perform in industrial settings characterised by harsh physical and chemical conditions.

INMARE partners will assess enzymatic potential using genetic resources available from previous research efforts, but will also construct novel gene libraries by collecting samples from new environments across about thirty hotspots of marine microbial biodiversity in the search for relevant enzymes and bioactive compounds.

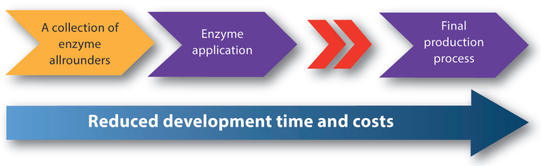
Value chain



Current timeline: 7 years



Research goal: timeline of 0-3 years



INMARE aims to shorten the biodiscovery pipeline, reducing the lengthy steps of enzyme optimisation and process development, and improve the upstream quality of metagenomics samples and library.

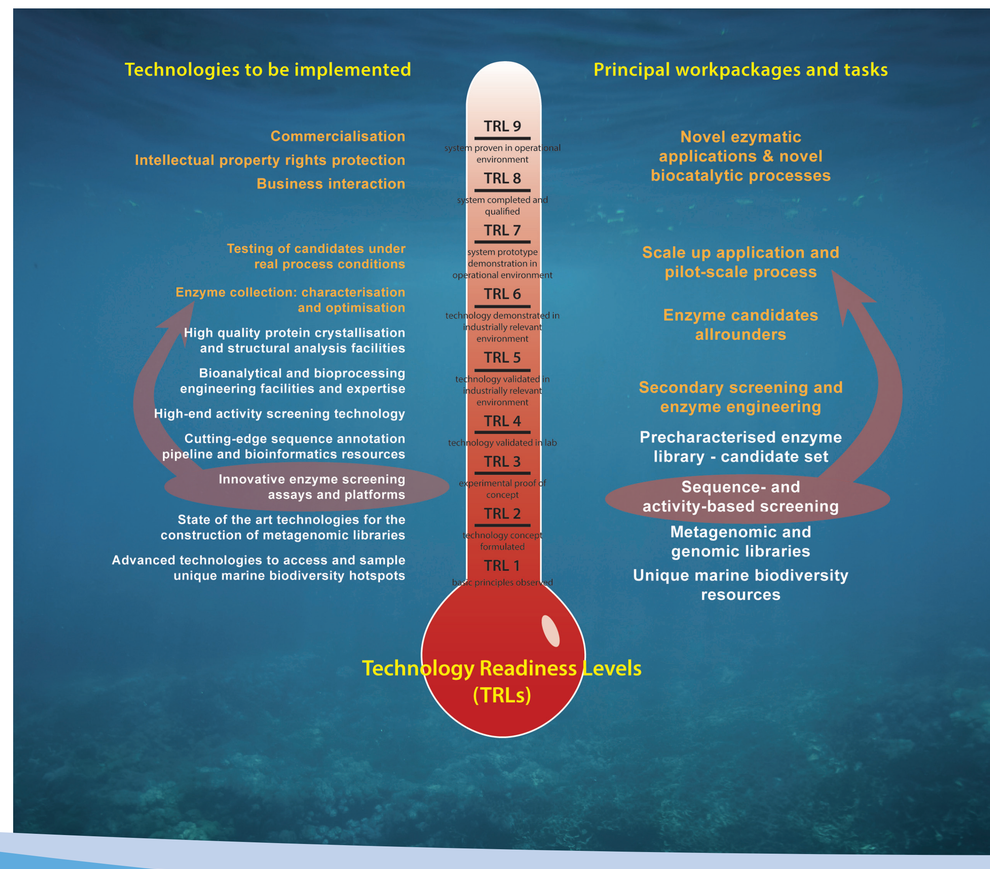
Graphic adapted from Ferrer et al., 2015.

Streamlining the enzyme discovery pipeline

Despite their potential for industrial applications, to date very few (marine) microbial enzymes have actually made it to the commercial market. While approaches such as metagenomics have provided new avenues for developing novel applications from marine microbes, many challenges remain. One of the major bottlenecks is the laborious, costly and unreliable enzyme optimisation process required to make enzymes more stable and perform better in industrial processes.

To circumvent this problem, the INMARE project will focus more attention on the early stages of the biodiscovery pipeline towards finding better natural enzyme variants - so called **enzyme-allrounders** - that perform a range of desirable functions under a set of realistic industrial conditions.

INMARE aims to streamline and shorten the biodiscovery pipeline, addressing all steps from sampling marine biodiversity hotspots, through to enzyme and bioactive compound discovery and development of prototypes. This involves state-of-the-art approaches and technologies covering various Technology Readiness Levels (TRL). Emphasis will be placed on TRL 1-6, with the development and implementation of innovative approaches to bypass or significantly shorten the cumbersome enzyme and expression optimisation stage. Within the lifetime of INMARE, new enzymatic applications corresponding to levels TRL 7-9 will be brought to the market.



Key INMARE activities

To achieve the project objectives, INMARE scientists will perform the following key activities:

- Explore novel biodiversity resources by sampling unique marine microbial biodiversity hotspots;
- Establish innovative screening platforms to identify relevant enzymes and bioactives;
- Construct and fine-tune sequence analysis pipelines for targeting enzymes and identification of pathways for drugs biosynthesis;
- Streamline gene identification in positive clone hits and in sequencing data;
- Expand the spectrum of hosts for heterologous protein and metabolite expression;
- Shorten the enzyme optimisation and processing steps by testing enzyme candidates under application conditions at the early discovery stage;
- Obtain enzyme-allrounders by screening collections against compounds representing challenging chemical steps in actual applications;
- Transfer the gained knowledge about allrounders to other enzyme classes;
- Identify new lead products and prototypes as well as delivery of new biocatalytic processes;
- Improve knowledge transfer pathways, enabling intellectual property protection and faster commercialisation.

The INMARE partnership

Bangor University, UK (Coordinator)
University of Hamburg, Germany
Heinrich Heine University of Düsseldorf, Germany
Consiglio Nazionale delle Ricerche, Italy
Agencia Estatal Consejo Superior de Investigaciones Científicas, Spain
Bayer Technology Services GmbH, Germany
Novozymes A/S, Denmark
University of Bergen, Norway
National University of Ireland, Cork, Ireland
Institute of Biochemistry, Vilnius University, Lithuania
Jacobs University, Germany
Pharma Mar S.A., Spain
Technical University of Crete, Greece
University of Bologna, Italy
Associação do Instituto Superior Técnico para a Investigação e Desenvolvimento, Portugal
evocatal GmbH, Germany
INOFEA Ltd, Switzerland
University of Applied Sciences and Arts, Switzerland
London School of Economics and Political Science, UK
Cluster Industrial Biotechnology CLIB2021, Germany
University of Toronto, Canada
Seascape Consultants Ltd, UK
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