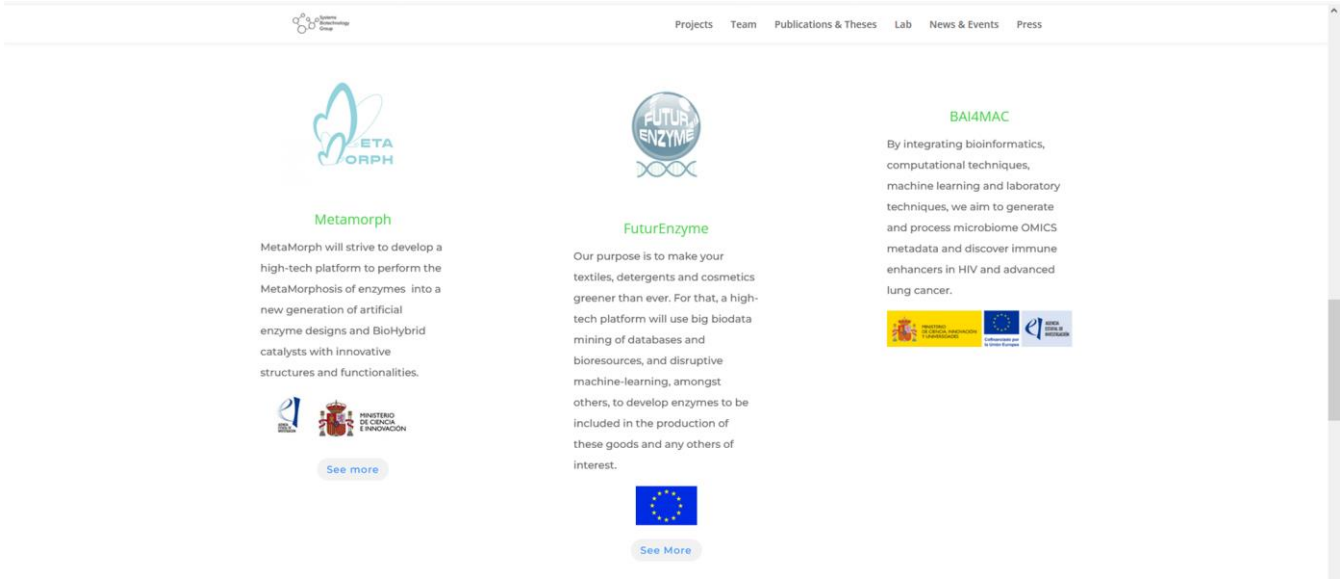
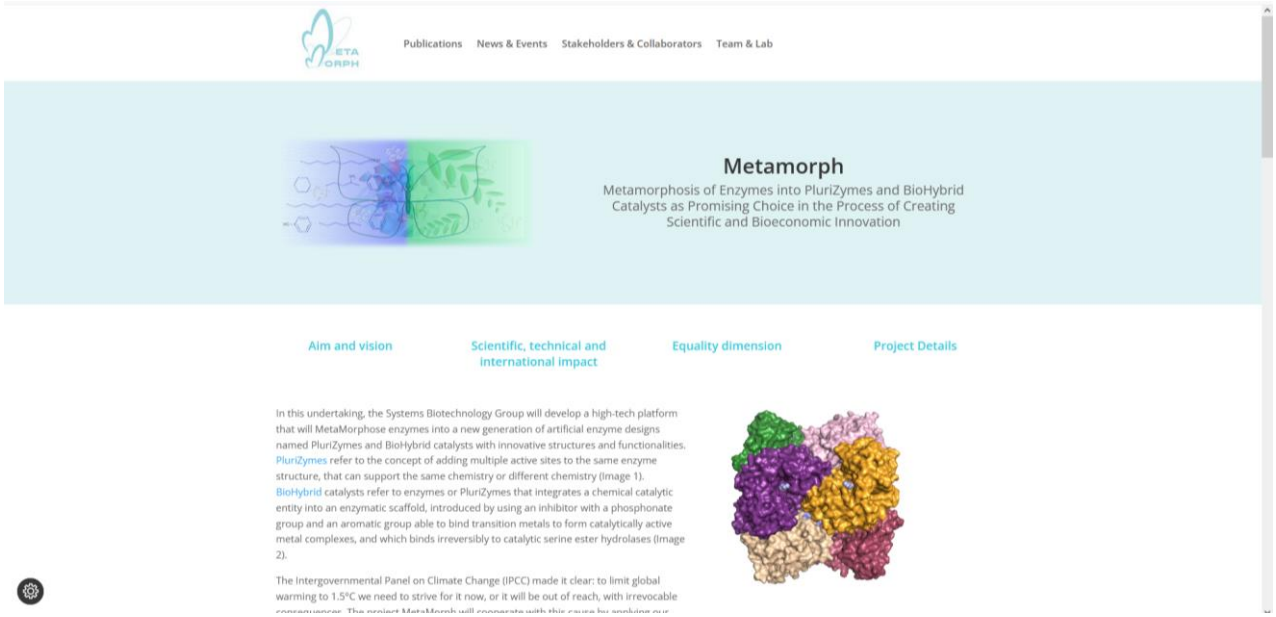
"METAMORFOSIS DE ENZIMAS A PLURIZIMAS Y CATALIZADORES BIOHIBRIDOS COMO OPCION PROMETEDORA EN EL PROCESO DE CREACION DE INNOVACION CIENTIFICA Y BIOECONOMICA", PID2020-112758RB-I00

Anexos

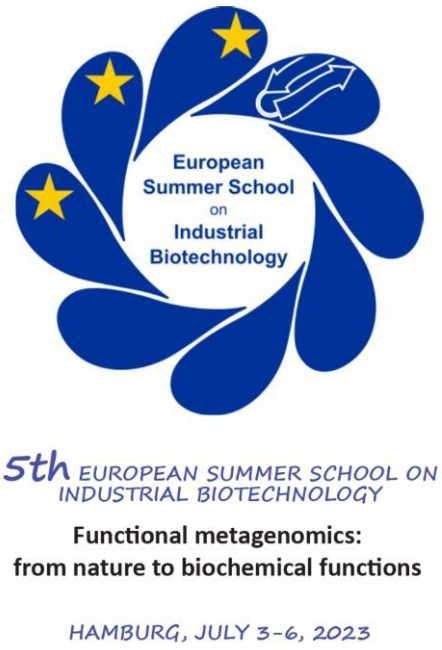
Imágenes/textos representativos que ejemplifican la referencia a la fuente de financiación

Web





Carteles/resúmenes (abstract)



Dr. Cristina Coscolín, Laura Fernández López & Paula Vidal Ramón
Institute of Catalysis – CSIC, Spain Poster #22 #23 #24

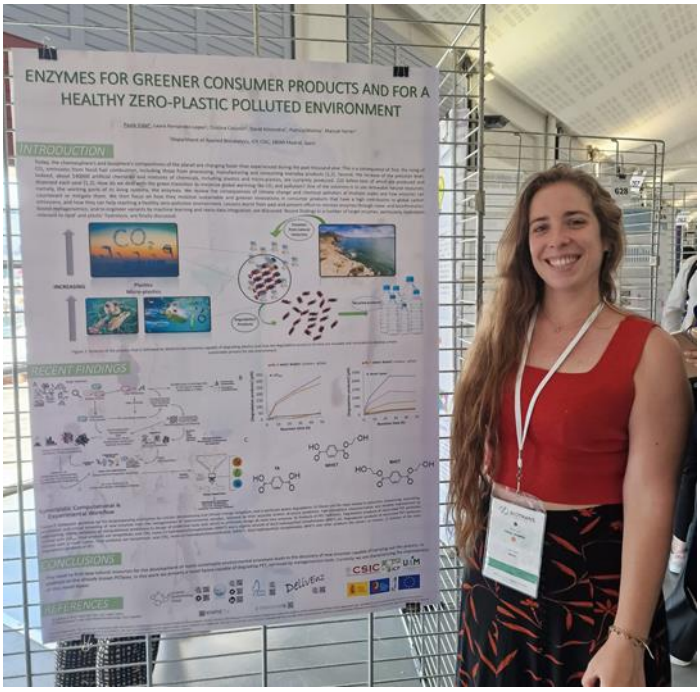
Current research topics: Biocatalysis, enzyme engineering

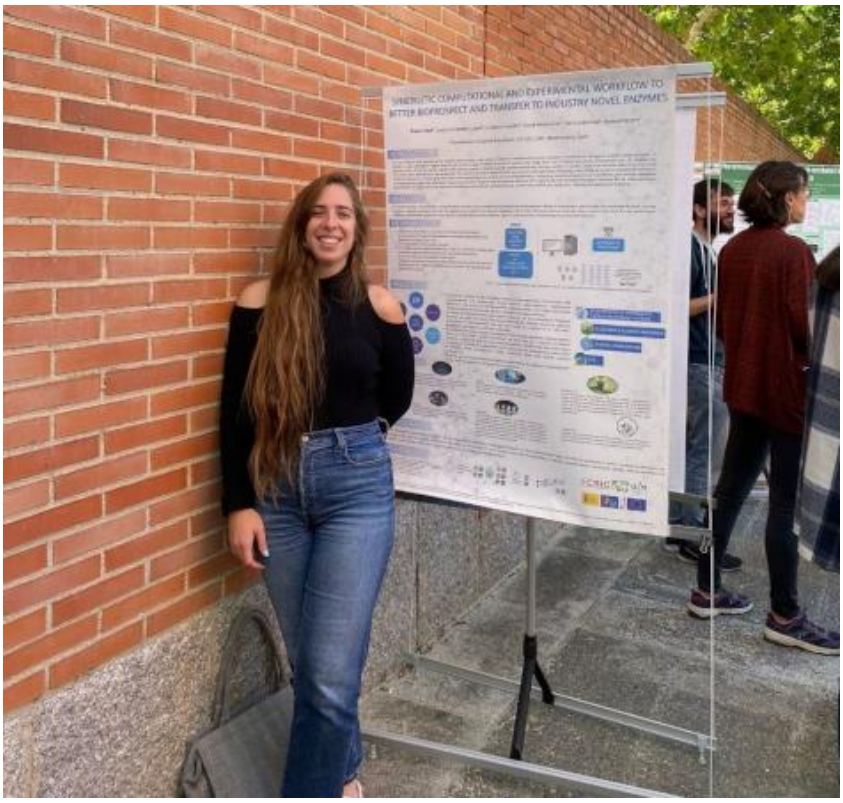
SysBio - Enzymes to the people: mitigate together climate change and promote circular bioeconomy

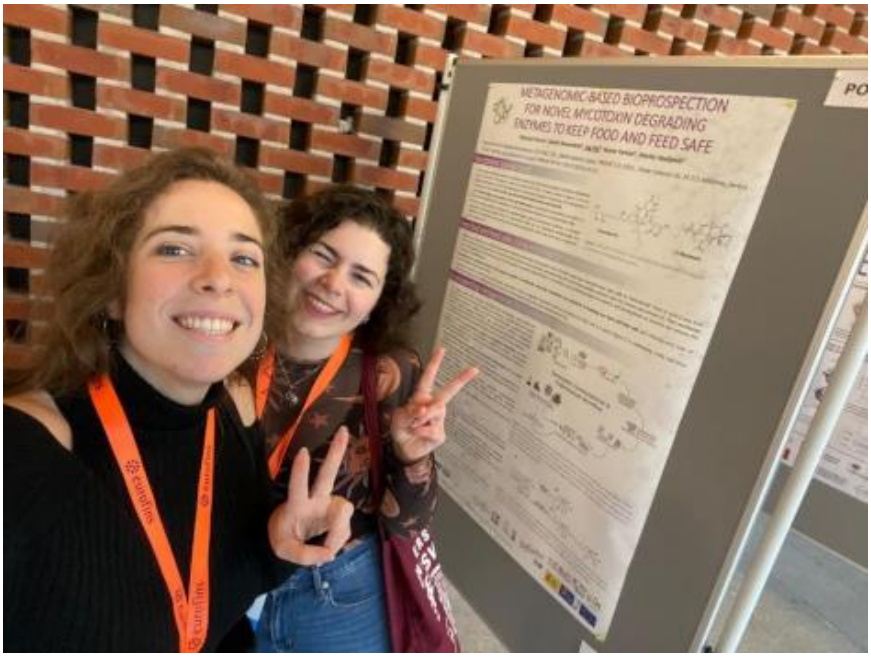
Laura Fernandez-Lopez[1], Paula Vidal[1], David Almendral[1], Patricia Molina-Espeja[1], Cristina Coscolín[1], Manuel Ferrer[1] [1]Instituto de Catalisis y Petroleoquimica, ICP, CSIC, Marie Curie 2, 28049, Madrid, Spain The Systems Biotechnology (SysBio) group (https://sysbio.csic.es/) is located at the Institute of Catalysis and Petrochemistry (ICP) (Madrid, Spain), which belongs to the Spanish National Research Council (CSIC).

Our scientific activity is marked into the biotechnology field, which uses microorganisms or parts of them to substitute traditional chemical reactions for greener and more efficient biological solutions. Our team is composed by chemists, biochemists and biologists which confer a multi- and inter-disciplinary view to all projects. The SysBio group offers and covers all steps from enzyme discovery (including meta-genomics) to engineering and implementation in multiple processes and products of interest for multiple industrial sectors. Subsequently, the accumulated knowledge of the bioprospecting and study of hundreds of new enzymes combined with engineering and material science techniques allowed the team to undertake leading investigations aimed at achieving a detailed understanding of the mechanisms underlying and tuning the properties of enzymes. Serve as examples recent works that investigate the mechanisms by which enzymes become promiscuous1, the adaptation of enzymes and the microbes that contain them to climate change2, and a recent investigation proposing a new strategy of enzyme supramolecular engineering based on a meticulous modification of a synthetic shell that surrounds an immobilized enzyme3. Most recently, the team members acquired expertise in computational techniques which have constituted the basis of a novel research addressing the design of a new generation of artificial enzymes with multiple active sites, the PluriZymes4,5. Bioinformatics and computational integration of multiple enzyme reactivity data is also allowing us to contribute to establishing the basis for predicting enzyme properties from enzyme sequence without the need for enzyme characterization6. To undertake all these activities, in the context of our effort to circular economy and climate change fighting7, it is crucial to know which are the requirements of industry. This is why we are constantly working with several companies in our different projects from a wide variety of sectors, such as those covering fine chemicals, food and feed, cosmetics, textiles, detergents, etc. Companies give us a set of necessities and real materials to start with, which constitute the base for bioprospecting and engineering enzymes a-la-carte. Science popularization and gender equality are also driven the SysBio group, and all our projects have an ecofriendly orientation. In this contribution, we summed up relevant investigations driven the SysBio commitment for the implementation of biocatalysts in our everyday life so we can help to mitigate climate change and move towards bioeconomy and circular economy7.

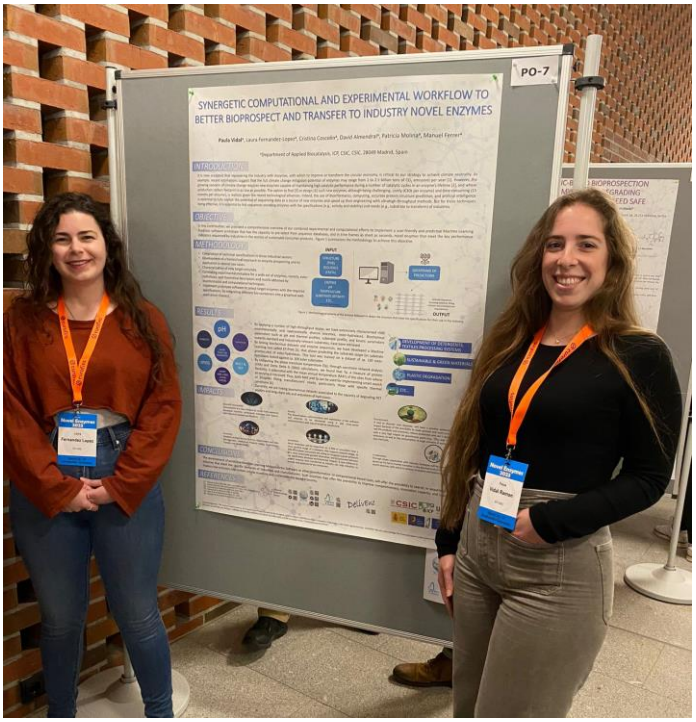
References 1Martínez-Martínez M, et al. ACS Chem Biol. 2018; 13:225-234. 2Marasco R, et al. Nat Commun. 2023; 14:1045. 3Giunta CI, et al. ACS Nano. 2020; 14:17652-17664. 4Alonso S, et al. Nat Catal 2020; 3:319-328. 5Roda S, et al. Angew Chem Int Ed Engl. 2022; 61:e202207344. 6Xiang R, et al. Biomolecules. 2022; 12:1529. 7Molina-Espeja P, et al. Oxford Open Climate Change, 2023; kgad003. Acknowledgements We acknowledge the FuturEnzyme Project funded by the European Union's Horizon 2020 Research and Innovation Programme (Grant Agreement No. 101000327), and the Grants PID2020-112758RB-I00, PDC2021-121534-I00, and TED2021-130544B-I00 from the Ministerio de Ciencia e Innovación, Agencia Estatal de Investigación (AEI) (Digital Object Identifier 10.13039/501100011033), and the European Union ("NextGenerationEU/PRTR").


ENZYMES FOR GREENER CONSUMER PRODUCTS AND FOR A HEALTHY ZERO-PLASTIC POLLUTED ENVIRONMENT
INTRODUCTION
RECENT FINDINGS
CONCLUSIONS
REFERENCES




METAGENOMIC-BASED BIOPROSPECTION
FOR NOVEL MYCOTOXIN DEGRADING
ENZYMES TO KEEP FOOD AND FEED SAFE


SYNERGETIC COMPUTATIONAL AND EXPERIMENTAL WORKFLOW TO
BETTER INSPROSPECT AND TRANSFER TO INDUSTRY NOVEL ENZYMES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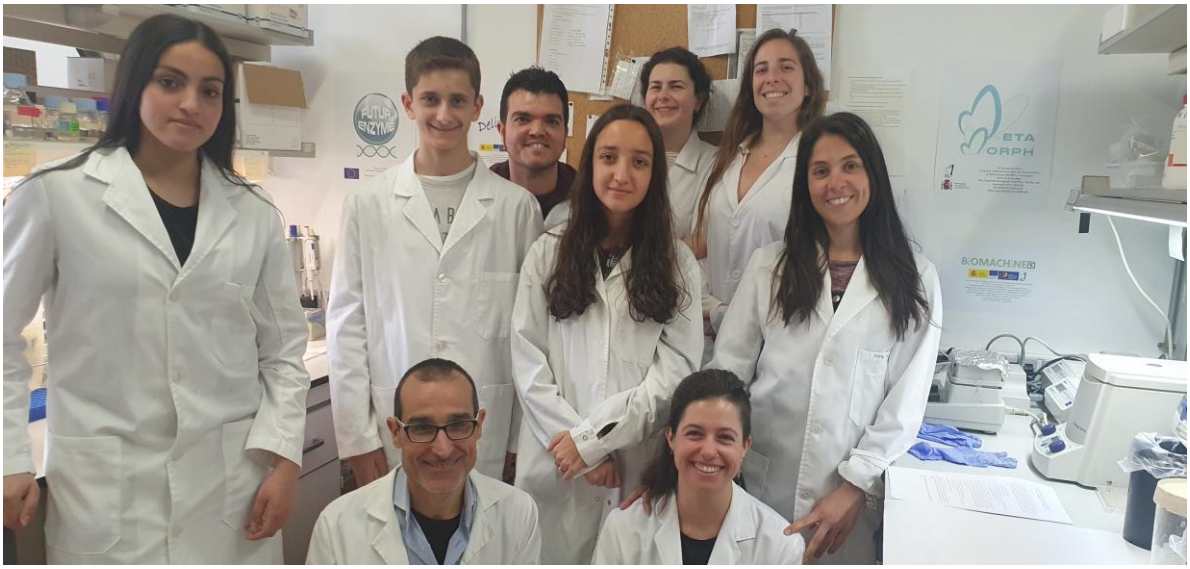
SYNERGETIC COMPUTATIONAL AND EXPERIMENTAL WORKFLOW TO BETTER BIOPROSPECT AND TRANSFER TO INDUSTRY NOVEL ENZYMES


FUTUR ENZYME
ETA ORPH
BIOMACHINES

SysBio - Enzymes To The People: Mitigate Together Climate Change And Promote Circular Bioeconomy

Laura Fernandez-Lopez[1], Paula Vidal[1], David Almendral[1], Patricia Molina-Espeja[1], Cristina Coscolín[1], Manuel Ferrer[1]

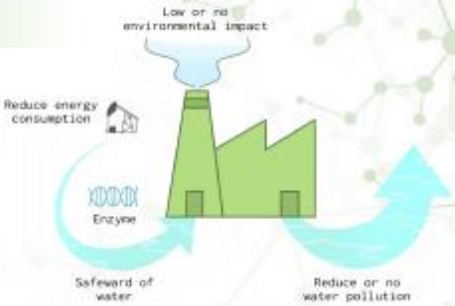
[1]Department of Applied Biocatalysis, ICP, CSIC, 28049 Madrid, Spain

SYSTEMS BIOTECHNOLOGY GROUP

CROSS-FUNCTIONAL TEAM

Biologists · Biochemists · Chemists

From enzyme discovery and the study of enzyme properties and adaptations [1,2] to engineering [3-5] and implementation of enzymes in industrial sectors [7].



DIVERSE INVESTIGATION

Circular bioeconomy: Enzymes are biodegradable molecular tools that can modify goods to make their materials reusable, slash energy consumption and replace hazardous chemicals while improving the quality of end-products [7].

FUTURENZYME

New "smart" enzymes implemented by screening and design can help improve real-life consumer products to become greener, more innovative and more functional. Having the least impact on the environment and higher acceptance in textile, cosmetic and detergent sectors.

METAMORPH

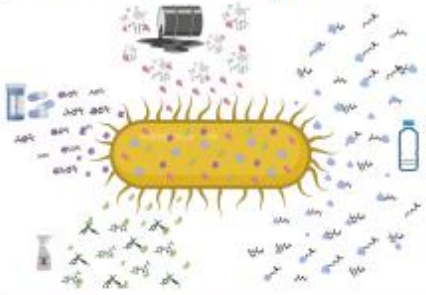
A high-tech platform to perform the MetaMorphosis of enzymes into a new generation of artificial enzyme designs (*PluriZymes*) and BioHybrid catalysts (using suicide inhibitors coordinated with metals, SI) fitting for circular bioeconomy [1,2].

NYMPHE

Usage of microbial interaction in the microbiome of real EU contaminated sites to remove the main contaminants and improve their biodiversity.

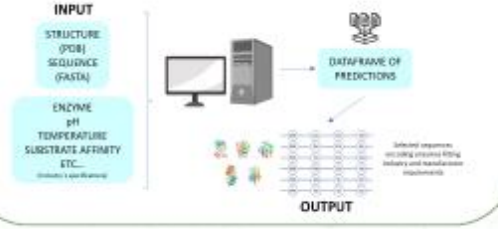
BIOMACHINES

"Nature-inspired" and "Artificial intelligent-edited" biologics with which to create and implement plastic degradation strategies.



DelivEnz

A predictive Machine Learning Metapredictor Software prototype that has the capacity to pre-select in time frames as short as minutes, enzymes that meet the key performance indicators (KPIs) requested by industry from any sequence database [6].



CONCLUSIONS

REDUCE · REUSE · RECYCLE

REFERENCES

[1] Martínez-Martínez M, et al. ACS Chem Biol. 2018; 13:215-234 [2] Maresca R, et al. Nat Commun. 2018; 19:1045 [3] Giuliani G, et al. ACS Nano. 2020; 14:17652-17664 [4] Alonso S, et al. Nat Catal 2020; 3:319-328 [5] Roda S, et al. Angew Chem Int Ed Engl. 2022; 61:e202207344 [6] Xiang R, et al. Biomolecules. 2022; 12:1529 [7] Molina-Espeja P, et al. Oxford Open Climate Change, 2023; kgad004.

Acknowledgements. We acknowledge the FuturEnzyme Project funded by the European Union's HorizonEU 2020 Research and Innovation Programme (Grant Agreement No. 101000937), and the Grants PID2020-113758RB-I00, PDC2021-121084-I00, and TED2021-130544B-I00 from the Ministerio de Ciencia e Innovación, Agencia Estatal de Investigación (AEI) (Digital Object Identifier 10.13039/501100011033), and the European Union ("NextGenerationEU/PRTR").

DESIGN OF AN IN-ONE PROTEASE-ESTERASE PLURIZYME FOR CASCADE REACTIONS

Laura Fernandez-Lopez[1], Sergi Roda[2], Jose L. Gonzalez-Alfonso[1], Francisco J. Plou[1], Víctor Guallar[2,3], and Manuel Ferrer[1]

[a]Department of Applied Biocatalysis, ICP, CSIC, 28049 Madrid, Spain
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Enzymes are one of the cornerstones of the circular bio-economy, since they are selective and specific, as well as a relevant sustainable and greener alternative to mitigate and even reverse climate change. Regardless of technological developments in terms of screening new naturally occurring enzymes, protein engineering and machine-learning methods are still an alternative for adjusting and repurposing enzyme scaffolds and activities. This potential is particularly noteworthy when addressing the development of novel enzymes for one-pot cascade reactions, considering that they require the engineering of the catalysts of each internal chemical reaction.

PluriZymes, enzymes with more than one active site, one native and one artificially introduced, are a new alternative to this problem. Previously successful *PluriZymes* had two active sites supporting similar (ester hydrolysis) or different (ester hydrolysis and amine transamination) chemistry [1,2]. Here, we present the first *PluriZyme* that combines one active site supporting esterolytic activity and another supporting proteolytic activity [3]. This *PluriZyme* was designed by introducing a cysteine-histidine dyad (which provides protease activity), that could accommodate bulky peptide substrates, in an exposed site of a serine-ester hydrolase. As a result, an in-one protease-esterase *PluriZyme* was produced, which could successfully perform the one-pot cascade synthesis of amino acid esters from dipeptides.

This study demonstrates that active sites supporting proteolytic activity can be artificially introduced into esterase scaffolds to design in-one protease-esterase *PluriZymes* for synthetic cascade reactions.

Acknowledgements. This research was funded by the FuturEnzyme Project, funded by the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No. 101000327 and 101000607. We also acknowledge the financial support under Grants PID2020-112758RB-I00, PID2019-106370RB-I00, PDC2021-121534-I00, and PID2019-105838RB-C31, from the Ministerio de Ciencia e Innovación, Agencia Estatal de Investigación (AEI) (Digital Object Identifier 10.13039/501100011033), Fondo Europeo de Desarrollo Regional (FEDER) and the European Union ("NextGenerationEU/PRTR"). SR thanks the Spanish Ministry of Science and Innovation for a PhD fellowship (FPU19/00608).

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[2] Roda S., Fernandez-Lopez L. *et al.* A Plurizyme with transaminase and hydrolase activity catalyzes cascade reactions (2022). Angewandte Chemie International Edition, 61(37):e202207344. DOI: 10.1002/anie.202207344.

[3] Fernandez-Lopez L., Roda S. *et al.* Design and Characterization of In-One Protease-Esterase PluriZyme (2022). International Journal of Molecular Sciences, 23(21):13337. DOI: 10.3390/ijms232113337.

DESIGN OF AN IN-ONE PROTEASE-ESTERASE *PLURIZYME* FOR CASCADE REACTIONS

Laura Fernandez-Lopez[1], Sergi Roda[2], Jose L. Gonzalez-Alfonso[1], Francisco J. Plou[1], Víctor Guallar[2,3], and Manuel Ferrer[1]

[1]Department of Applied Biocatalysis, ICP, CSIC, CSIC, 28049 Madrid, Spain, [2]Department of Life Sciences, Barcelona Supercomputing Center (BSC), 08034 Barcelona, Spain, [3]Institution for Research and Advanced Studies (ICREA), 08010 Barcelona, Spain

PLURIZYMES: BACKGROUND

PluriZymes are enzymes that preserve their native active site while having more computationally added (Fig. 1). The well-known advantages of biocatalysts -selectivity and specificity, driven by the architecture of active sites, and sustainability-, can be extended by the addition of active sites, which by supporting complementary selective chemistry allows a sole enzyme performing one-pot cascade reactions.

We have successfully designed *PluriZymes* that had two active sites supporting similar (ester hydrolysis) or different (ester hydrolysis and amine transamination) chemistries [1,2]. Here, we further extend our computational effort to design a *PluriZyme* with both esterase and protease activity (Fig. 2).

Figure 1. *PluriZyme* design scheme: introduction of an artificial active site.

EH_{1AB1C}: FROM AN ESTERASE TO A PROTEASE-ESTERASE *PLURIZYME*

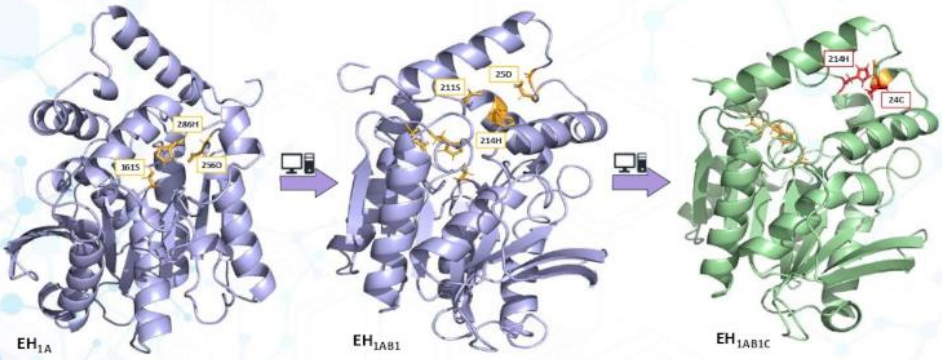

Figure 2. Schematic representation of the design of the protease-esterase *PluriZyme* EH_{1AB1C}. We used as target the *Plurizyme* EH_{1AB1} [1], that contained two ester hydrolase active sites, one native (EH_{1A}) and one artificially introduced (EH_{1B1}). EH_{1AB1C} [3] was further designed by introducing catalytic residues supporting proteolytic activity in the vicinity of the artificially introduced EH_{1B1}. Esterase active sites shown in yellow (**A**: 161S, 256D, 286H; **B**: 211S, 25D, 214H). Protease active site shown in red (**C**: 214H, 24C).

ONE-POT CONVERSION OF L-CARNOSINE

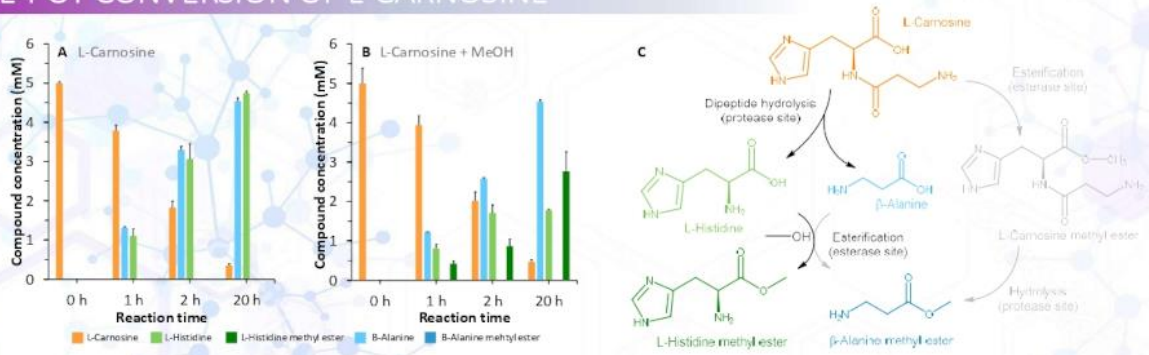

Figure 3. Concentration of reaction products obtained for the conversion of L-carnosine (β-alanine-L-histidine) by EH_{1AB1C} in the absence (A) or presence (B) of methanol. Schematic representation of the main product obtained in a one-pot reaction with L-carnosine and methanol (C). The preferential route is the production of L-histidine methyl ester via the hydrolysis of L-carnosine at the protease site and the selective esterification with methanol of L-histidine (but not β-alanine) at the esterase site.

CONCLUSIONS

This study demonstrates that active sites supporting proteolytic activity can be artificially introduced into esterase scaffolds to design in-one protease-esterase *PluriZymes* for synthetic cascade reactions, herein exemplified by the one-pot synthesis of amino acid esters from dipeptides.

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[2] Roda S., Fernandez-Lopez L. *et al.* Angewandte Chemie International Edition, 2022, 61(37):e202207944.

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Acknowledgements. This research has funded by the FuturEnzyme Project, funded by the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No. 101000327 and 101000607. We also acknowledge the financial support under Grants PID2020-112750RB-I00, PID2019-106870RB-I00, PDC2021-121594-I00, and PID2019-105881RB-C31, from the Ministerio de Ciencia e Innovación, Agencia Estatal de Investigación [AEI | (Digital Object Identifier 10.13039/501100011033), Modo Europeo de Desarrollo Regional [FEDER] and the European Union ["NextGenerationEU/PRTR"]. JA thanks the Spanish Ministry of Science and Innovation for a PhD fellowship (PRE2020-0000).

METAGENOMIC-BASED BIOPROSPECTION FOR NOVEL MYCOTOXIN DEGRADING ENZYMES TO KEEP FOOD AND FEED SAFE

Manuel Ferrer[1], David Almendral[1], Jog Raj[2], Hunor Farkaš[2], Marko Vasiljević[2]

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Mycotoxins: background

Many species of fungi capable of growing in grain and animal feed produce secondary metabolites called mycotoxins. Mycotoxins, such as fumonisin FB1 and T-2 toxins shown in Figure 1, are the biggest challenge for animal feed producers and therefore, regular monitoring and remediation is necessary, as these **toxins can be very detrimental to both humans and animals**.

The **economic loss of mycotoxins in the agri-food sector** is estimated to be billions of dollars, so the economic potential of protection or mycotoxin removal measures is correspondingly high.

There are already different measures available today, such as mechanical, thermic, or chemical approaches. However, these kinds of approaches have as an associated disadvantage the possibility of unknown or unintended side products generation which may turn out as dangerous as the original toxin.

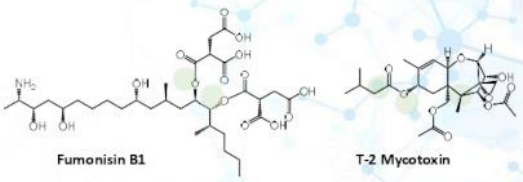

Figure 1. FB1 and T-2 toxins. The potential sites potentially be attacked by enzymes are highlighted in green.

Keep food and feed safe: Using enzymes for mycotoxin removal

Enzymes are proteins that catalyze biochemical reactions that make life possible since 3.8 billion years ago. Scientists have been able to "domesticate" them in such a way that enzymes are now key players for the circular economy and for the processing, manufacturing and consuming everyday products, both for humans and animals [2]. Their worldwide production reached 117 Kilo-tons per year. In this context, enzymatic detoxification is currently a very promising subject of research and development, as enzymes can remove the mycotoxins in a defined way.

Repowering the agri-food industry with enzymes capable of efficiently removing mycotoxins can contribute to keeping our food and feed safe and reducing carry over of mycotoxins form animals to humans.

However, the option to find such new enzymes, particularly those to degrade mycotoxins such as fumonisin B1 (FB1) and T-2 toxins (Figure 1) is challenging, costly, and time-consuming. Indeed, a few number of enzymes are known that degrade both toxins (for example see ref. [1]).

Bio-prospecting metagenomes for mycotoxins-degrading enzymes

The option to find new enzymes, although being challenging, costly (€30k per enzyme) and time-consuming (15 months per enzyme), is realistic given the recent technological advances. Indeed, the use of bioinformatics, machine-learning, accurate protein structure prediction, and data-driven artificial intelligence techniques, combined with naïve screens with appropriated substrates, are essential to fully exploit the potential of sequencing data and as a source of new enzymes.

In order to access to **new enzymes capable of degrading mycotoxins**, we have established a comprehensive and synergetic platform to better bio-prospect environmental metagenomes for novel such rare enzymes, summarized in Figure 2. It consists in the following steps:

- **Extraction and sequencing of DNA from microbial communities** (the so-called metagenome) of a large number of environmental samples.
- **Bioinformatic processing** of the sequences representing the metagenomes to filter for those enzymes in the metagenome potentially degrading FB1 and T-2 toxins, namely, hydrolases.
- **Computational docking analysis** to further provided computational quantum/molecular mechanics (QM/MM) analysis to identify, through quantifying the catalytic events, which of the selected enzymes can bind and potentially degrade FB1 and T-2 toxins.
- Finally, the **experimental validation**: gene synthesis, production, purification and characterization.

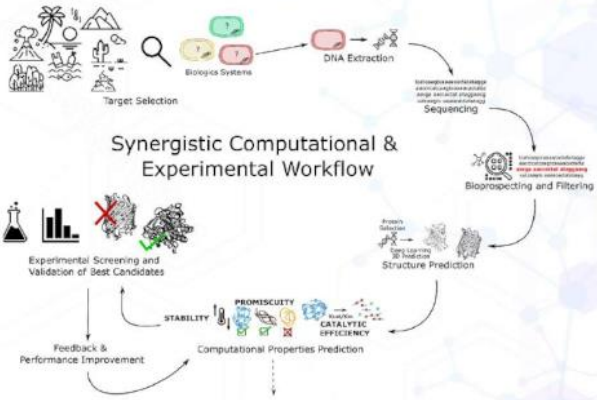

Figure 2. Schematic workflow for the bioprospecting of enzymes capable of degrading toxins. Shown are the steps related to extraction, sequencing, assembling, annotation and virtual screening of new enzymes from the metagenomes of environmental samples, followed by their accurate protein structure prediction, high throughput characterization, and iterative improvement by engineering.

CONCLUSIONS

Through the application of our synergetic platform, we have successfully bio-prospected environmental metagenomes and **found several FB1 and T-2 toxins degrading hydrolases**, to highlight:

- A family VIII esterase, isolated from the metagenomic DNA of microbial communities inhabiting the seashore area of Milazzo Harbor (Sicily, Italy), capable of degrading T-2 toxin (Figure 3) without producing HT-2 intermediate [1].
- An esterase capable of degrading 2-10 ppm FB1 (100% degradation) after 5 min reaction time at concentrations as low as 5 µg/mL at 37-90ºC [3].

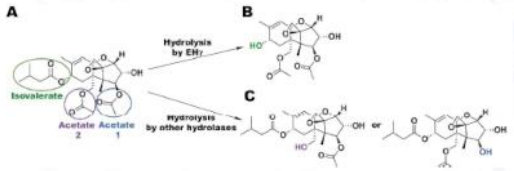

Figure 3. (A) Structure of toxin T-2. Different ester bonds that can be hydrolyzed are colored. Product(s) obtained by the degradation of toxin T-2 through the isovalerate group by the esterase EH7 (B) and by the hydrolysis of both acetates by different hydrolases (C).

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Acknowledgements. M.F. acknowledge the financial support under Grants PID2019-112758RB-I00 and PDC2021-121534-I00 from the MCIN/AEI/10.13039/501100011033 and the European Union ("NextGenerationEU/PRTR")

SYNERGETIC COMPUTATIONAL AND EXPERIMENTAL WORKFLOW TO BETTER BIOPROSPECT AND TRANSFER TO INDUSTRY NOVEL ENZYMES

Paula Vidal[a], Laura Fernandez-Lopez[a], Cristina Coscolín[a], David Almendral[a], Patricia Molina[a], Manuel Ferrer[a]

[a]Department of Applied Biocatalysis, ICP, CSIC, CSIC, 28049 Madrid, Spain

INTRODUCTION

It is now accepted that repowering the industry with enzymes, with which to improve or transform the circular economy, is critical to our strategy to achieve climate neutrality. As example, recent estimations suggest that the full climate change mitigation potential of enzymes may range from 1 to 2.5 billion tons of CO_2 emissions per year [1]. However, the growing concern of climate change requires new enzymes capable of maintaining high catalytic performance during a number of catalytic cycles in an enzyme's lifetime [2], and whose production carbon footprint is as low as possible. The option to find [3] or design [4] such new enzymes, although being challenging, costly (€30k per enzyme) and time-consuming (15 months per enzyme), is realistic given the recent technological advances. Indeed, the use of bioinformatics, computing, accurate protein structure prediction, and artificial intelligence is essential to fully exploit the potential of sequencing data as a source of new enzymes and speed up their engineering with ultrahigh-throughput methods. But for these techniques being effective, it is essential to link sequences encoding enzymes with the specifications (e.g., activity and stability) and needs (e.g., substrate to transform) of industries.

OBJECTIVE

In this contribution, we provided a comprehensive overview of our combined experimental and computational efforts to implement a user-friendly and predictive Machine Learning Predictor software prototype that has the capacity to pre-select from sequence databases, and in time frames as short as seconds, novel enzymes that meet the key performance indicators requested by industries in the sectors of sustainable consumer products. Figure 1 summarizes the methodology to achieve this objective.

METHODOLOGY

- Compilation of technical specifications in three industrial sectors.
- Development of a hierarchical approach to enzyme prospecting and its application in several use cases.
- Characterization of new target enzymes.
- Correlating experimental metadata for a wide set of enzymes, namely, ester-hydrolases, and theoretical descriptors and motifs obtained by bioinformatics and computational techniques.
- Implement prototype software to select target enzymes with the required specifications, by integrating different bio-containers into a graphical web application (Galaxy).

Figure 1. Methodological scheme of the process followed to obtain the enzymes that meet the specifications for their use in the industry.

RESULTS

- By applying a number of high-throughput assays, we have extensively characterized +500 environmentally and taxonomically diverse enzymes, ester-hydrolases. Biochemical parameters such as pH and thermal profiles, substrate profile, and kinetic parameters towards standard and industrially-relevant substrates, have been retrieved.
- By linking biochemical datasets and enzyme sequences, we have developed a Machine Learning tool called EP-Pred [5], that allows predicting the substrate scope (or substrate promiscuity) of ester-hydrolases. This tool was trained on a dataset of ca. 150 ester-hydrolases tested against ca. 100 ester substrates.
- By computing the phase transition temperature (Tp), through constraint network analysis (CNA) and Delta Delta G (DDG) calculations, we found that Tp, a measure of protein flexibility, is associated with the mean annual temperature (MAT) of the sites from where an enzyme is retrieved. Thus, both MAT and Tp can be used for implementing smart search of enzymes fitting manufacturers' needs, particularly those with specific thermal conditions [6].
- Currently, we are linking biochemical datasets associated to the capacity of degrading PET plastics and long-chain oils and sequences of hydrolases.

IMPACTS

Scientific innovation:
Development of a new software to screen from sequence databases enzymes, particularly esterases and lipases, with industrial needed specifications.

Society:
The dissemination, communication and exploitation of the software and enzymes to be discovered using it and cross-sector interconnections with industries will be established.

Environment:
A tool to discover new enzymes, will have a positive environmental impact because of the possibility to make greener and more innovative real-life products and processes, whose production and use is associated with a very high impact on greenhouse gases (e.g., CO_2) and chemical emissions, as well as the consumption of large amounts of energy, water and chemicals.

Economy:
Establish an Open Access/Science, Digitalization and Data Management, Intellectual Property Rights, Exploitation, Transfer and Market Plans.

Innovation:
Social innovation will be supported, as: i) 90% of consumers have a more positive image of a company that supports biotechnology,; ii) 50% of European consumers are willing to recognize a green premium for a more sustainable greener alternative; and iii) consumer behavior can significantly decrease environmental impacts. A new software to predict enzymes best transferred to industry can help industries to provide new products for eco-consumers.

Cooperation:
Through closer cooperation with industry, strategies will be developed to speed up the lab to market transition in the development of a software to search enzymes with which to achieve innovation and economic gain.

CONCLUSIONS

The development of predictive Machine Learning Metapredictor Software or other bioinformatics- or computational-based tools, will offer the possibility to search, in sequence databases, for enzymes that meet the specific demands of industries and manufacturers. Such enzymes may offer the possibility to improve competitiveness, innovation capacity, and sustainability in a modern low emission, low-carbon circular economy and sustainable bio-based economy.

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ENZYMES FOR GREENER CONSUMER PRODUCTS AND FOR A HEALTHY ZERO-PLASTIC POLLUTED ENVIRONMENT

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INTRODUCTION

Today, the chemosphere's and biosphere's compositions of the planet are changing faster than experienced during the past thousand year. This is a consequence of, first, the rising of CO_2 emissions from fossil fuel combustion, including those from processing, manufacturing and consuming everyday products [1,2]. Second, the increase of the pollution level; indeed, about 140000 artificial chemicals and mixtures of chemicals, including plastics and micro-plastics, are currently produced, 220 billion-tons of which are produced and disposed each year [1,2]. How do we deal with the green transition to minimize global warming like CO_2 and pollution? One of the solutions is to use renewable natural resources, namely, the working parts of its living systems, the enzymes. We review the consequences of climate change and chemical pollution at multiple scales and how enzymes can counteract or mitigate them. We then focus on how they mobilize sustainable and greener innovations in consumer products that have a high contribution to global carbon emissions, and how they can help reaching a healthy zero-pollution environment. Lessons learnt from past and present effort to retrieve enzymes through naïve- and bioinformatics-based metagenomics, and to engineer variants by machine learning and meta-data integration, are discussed. Recent findings in a number of target enzymes, particularly, hydrolases relevant to lipid' and plastic' hydrolysis, are finally discussed.

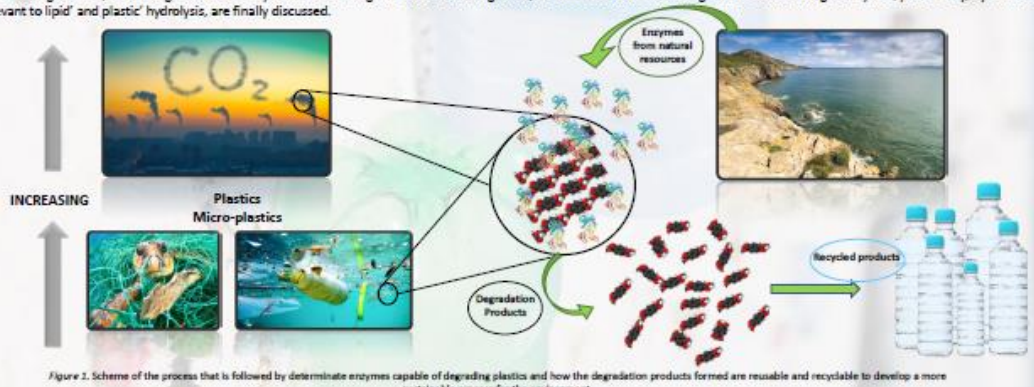

Figure 1. Scheme of the process that is followed by determinate enzymes capable of degrading plastics and how the degradation products formed are reusable and recyclable to develop a more sustainable process for the environment.

RECENT FINDINGS

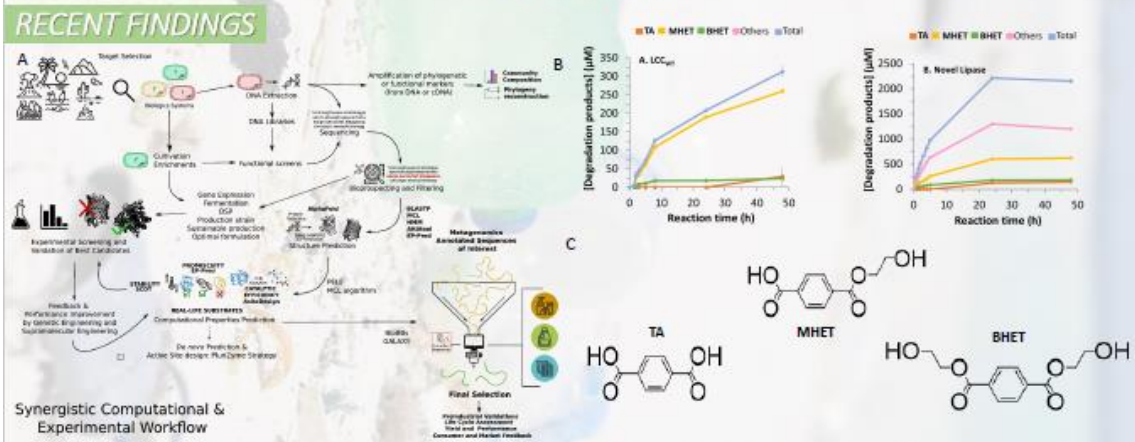

Figure 2. Schematic workflow for the bioprospecting of enzymes for circular (bio)economy and climate change mitigation, and in particular plastic degradation. A) Shown are the steps related to extraction, sequencing, assembling, annotation and virtual screening of new enzymes from the metagenomes of environmental samples, followed by their accurate protein structure prediction, high-throughput characterization and iterative improvement by engineering; finally, validation of computational predictions to design of predictive tools with which to artificially design *de novo* new enzymes. B) Products of PET hydrolysis. Degradation products of nano-sized PET particules formed with LCC$_{ICCG}$. Final products are terephthalic acid (TA), mono-(2-hydroxyehyl)terephthalate (MHET) and a slightly amount of bis(2-hydroxyethyl) terephthalate (BHET) (A). Degradation products of nano-sized PET particules formed with a novel Lipase. Final products are terephthalic acid (TA), mono-(2-hydroxyehyl)terephthalate (MHET), bis(2-hydroxyethyl) terephthalate (BHET) and other products like dimers or trimers. C) Scheme of the main degradation products of PET.

CONCLUSIONS

The need to find new natural resources for the development of more sustainable environmental processes leads to the discovery of new enzymes capable of carrying out this process. In addition to the already known PETases, in this work we present a novel lipase capable of degrading PET, retrieved by metagenomics tools. Currently we are characterizing the improvement of this novel lipase.

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Publicaciones y capítulos de libro

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ORIGINAL RESEARCH

Metagenomic Mining for Esterases in the Microbial Community of Los Rueldos Acid Mine Drainage Formation

Paula Vidal[1], Mónica Martínez-Martínez[1*], Laura Fernandez-Lopez[1], Sergi Roda[1], Celia Méndez-García[2], Olga V. Golyshina[3], Víctor Guallar[4,5], Ana I. Peláez[2] and Manuel Ferrer[1*]

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A Plurizyme with Transaminase and Hydrolase Activity Catalyzes Cascade Reactions

Sergi Roda, Laura Fernandez-Lopez, Marius Benedens, Alexander Bollinger, Stephan Thies, Julia Schumacher, Cristina Coscolín, Masoud Kazemi, Gerard Santiago, Christoph G. W. Gertzen, Jose L. Gonzalez-Alfonso, Francisco J. Plou, Karl-Erich Jaeger, Sander H. J. Smits, Manuel Ferrer, and Víctor Guallar**

Abstract: Engineering dual-function single polypeptide catalysts with two abiotic or biotic catalytic entities (or combinations of both) supporting cascade reactions is becoming an important area of enzyme engineering and catalysis. Herein we present the development of a *PluriZyme*, TR$_1$E$_2$, with efficient native transaminase (k_{cat}: 69.49 ± 1.77 min^{-1}) and artificial esterase (k_{cat}: 3908-0.41 min^{-1}) activities integrated into a single scaffold, and evaluate its utility in a cascade reaction. TR$_1$E$_2$ (pH$_{opt}$: 8.0-9.5; T_{opt}: 60-65 °C) efficiently converts methyl 3-oxo-4-(2,4,5-trifluorophenyl)butanoate into 3-(*R*)-amino-4-(2,4,5-trifluorophenyl)butanoic acid, a crucial intermediate for the synthesis of antidiabetic drugs. The reaction proceeds through the conversion of the β-keto ester into the β-keto acid at the hydrolytic site and subsequently into the β-amino acid (*e.e.* >99 %) at the transaminase site. The catalytic power of the TR$_1$E$_2$ *PluriZyme* was proven with a set of β-keto esters, demonstrating the potential of such designs to address bioinspired cascade reactions.

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Crystal structure of a family VIII β-lactamase fold hydrolase reveals the molecular mechanism for its broad substrate scope

Isabel Cea-Rama[1], Cristina Coscolín[2], Jose L. Gonzalez-Alfonso[2], Jog Raj[3], Marko Vasiljević[3], Francisco J. Plou[2], Manuel Ferrer[2] and Julia Sanz-Aparicio[1]

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(PDB code 4IVK). The structure of the complex was solved by difference Fourier synthesis using the coordinates of the EH_7 native crystals. Crystallographic refinement was performed using the program REFMAC [39] within the CCP4 suite with automatic local noncrystallographic symmetry (NCS). For the wild-type, amplitude-based twin refinement was applied. The free R-factor was calculated using a subset of 5% randomly selected structure-factor amplitudes that were excluded from automated refinement. At the later stages, ligands were manually built into the electron density maps with Coot8 [40], and water molecules were included in the model, which, combined with more rounds of restrained refinement, reached the R factors listed in Table S3. For M-4NHP and O-4NHP, which are not present in the Protein Data Bank, a model was built using MacPyMOLX11Hybrid (The PyMOL Molecular Graphics System, Version 2.0, Schrödinger, LLC, New York, NY.

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Article

EP-Pred: A Machine Learning Tool for Bioprospecting Promiscuous Ester Hydrolases

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Data Availability Statement: The code, features and the results of the training can be downloaded from https://github.com/etiur/EP-pred.

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Conflicts of Interest: The authors declare no conflict of interest.

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Article

Design and Characterization of In-One Protease-Esterase PluriZyme

Laura Fernandez-Lopez [1,†], Sergi Roda [2,†], Jose L. Gonzalez-Alfonso [1], Francisco J. Plou [1], Víctor Guallar [2,3,*] and Manuel Ferrer [1,*]

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† These authors contributed equally to this work.

Abstract: Proteases are abundant in prokaryotic genomes (~10 per genome), but their recovery

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ENZYMOLOGY AND PROTEIN ENGINEERING

The Mobility of the Cap Domain Is Essential for the Substrate Promiscuity of a Family IV Esterase from Sorghum Rhizosphere Microbiome

Marco Distaso,[a] Isabel Cea-Rama,[b] Cristina Coscolín,[c] Tatyana N. Chernikova,[a] Hai Tran,[a] Manuel Ferrer,[c] Julia Sanz-Aparicio,[b] Peter N. Golyshin[a]

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We declare no conflict of interest.

P.N.G., M.F., and J.S.-A. developed the conceptual framework; M.D., C.C., T.N.C., and H.T. developed the experimental design; I.C.-R. and J.S.-A. performed the crystallization and X-ray structure determinations, analysis, and interpretation; M.D., M.F., and P.N.G. interpreted the experimental data; P.N.G., M.F., and J.S.-A. wrote the initial manuscript. All authors edited the manuscript. All authors read and approved the final manuscript.

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ENVIRONMENTAL MICROBIOLOGY

Thermophilic Carboxylesterases from Hydrothermal Vents of the Volcanic Island of Ischia Active on Synthetic and Biobased Polymers and Mycotoxins

Marco A. Distaso,[a] Tatyana N. Chernikova,[a] Rafael Bargiela,[a] Cristina Coscolín,[b] Peter Stogios,[c] Jose L. Gonzalez-Alfonso,[b] Sofia Lemak,[c] Anna N. Khusnutdinova,[a] Francisco J. Plou,[b] Elena Evdokimova,[c] Alexei Savchenko,[c,d] Evgenii A. Lunev,[a,e] Michail M. Yakimov,[f] Olga V. Golyshina,[a] Manuel Ferrer,[b] Alexander F. Yakunin,[a,c] Peter N. Golyshin[a]

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ENZYMOLOGY AND PROTEIN ENGINEERING

Increased Thermostability of an Engineered Flavin-Containing Monooxygenase to Remediate Trimethylamine in Fish Protein Hydrolysates

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G.E.K.B. and P.P. performed the PROSS analysis. M.G. planned experiments, cloned and purified all constructs, conducted biochemical experiments and analyzed all data. I.C.-R. and J.S.-A. conducted crystallography and structural analysis. R.R. conducted kinetic analyses. D.A. conducted CD experiments. M.F. supervised and prepared all mass spectrometry experiments together with M.G. G.E.K.B. secured the main funding, conceptualized the study, and supervised the project together with P.P. and M.F. M.G. and P.P. wrote the paper with input from I.C.-R., J.S.-A., R.R., M.F., and G.E.K.B. All authors read and revised the manuscript.

We declare no conflict of interest.

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Transforming an esterase into an enantioselective catecholase through bioconjugation of a versatile metal-chelating inhibitor†

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bEH_{1A81} was found to preferentially oxidize (−)-catechin (Fig. S6 and S8, ESI†). It is generally accepted that the apparent enantioselectivity (E_{app}) of soluble enzymes can be calculated as the ratio between the conversion rates of the preferred chiral substrate and the non-preferred substrate obtained by testing the two enantiomers separately. Using the oxidation rates (in min^{-1}) values for each biomimetic and enantiomer (Fig. S8, ESI†), E_{app} of 91.9 ± 0.5 for bEH_3 ((+), preferred) and 3.9 ± 0.7 for bEH_{1A81} ((−), preferred) were obtained. It is plausible that the higher number of methionine residues in close and flexible regions of the bEH_3 complex compared to that of bEH_{1A81} might provide additional ligands for Cu^{2+}, probably stabilizing the metal complex, which has higher accessibility from the solvent (Fig. 3d and e); this may promote the entrance of the substrates influencing the observed catalytic activity and enantioselectivity.

In summary, we synthesized a versatile inhibitor that enables the transformation of esterases into biomimetic catecholases without manipulating the protein sequence by genetic engineering. Indeed, the introduction of Cys,[6a,9] Lys,[6a,b,e] His,[6b] non-natural aminoacids,[6c] and other mutations[10] has been reported as being necessary for designing metalloenzymes. It also obviates the use of computational efforts commonly needed to find sites that can accommodate a biomolecule in protein scaffolds.[9–11] We applied this molecule to an esterase and determined the structure of the biomimetics using single-crystal X-ray crystallography. The synthetic relevance and the possibility of using **2** and the resulting biomimetics for enantioselective conversions, either modulated by the orientation of the competent organometallic complex or by the nano-environment of the active site, needs to be further evaluated. Although yet to fully elucidate the nature of the copper site in the biomimetic bEH_3 and how it is modulated for catecholase function, it is plausible that the catalytic cycle of the biomimetic herein designed proceeds as mononuclear copper complexes containing N4 donors,[17] in contrast to natural catecholases that often have binuclear copper centres.[18] In brief, the non-protonated catecholate anion first binds to the Cu^{2+} centre of the biomimetic. This intermediate then oxidizes the coordinated catecholate anion forming Cu^{+} species; these species then react with dioxygen to give a copper dioxygen complex which yields catechin quinone and H_2O_2, which would be decomposed to oxygen and two molecules of H_2O and the catalyst is regenerated in its original active form in closing up the catalytic cycle.

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Conflicts of interest

There are no conflicts to declare.

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Microbiome-derived cobalamin and succinyl-CoA as biomarkers for improved screening of anal cancer

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Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The data used for these analyses are available as supporting material at https://github.com/sajanraju/SCRAtCH-Codes. All of the sequences are publicly available in the European Nucleotide Archive database under accession number PRJEB58898. The mass spectrometry proteomics data have been deposited with the ProteomeXchange Consortium via the PRIDE partner repository[70] with the dataset identifier PXD037268.

Code availability

The code used for these analyses is available as supporting material at https://github.com/sajanraju/SCRAtCH-Codes.

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RESEARCH ARTICLE

Nanohaloarchaea as beneficiaries of xylan degradation by haloarchaea

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spectrometry proteomics data have been deposited in the ProteomeXchange Consortium via the PRIDE partner repository with the data set identifier PXD036877.

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Sub-micro- and nano-sized polyethylene terephthalate deconstruction with engineered protein nanopores

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Author contributions

A.R.-M., R.A.-S., and L.F.-L. contributed equally to this work. V.G., S.G.-L. and M.F. lead this contribution. V.G., A.M.-P. and M.F. wrote the original manuscript, which was further prepared through the contributions of A.R.-M., S.R., S.G.-L., R.P. and M.A.B. All the authors have given approval to the final version of the manuscript. R.A.-S., D.H.-M., A.M.-P. and S.G.-L. contributed to the production, purification and haemolytic and structural characterization of the FraC pore-forming proteins. J.L.G.-A. and F.J.P. contributed to the HPLC analysis. L.F.-L., C.C., D.A. and M.F. performed the ester and

additional active site. Depending on the placement of this artificial active center and the accessibility of the protrusions, we achieved varied degradation pathways for the nanoparticles. Thus, we found ourselves charting exciting new territory in the quest to enhance the capture and break down of sub-micro and nano-sized PET, for example, in wastewater treatment plants. **M.F., A.R.-M., S.G.-L., A.M.-P., and V.G.**

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Review

Enzymes for consumer products to achieve climate neutrality

Patricia Molina-Espeja [1], Julia Sanz-Aparicio [2], Peter N. Golyshin [3], Ana Robles-Martín [4], Víctor Guallar [4,5], Fabrizio Beltrametti [6], Markus Müller [7], Michail M. Yakimov [8], Jan Modregger [9], Moniec van Logchem[10], Philippe Corvini [11], Patrick Shahgaldian [11], Christian Degering[12], Susanne Wieland[12], Anne Timm[13], Carla C. C. R. de Carvalho [14], Ilaria Re [15], Sara Daniotti [15], Stephan Thies [16], Karl-Erich Jaeger [16,17], Jennifer Chow [18], Wolfgang R. Streit [18], Roland Lottenbach[19], Rainer Rösch[19], Nazanin Ansari [19], Manuel Ferrer [1,*] (The FuturEnzyme Consortium)

species are being described to date through the Earth Biogenome Project [145]. The grand aim is to minimize the influence on, or even rehabilitate or restore, the biodiversity of our ecosystems. Enzymes, as part of the nature-based solutions and circular bio-based systems, have the potential to substantially contribute to avoid the release of chemicals to, and remove pollutants from, environmental sites to improve the biodiversity status, thus extending the Natura 2000 network, that marked a significant step forward in environmental management [146]. Access to new enzymes that are not only capable of producing biobased chemicals but also help degrade pollutants in our ecosystems is critical to maintaining biodiversity and the health of our planet [147].

Conclusions

Climate change is here to stay unless humankind manages to knock it off. The only feasible approach encompasses the development of new methods, techniques and processes, mainly aiming at reducing GHG emissions. This is not an easy path, not all will be fixed by tomorrow, but it is in our hands to gradually reduce the damage to our environment, which also means to ourselves and all living forms. It is important to remark that signs of the effectiveness of the measures tackled are already beginning to be visible. For instance, in the EU Member States and the UK, fossil emissions in 2019 decreased by nearly 3.8% [148]. This tendency needs to be extended to the whole planet and maintained

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Conflict of interest

None declared.

Authors' contributions

Patricia Molina-Espeja (Project administration [equal], Writing—original draft [equal], Writing—review and editing [equal]), Julia Sanz-Aparicio (Writing—review and editing [equal]), Peter N. Golyshin (Writing—review and editing [equal]), Ana Robles (Writing—review and editing [equal]), Víctor Guallar (Writing—

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Enzyme adaptation to habitat thermal legacy shapes the thermal plasticity of marine microbiomes

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modelling, identified CARs, and performed CNA runs, H.G. supervised the modelling and simulation work; R.Mar. and M.Fu. wrote the first version of the manuscript with contributions from C.C., M.Fe and D.D.; All authors contributed to the revision of the manuscript.

Competing interests

The authors declare no competing interests.

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Exploiting cyclodextrins as artificial chaperones to enhance enzyme protection through supramolecular engineering†

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Clinical Proteomics

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Proteomic snapshot of saliva samples predicts new pathways implicated in SARS-CoV-2 pathogenesis

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AGC	Automatic gain control
CAA	Chloroacetamide
DE	Differentially expressed
FA	Formic acid
FDR	False discovery rate
GO	Gene Ontology
HCD	Higher-energy collisional dissociation
IPA	Ingenuity Pathway Analysis
IS	Internal standard
KEGG	Kyoto Encyclopedia of Genes and Genomes
Kos	KEGG Ontologies
LC–ESI–MS/MS	Liquid Chromatography Electrospray Ionization Tandem Mass Spectrometric
Mcov	Moderate COVID-19
NcNs	Non-COVID and nonsusceptible individuals
NcSus	Non-COVID and susceptible individuals
PSMs	Peptide spectral matches
ROS	Reactive oxygen species
Scov	Severe COVID-19
SDB-RPS	Reversed-phase Stage-Tips
TCEP	Tris(2–24 carboxyethyl) phosphine
TEAB	Triethylammonium bicarbonate
TMT	Tandem mass tags

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12014-024-09482-9.

Additional file 1: Figure S1. Main interaction network from IPA analysis for DE proteins in saliva of the comparison of Moderate COVID (Mcov) vs Non-COVID nonsusceptible (NcNs). **Figure S2.** Main interaction networks from IPA analysis for DE proteins in saliva of the comparison of Moderate COVID (Mcov) vs Non-COVID susceptible (NcSus). **Figure S3.** Main interaction network from IPA analysis for DE proteins in saliva of the comparison of severe COVID (Scov) vs non-COVID susceptible (NcSus). **Figure S4.** Main interaction networks from IPA analysis for DE proteins in saliva of the comparison of severe COVID (Scov) vs non-COVID nonsusceptible (NcNs). **Figure S5.** Main interaction networks from IPA analysis for DE proteins in saliva of the comparison of severe COVID (Scov) vs moderate COVID (Mcov). **Figure S6.** Comparisons with other databases were performed to infer the main transcription factors, transcription factor targets, cell types, and tissues. **Table S1.** Quality-filtered nonredundant human proteins identified from saliva samples, their expression level, and their functional annotation. **Table S2.** Lists of DE human proteins identified from saliva samples that were used for functional analysis based on IPA. **Table S3.** Discriminatory pathways associated with DE human proteins herein identified in saliva samples of all conditions compared to those in all the -omic studies published related to COVID-19 by using Metascape. **Table S4.** Quality-filtered nonredundant microbial-produced proteins identified from the saliva samples and their expression levels.

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Author contributions

Conceptualizations: SSV, MF, FC, EM. Methodology: SSV, MF, FC, EM, SC, DJ, RB, SSC, SF. Patient recruitment: SSV, JMS, PV, RR, MSC. Laboratory measurements: EM, SC, DJ, SF, FC, MF. Funding acquisition: SSV, MF, FC. Supervision: SSV, MF, FC. Writing—original draft: EM. Writing—review and editing: EM, SC, DJ, JMS, PV, RR, MSC, RB, SSC, SM, SF, FC, MF, SSV.

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Availability of data and materials

The datasets supporting the conclusions of this article are included within the article (and its additional files). The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository [96] with the dataset identifiers PXD032333 andhttps://doi.org/10.6019/PXD032333.

Declarations

Ethics approval and consent to participate

The study was carried out at the Ramón and Cajal University Hospital in Madrid (Spain) and was approved by the local research ethics committee (Comite etico de investigacion clinica GAE Ramon y Cajal, ceic.hrc@salud.madrid.org, approval number 095/20). Informed consent was obtained from all subjects and/or their legal guardian(s). All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

Outside the submitted work, S. S.-V. Reports personal fees from ViV Healthcare, Janssen Cilag, Gilead Sciences, and MSD as well as nonfinancial support from ViV Healthcare and Gilead Sciences and research grants from MSD and Gilead Sciences. J.M.-S. nonfinancial support from ViV Healthcare, nonfinancial support from Janssen Cilag, nonfinancial support from Gilead Sciences, outside the submitted work. E.M. has received mobility grants for conferences from Gilead and ViV Healthcare; S.M. reports grants, personal fees and nonfinancial support from ViV Healthcare, personal fees and nonfinancial support from Janssen, grants, personal fees and nonfinancial support from MSD, grants, personal fees and nonfinancial support from Gilead, outside the submitted work. There are no potential conflicts of interest.

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Unlocking a Key Residue in a Lipase for Efficient Polyethylene Terephthalate (PET) Hydrolysis and Influencing Depolymerization Product Profiles

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Polyethylene terephthalate (PET) pollution is a global challenge. Advancing the bioprospecting of PET-degrading enzymes through metagenomics and using computational and functional methods to identify key positions influencing the catalytic rate and selectivity are part of the solution. Here, we report PETase activity in the metagenomic lipase Lip_{MEH9}, which exhibits peak activity at 30 °C and pH 9.0 and has a denaturation temperature of 42 °C. In addition to acting on long-chain triglycerides (up to ~13 units (U)/mg, pH 8.0, 30 °C) and a wide range of 34 other esters (up to ~228 U/g), Lip_{MEH9} hydrolyses mono(2-hydroxyethyl) terephthalate (~57 U/g) and bis(2-hydroxyethyl) terephthalate (~131 U/g). It also efficiently deconstructs GoodFellow amorphous submicro- and nanosized PET particles (~984/2238 μM degradation products at 30/40 °C, pH 7.0, 21.5 h) and films (~112/198 μM degradation products at 30/40 °C, pH 7.0, 7 days). Through molecular modelling and experimental analysis, the active site of Lip_{MEH9} was revealed, identifying a key residue contributing to its PETase activity compared with those of its closest homologues. This residue plays a crucial role in determining the distinct profiles of degradation products from PET hydrolysis and should be studied in other PETases for its influence on the catalytic process.

Introduction

The environmental challenges posed by polyethylene terephthalate (PET), a common plastic that is extensively used, have spurred significant interest in its use in enzymatic degradation as a sustainable and efficient solution for recycling and upcycling, which has been explored at the industrial scale.[1–5] This journey began with the discovery of *Thermobifida fusca*, a bacterium from which the cutinase TfH was isolated, showing its ability to degrade PET with 10% crystallinity over three weeks.[6] The isolation of *Ideonella sakaiensis*,[7] which encodes a PET hydrolase (or PETase, *Is*PETase) that initiates the hydrolysis of PET into bis(2-hydroxyethyl) terephthalate (BHET or **ETE**[8]) and a MHETase that further breaks down mono-(2-hydroxyethyl) terephthalate (MHET or **TE**[8]) to terephthalic acid (TA or **T**[8]) and ethylene glycol (EG or **E**[8]), has allowed us to delve deeper into the PET degradation process.[7]

However, these natural enzymes are not sufficient to address the challenges associated with recycling and upcycling PET effectively.[1,2] The search for other PET-degrading enzymes using cultivation-dependent functional screening methods and large-scale genome and metagenome mining and the subsequent optimization of microbial systems for enzyme production and enzyme engineering have been recognized as part of the solution to PET pollution.

Through cultivation approaches, various species within *Actinomyces*, *Bacillus*, *Bacteroidetes*, and *Proteobacteria*, as well as certain fungi, have been identified as capable of degrading PET, and their respective enzymes have undergone extensive characterization.[9–17] Furthermore, the development of culture-independent genomics and metagenomics tools has significantly enhanced our understanding of the global distribution of plastic-depolymerizing enzymes, including those that degrade PET, and has expanded the repertoire of PETases characterized from environmental metagenomes.[18–23] This progress has been facilitated by advancements in bioinformatic algorithms and machine learning methods,[19,24] although these studies also indicate that current sequence-based approaches restrict the discovery of novel PET-degrading enzymes to a limited sequence space surrounding known PETases.[24] Currently, the

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Oxyplasma meridianum gen. nov., sp. nov., an extremely acidophilic organotrophic member of the order *Thermoplasmatales*

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Abstract

A mesophilic, hyperacidophilic archaeon, strain M1^T, was isolated from a rock sample from Vulcano Island, Italy. Cells of this organism were cocci with an average diameter of 1 µm. Some cells possessed filaments. The strain grew in the range of temperatures between 15 and 52 °C and pH 0.5–4.0 with growth optima at 40 °C and pH 1.0. Strain M1^T was aerobic and chemoorganotrophic, growing on complex substrates, such as casamino acids, trypticase, tryptone, yeast and beef extracts. No growth at expenses of oxidation of elemental sulphur or reduced sulphur compounds, pyrite, or ferrous sulphate was observed. The core lipids were glycerol dibiphytanyl glycerol tetraether lipids (membrane spanning) with 0 to 4 cyclopentane moieties and archaeol, with trace amounts of hydroxy archaeol. The dominant quinone was MK-7:7. The genome size of M1^T was 1.67 Mbp with a G+C content of 39.76 mol%, and both characteristics were well within the common range for *Thermoplasmatales*. The phylogenetic analysis based on 16S rRNA gene sequence placed the strain M1^T within the order *Thermoplasmatales* with sequence identities of 90.9, 90.3 and 90.5% to the closest SSU rRNA gene sequences from organisms with validly published names, *Thermoplasma acidophilum*, *Thermoplasma volcanium* and *Thermogymnomonas acidicola*, respectively. Based on the results of our genomic, phylogenetic, physiological and chemotaxonomic studies, we propose that strain M1^T (=DSM 116605^T=JCM 36570^T) represents a new genus and species, *Oxyplasma meridianum* gen. nov., sp. nov., within the order *Thermoplasmatales*.

INTRODUCTION

Archaea of the order *Thermoplasmatales* are ubiquitous across most terrestrial acidic environments of various scale and origin (geothermal and anthropogenic sulphide-ore-containing mining biotopes with temperatures between 10 and 60 °C) [1–3]. These archaea occur in a variety of sites in significant abundance, suggesting they contribute substantially to element cycling and community composition [4–6]. However, most of these archaea were detected by obtaining metagenomes worldwide and, thus, remain uncultured. Up to now, there are six genera with validly published names within the order *Thermoplasmatales*: *Thermoplasma*, *Picrophilus*, *Ferroplasma*, *Thermogymnomonas*, *Acidiplasma* and *Cuniculiplasma* [7]. The scarcity of isolated and described members limits our knowledge about the ecological, physiological, morphological, and chemotaxonomic properties of these organisms. The phylogenetic position of the order *Thermoplasmatales* has been recently changed. Originally, the order was affiliated with the phylum *Euryarchaeota* [2]. However, an updated phylogenetic reconstruction from Genome Taxonomy Database (GTDB) firmly placed these organisms as a separate phylum, namely *Thermoplasmatota* [8, 9]. According to this classification, the phylum *Thermoplasmatota* comprises classes '*Ca.* Poseidonia' and *Thermoplasmata*, with

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Keywords: acidic environments; acidophilic archaea; geothermal environments; *Oxyplasma*; *Thermoplasmatales*.
Abbreviations: DSMZ, German Collection of Microorganisms and Cell Cultures GmbH; TCA cycle, the citric acid cycle; TEM, transmission electron microscopy.
The GenBank accession number for the 16S rRNA gene of strain M1^T is OR949061. The GenBank accession number for the complete genome sequence of strain M1^T is CP133772.
Three supplementary tables are available with the online version of this article.

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Research Article

Moderately thermostable GH1 *β*-glucosidases from hyperacidophilic archaeon *Cuniculiplasma divulgatum* S5

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Abstract

Family GH1 glycosyl hydrolases are ubiquitous in prokaryotes and eukaryotes and are utilized in numerous industrial applications, including bioconversion of lignocelluloses. In this study, hyperacidophilic archaeon *Cuniculiplasma divulgatum* ($S5^T$=JCM 30642^T) was explored as a source of novel carbohydrate-active enzymes. The genome of *C. divulgatum* encodes three GH1 enzyme candidates, from which CIB12 and CIB13 were heterologously expressed and characterized. Phylogenetic analysis of CIB12 and CIB13 clustered them with *β*-glucosidases from genuinely thermophilic archaea including *Thermoplasma acidophilum*, *Picrophilus torridus*, *Sulfolobus solfataricus*, *Pyrococcus furiosus*, and *Thermococcus kodakarensis*. Purified enzymes showed maximal activities at pH 4.5–6.0 (CIB12) and 4.5–5.5 (CIB13) with optimal temperatures at 50°C, suggesting a high-temperature origin of *Cuniculiplasma* spp. ancestors. Crystal structures of both enzymes revealed a classical $(\alpha/\beta)_8$ TIM-barrel fold with the active site located inside the barrel close to the C-termini of *β*-strands including the catalytic residues Glu204 and Glu388 (CIB12), and Glu204 and Glu385 (CIB13). Both enzymes preferred cellobiose over lactose as substrates and were classified as cellobiohydrolases. Cellobiose addition increased the biomass yield of *Cuniculiplasma* cultures growing on peptides by 50%, suggesting that the cellobiohydrolases expand the carbon substrate range and hence environmental fitness of *Cuniculiplasma*.

Keywords: acidic environments; acidophilic archaea; *β*-glucosidase; cellobiohydrolase; *Cuniculiplasma*; extremozymes; GH1; Thermoplasmatales

Introduction

Extremophiles thriving in environments with physico-chemical conditions hostile to common microorganisms, are widely distributed across the globe. Archaea often outcompete bacteria and eukaryotes in extreme environments, and flourish at high temperatures, at low or high pH values and at elevated salinities (Shu and Huang 2022). They employ various and often unique physiological properties, which result in products of biotechnological importance useful for applications in different industries (Elleuche et al. 2014). One of such organisms is *Cuniculiplasma divilgatum*, ubiquitous in moderate-to-low temperature acid mine drainage systems, with pH optimum at 1.0–1.2 (Golyshina et al. 2016a,b). *Cuniculiplasma* spp. are also found in geothermal areas worldwide, pointing at their global distribution in acidic environments of different origin and at variety of temperature adaptations in these archaea (Golyshina et al. 2019). Taxonomically, the genus *Cuniculiplasma* is included in the order *Thermoplasmatales*, which contains organisms with the lowest pH values for growth ever recorded (Golyshina et al. 2019). Potentially, *Cuniculiplasma* spp. can serve as a source of extremozymes, enhancing our comprehension of these enzymes' functions and their significance in the life strategies and ecology of extremophilic archaea, while also offering promise for potential biotechnological uses.

Cuniculiplasma divulgatum S5 genome encodes 22 glycoside hydrolases (GHs), according to CAZY records (http://www.cazy.org/a7595.html; Cantarel et al. 2009), three of which belong to the Glycosyl Hydrolases Family 1 (GH1) that encompasses a large set of enzymes sharing a catalytic domain with a $(\alpha/\beta)8$ TIM-barrel fold and a retaining mechanism of catalysis with activities spread across 34 EC numbers (CAZY database; Cantarel et al. 2009). These enzymes are ubiquitous across all domains of life and play fundamental roles, such as in vivo degradation of lignocellulosic materials for nutrient uptake. Additionally, they have a wide range of in vitro applications in food, medicine, and the production of bio-based chemicals and renewable energy sources (Cantarel et al. 2009, Ketudat Cairn and Esen 2010). GH1 enzymes are encoded in genomes of archaea, with 25 enzymes functionally characterized, including from two taxonomic neighbours of *C. divulgatum*, *Thermoplasma acidophilum* DSM 1728 (Kim et al. 2009), and from *Picrophilus torridus* DSM 9790 (Murphy and Walsh 2019). *Cuniculiplasma divulgatum* encodes three such GH1 proteins, one of which was partially characterized, however, only with model, p-nitrophenyl (pNP) glucoside substrate, with no activity determined against natural substrates (He et al. 2023).

Cuniculiplasma spp. are known (Golyshina et al. 2016a,b), like their closest relatives from *Thermoplasmatales* (Huber and

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Enhancing the Hydrolytic Activity of a Lipase towards Larger Triglycerides through Lid Domain Engineering

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Abstract: Lipases have valuable potential for industrial use, particularly those mostly active against water-insoluble substrates, such as triglycerides composed of long-carbon chain fatty acids. However, in most cases, engineered variants often need to be constructed to achieve optimal performance for such substrates. Protein engineering techniques have been reported as strategies for improving lipase characteristics by introducing specific mutations in the cap domain of esterases or in the lid domain of lipases or through lid domain swapping. Here, we improved the lipase activity of a lipase (WP_075743487.1, or Lip_{MRD}) retrieved from the Marine Metagenomics MarRef Database and assigned to the *Actinoalloteichus* genus. The improvement was achieved through site-directed mutagenesis and by substituting its lid domain (FRGTEITQIKDWLTDA) with that of *Rhizopus delemar* lipase (previously *R. oryzae*; UniProt accession number, I1BGQ3) (FRGTNSFRSAITDIVF). The results demonstrated that the redesigned mutants gain activity against bulkier triglycerides, such as glyceryl tridecanoate and tridodecanoate, olive oil, coconut oil, and palm oil. Residue W89 (Lip_{MRD} numbering) appears to be key to the increase in lipase activity, an increase that was also achieved with lid swapping. This study reinforces the importance of the lid domains and their amino acid compositions in determining the substrate specificity of lipases, but the generalization of the lid domain swapping between lipases or the introduction of specific mutations in the lid domain to improve lipase activity may require further investigation.

Keywords: lipase; lid domain; protein engineering; rational design

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1. Introduction

Ester hydrolases (Enzyme Commission (EC) number 3.1.-.-) are enzymes responsible for the cleavage (under hydrolysis conditions) or formation (under synthetic conditions, e.g., transesterification) of ester bonds [1]. Specifically, those enzymes that carry out the hydrolysis of carboxylic esters into their respective acid and alcohol are known as carboxylic ester hydrolases (EC 3.1.1.1.-). This group is further divided into esterases (EC 3.1.1.1) and lipases (EC 3.1.1.3), which have been differentiated on the basis of their sequences and substrate specificity. Esterases hydrolyse water-soluble short-chain (<10–12 carbon atoms) acyl esters (e.g., *p*-nitrophenyl butyrate, *p*-NP butyrate) and are mostly inactive against water-insoluble long-chain (>12–18 carbon atoms) triacylglycerols (e.g., triolein), which, in turn, are specifically hydrolysed by lipases [2,3]. The difference between lipases and esterases has been a subject of continuing controversy, although most of the "true

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BIOTECHNOLOGICAL PRODUCTS AND PROCESS ENGINEERING

Synthesis of 12-aminododecenoic acid by coupling transaminase to oxylipin pathway enzymes

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Abstract

Biobased polymers derived from plant oils are sustainable alternatives to petro based polymers. In recent years, multienzyme cascades have been developed for the synthesis of biobased ω-aminocarboxylic acids, which serve as building blocks for polyamides. In this work, we have developed a novel enzyme cascade for the synthesis of 12-aminododeceneoic acid, a precursor for nylon-12, starting from linoleic acid. Seven bacterial ω-transaminases (ω-TAs) were cloned, expressed in *Escherichia coli* and successfully purified by affinity chromatography. Activity towards the oxylipin pathway intermediates hexanal and 12-oxododecenoic acid in their 9(*Z*) and 10(*E*) isoforms was demonstrated for all seven transaminases in a coupled photometric enzyme assay. The highest specific activities were obtained with ω-TA from *Aquitalea denitrificans* (TR_{AD}), with 0.62 U mg^{-1} for 12-oxo-9(*Z*)-dodecenoic acid, 0.52 U mg^{-1} for 12-oxo-10(*E*)-dodecenoic acid and 1.17 U mg^{-1} for hexanal. A one-pot enzyme cascade was established with TR_{AD} and papaya hydroperoxide lyase ($HPL_{CP\text{-}N}$), reaching conversions of 59% according to LC-ELSD quantification. Starting from linoleic acid, up to 12% conversion to 12-aminododecenoic acid was achieved with a 3-enzyme cascade comprising soybean lipoxygenase (LOX-1), $HPL_{CP\text{-}N}$ and TR_{AD}. Higher product concentrations were achieved by the consecutive addition of enzymes compared to simultaneous addition at the beginning.

Key points

- *Seven ω-transaminases converted 12-oxododecenoic acid into its corresponding amine.*
- *A three-enzyme cascade with lipoxygenase, hydroperoxide lyase, and ω-transaminase was established for the first time.*
- *A one-pot transformation of linoleic acid to 12-aminododecenoic acid, a precursor of nylon-12 was achieved.*

Keywords Transaminase · 12-aminododecenoic acid · Polyamide · Nylon-12 · Enzyme cascade

Introduction

Polyamides are important industrial polymers. Among them, nylon-12 exhibits properties that are centered between short-chain aliphatic nylons (e.g. nylon-6) and high-molecular-weight polymers (e.g., polyethylene). Nylon-12, as a high-performance polymer with good heat, UV and chemical resistance, is manufactured by ring opening polymerization of ω-laurolactam (Ladkau et al. 2016). Laurolactam is synthesized in a complex reaction cascade starting from the trimerization of petro-derived butadiene followed by cyclododecane oxime synthesis and Beckmann rearrangement (Karau et al. 2015). An increasing demand exists to replace fossil resources with renewable materials, forcing a switch in polymer production. For polyamide precursors, engineered whole-cell biocatalysts were used for their synthesis from fatty acids in multistep enzyme cascades. For example, 11-aminoundecanoic acid, a precursor for nylon-11, was obtained from 12-hydroxystearic acid using alcohol dehydrogenase, Baeyer–Villiger monooxygenase, esterase, and ω-transaminase (ω-TA) (Song et al. 2014). Furthermore, a whole-cell biocatalyst was designed using the alkane monooxygenase AlkBGT from *Pseudomonas putida* GPo1 and the ω-TA CV2025 from

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The bone-degrading enzyme machinery: From multi-component understanding to the treatment of residues from the meat industry

Laura Fernandez-Lopez [a,1], Sergio Sanchez-Carrillo [a,1], Antonio García-Moyano [b,1], Erik Borchert [c,*,1], David Almendral [a], Sandra Alonso [a], Isabel Cea-Rama [d], Noa Miguez [a], Øivind Larsen [b], Johannes Werner [e], Kira S. Makarova [f], Francisco J. Plou [a], Thomas G. Dahlgren [b], Julia Sanz-Aparicio [d], Ute Hentschel [c,g], Gro Elin Kjæreng Bjerga [b], Manuel Ferrer [a,*]

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ABSTRACT

Many microorganisms feed on the tissue and recalcitrant bone materials from dead animals, however little is known about the collaborative effort and characteristics of their enzymes. In this study, microbial metagenomes from symbionts of the marine bone-dwelling worm *Osedax mucofloris*, and from microbial biofilms growing on experimentally deployed bone surfaces were screened for specialized bone-degrading enzymes. A total of 2,043 taxonomically (closest match within 40 phyla) and functionally (1 proteolytic and 9 glycohydrolytic activities) diverse and non-redundant sequences (median pairwise identity of 23.6%) encoding such enzymes were retrieved. The taxonomic assignation and the median identity of 72.2% to homologous proteins reflect microbial and functional novelty associated to a specialized bone-degrading marine community. Binning suggests that only one generalist hosting all ten targeted activities, working in synergy with multiple specialists hosting a few or individual activities. Collagenases were the most abundant enzyme class, representing 48% of the total hits. A total of 47 diverse enzymes, representing 8 hydrolytic activities, were produced in *Escherichia coli*, whereof 13 were soluble and active. The biochemical analyses revealed a wide range of optimal pH (4.0–7.0), optimal temperature (5–65 °C), and of accepted substrates, specific to each microbial enzyme. This versatility may contribute to a high environmental plasticity of bone-degrading marine consortia that can be confronted to diverse habitats and bone materials. Through bone-meal degradation tests, we further demonstrated

Abbreviations: COLL, collagenases (peptidases families U32 and M9); DNS, dinitrosalicylic acid; FALGPA, N-[3-(2-furyl)acryloyl]-L-leucyl-glycyl-L-prolyl-L-alanine; HPAEC-PAD, High performance anion-exchange chromatography with pulsed amperometric detection; HEPES, 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; HMM, Hidden Markov Models; MAG, Metagenome Assembled Genome; Neu5Ac-GM_3, N-acetyl-galactose-β-1,4-[N-acetylneuraminidate-α-2,3-]-galactose-β-1,4-glucose-α-ceramide; Neu5Ac-GM_3, Neu5Acα2-3Galβ1-4Glcβ1-ceramide; Ni-NTA, nickel-nitrilotriacetic acid; PEPT, peptidase (families S1, S8, S53, M61); pNP-NAβGal, pNP-N-acetyl-β-galactosaminide; pNP-NAβGlu, pNP-N-acetyl-β-glucosaminide; pNP-Neu5Ac, 2-O-(*p*-nitrophenyl)-α-acetylneuraminic acid; pNP-sugars, *p*-nitrophenyl-sugars; pNP-αAFur, pNP-α-arabinofuranoside; pNP-αAPyr, pNP-α-arabinopyranoside; pNP-αFuc, pNP-α-fucopyranoside; pNP-αGal, pNP-α-galactopyranoside; pNP-αGlu, pNP-α-glucopyranoside; pNP-αMal, pNP-α-maltoside; pNP-αMan, pNP-α-mannopyranoside; pNP-αRham, pNP-α-rhamnopyranoside; pNP-αXyl, pNP-α-xylopyranoside; pNP-βAPyr, pNP-β-arabinopyranoside; pNP-βCel, pNP-β-cellobioside; pNP-βFuc, pNP-β-fucopyranoside; pNP-βGal, pNP-β-galactopyranoside; pNP-βGlu, pNP-β-glucopyranoside; pNP-βGlucur, pNP-β-glucuronide; pNP-βLac, pNP-β-lactoside; pNP-βMan, pNP-β-mannopyranoside; pNP-βXyl, pNP-β-xylopyranoside; RHAM, α-rhamnosidases; SIAL, sialidases; αFUC, α-fucosidases; αGAL, α-galactosidases; αMAN, α-mannosidases; αNAG, α-N-acetyl-hexosaminidases; βGAL, β-galactosidases; βGLU, β-glucosidases; βNAG, β-N-acetyl-hexosaminidases.

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c0007 Chapter 7

Metagenomics and new enzymes for the bioeconomy to 2030

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s0035 **Acknowledgments**

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Chapter 13

Assigning Functions of Unknown Enzymes by High-Throughput Enzyme Characterization

Patricia Molina, Laura Fernandez-Lopez, Peter N. Golyshin, and Manuel Ferrer

Abstract

The discovery of new enzymes is strongly enabled by the implementation of high-throughput screening methods to detect enzymatic activity in single organisms or clone expression libraries, or to benchmark their performances against known prototypes. In this chapter, a number of methods, applicable at high-throughput scale, are described that allow the screening and characterization of enzymes relevant to biotechnology, particularly, ester-hydrolases (esterases, lipases, phospholipases, and polyester hydrolases).

Key words Ester-hydrolases, Esterase, Lipase, High-throughput assays, Enzyme characterization, Metagenomics

Acknowledgements

This study was conducted under the auspices of the FuturEnzyme Project funded by the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No. 101000327. We also acknowledge financial support under Grants PCIN-2017-078 (within the Marine Biotechnology ERA-NET, GA No. 604814), BIO2017-85522-R (M.F.), PID2020-112758RB-I00 (M.F.), andand PDC2021-121534-I00 (M.F.), from the Ministerio de Economía, Industria y Competitividad, Ministerio de Ciencia e Innovación, Agencia Estatal de Investigación (AEI) (Digital Object Identifier 10.13039/501100011033), Fondo Europeo de Desarrollo Regional (FEDER) and the European Union ("NextGen-erationEU/PRTR"), and Grant 2020AEP061 (M.F.) from the Agencia Estatal CSIC. P.N.G. acknowledges the support of the Centre for Environmental Biotechnology Project, co-funded by the European Regional Development Fund (ERDF) via the Welsh Government (WEFO) and Ser Cymru-funded Project BioPol4Life.

2

Metagenomic protocols and strategies

Rafael Bargiela[a], Celia Méndez-García[b], Mónica Martínez-Martínez[b], and Manuel Ferrer[b]

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1 Introduction

We have always used microbiological cultures to determine the microbial composition, but at present we know that a large proportion of microorganisms in each ecosystem cannot be cultured with traditional tools, and their detection is only possible with the DNA sequencing of their genetic fingerprint, the so-called metagenome [1]. Characterization of the metagenome can be performed through at least three types of approaches, as follows: (i) to determine the composition of total microorganisms present (including those that are dead, dormant, or inactive), through the massive sequencing of the 16S ribosomal RNA (16S rRNA) gene amplified from DNA; (ii) to identify the potentially active bacteria that are dividing, through the massive sequencing of complementary DNA (cDNA) produced from the 16S rRNA molecule; and (iii) to analyze the genomic content through massive sequencing of DNA or cDNA, or functional screens in clone libraries. The aim of this chapter is to provide the basis and standard methods to cover these approaches. Before detailing the strategies to each approach, it is important to mention that there are several methods and techniques that can be used for the analysis of both the composition and the functionality of microbial communities. Before describing them, some prior circumstances that can lead to an important bias and influence the final result should be described. These circumstances are the selection, preservation, and transport of the sample and the method used for nucleic acid extraction, to cite just a few.

2 Wet-lab techniques for sample collection, preservation, and transport

The recommendation is to collect the samples and to freeze them immediately at −80°C, although higher temperatures are also acceptable (up to −20°C). In some cases, storage under strict anaerobic conditions is recommended to ensure the viability and

Metagenomics. https://doi.org/10.1016/B978-0-323-91631-8.00018-4

2. Add 10 µL of each dilution to 100 µL ready-to-use *E. coli* EPI300-T1^{R}, and incubate at 37°C over 20 min.
3. Plate the resulting cells on 12.5 µg L^{-1} chloramphenicol-LB agar plates.
4. After overnight incubation at 37°C, the colonies are quantified as follows: if there were 200 colonies on the plate streaked with the 1:10^4 dilution, then the titer in cfu L^{-1} (where cfu represents colony-forming units) of this reaction would be:
(# of colonies) (dilution factor) (1000 µL L^{-1})/(volume of phage plated [µL])
That is: (200 cfu) (10^4) (1000 µL L^{-1})/(10 µL) = 2×10^8 cfu L^{-1}

Based on the titer of the phage particles determined previously, dilute the phage particles with PD buffer to obtain the desired number of clones and clone density on the plate, which will be prepared as previously described. Subsequently these clones are plated with the help of a colony-picker robot, in 384-well plates (LB, 12.5 µg L^{-1} chloramphenicol and 15% of glycerol). Plates are incubated overnight without shaking at 37°C. The colony-picker robot is again used to produce copies of the 384-well plates.

Once the clone library is prepared, the clones are ready for activity screening. Extensive descriptions of assay methods have been reviewed elsewhere [30–32].

Acknowledgments

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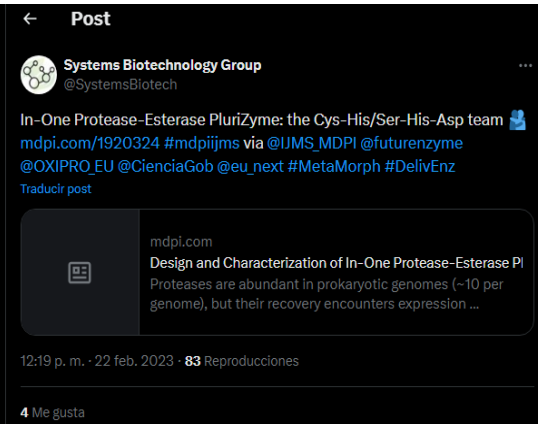

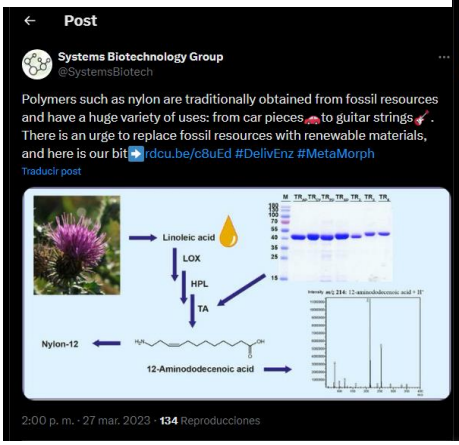

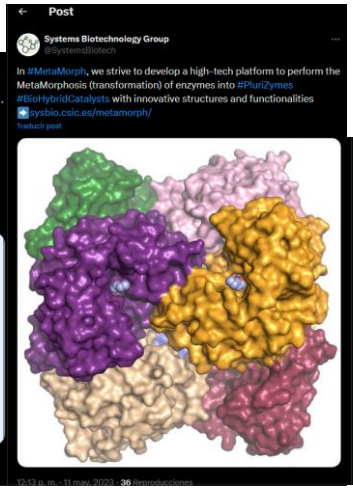

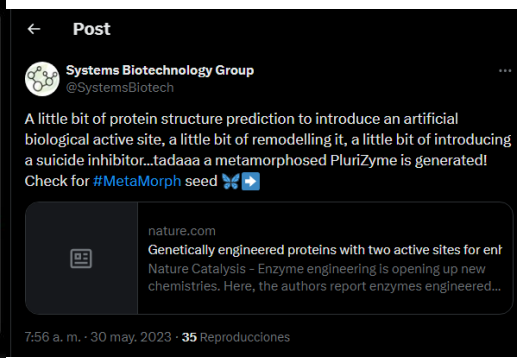

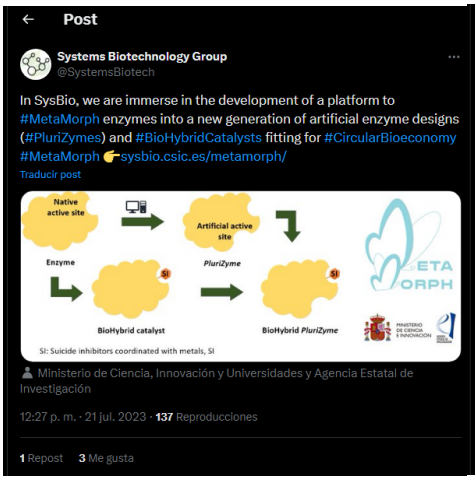


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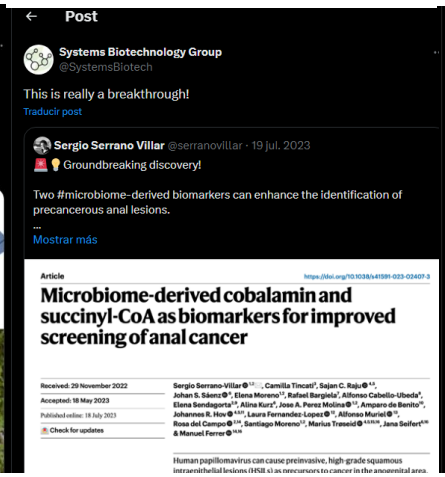
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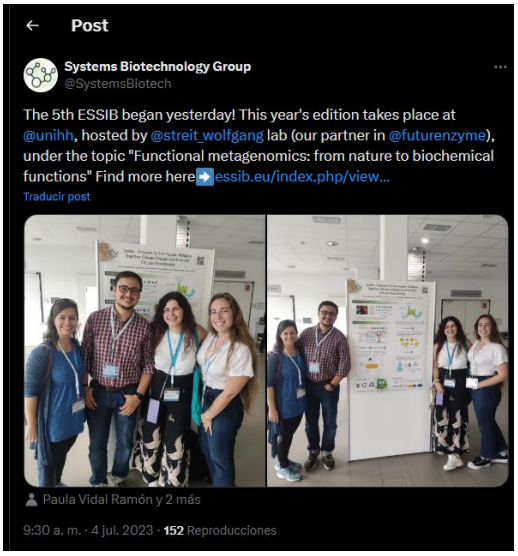
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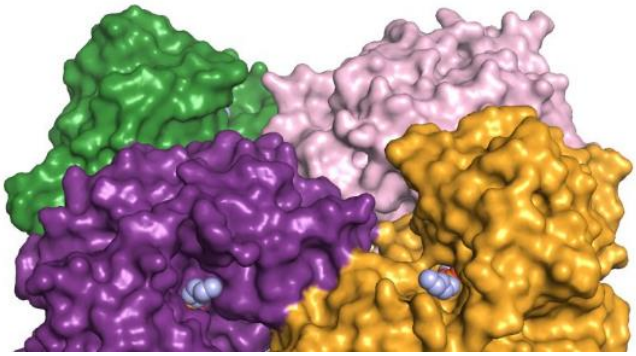

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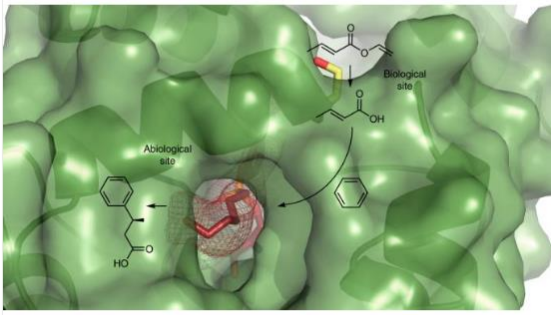

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#DelivEnz #MetaMorph #BioMachine

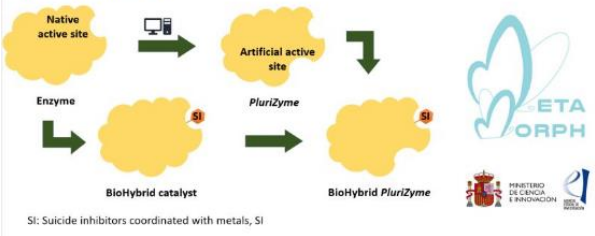
Todavía queda mucho por hacer: la justicia ambiental es una necesidad, y una realmente urgente

Why ideas of 'planetary boundaries' must uphold environmental justice
nature.com

1

Systems Biotechnology Group
160 seguidores
1 año

In SysBio, we are immerse in the development of a platform to #MetaMorph enzymes into a new generation of artificial enzyme designs (#PluriZymes) and #BioHybridCatalysts fitting for #CircularBioeconomy #MetaMorph
https://lnkd.in/ddyaA_p5



6

Recomendar Comentar Compartir

Inicia sesión para ver o añadir un comentario.

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The base idea of #MetaMorph 🦋 is to design #enzymes with more than one active site, hypothesizing that, by synergy, the catalytic performance can be significantly improved, and...yes, #PluriZymes made their appearance!

Then we wanted to design PluriZymes with 2 reactive groups for different chemistry: we synthesized a suicide catalytic inhibitor which selectively "sticks" to the active center, driving to an activity metamorphosis! Our PluriZyme was now a #BiohybridCatalyst with 2 active sites.

Now we aim at following this lead by adding to the approach disruptive engineering computational tools and supramolecular engineering, to further tune the properties of enzyme designs that fit industrial' needs for more #sustainable goods. 🌍 🎄

Visit us for more info 👉 https://lnkd.in/ddyaA_p5

Systems Biotechnology Group
160 seguidores
2 meses · Editado

Our group participates on the IV Spanish Congress of Biocatalysis (JEB), represented by Laura Fernandez-Lopez (talk) and Fadia Cervantes (poster). Celebrated in San Sebastian and organized by SEBiot - Sociedad Española de Biotecnología and CIC biomaGUNE, this Congress is full of networking and opportunities to learn more on the future of biocatalysis.

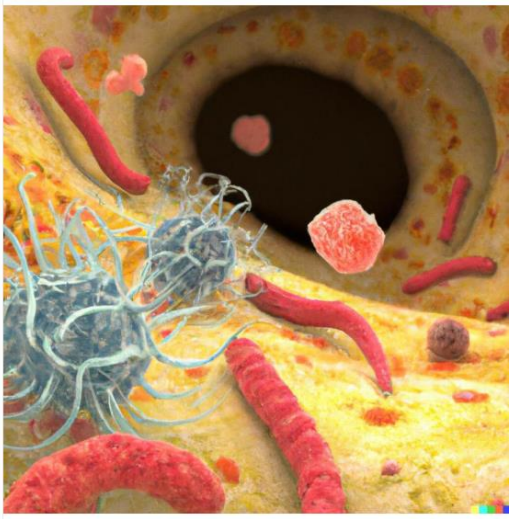
Nuestro grupo participa en las IV Jornadas Españolas de Biocatálisis, representado por Laura Fernández-López (comunicación oral) y Fadia Cervantes (póster). Este congreso, organizado en San Sebastián por SEBiot y CIC biomaGUNE es una gran oportunidad para ampliar la red de los investigadores y saber más sobre el futuro de la biocatálisis.

FuturEnzyme Nymphe #BioMachine #DelivEnz #MetaMorph

25

Laboratorios Normon
122.045 seguidores
1 año

Un equipo de investigadores españoles ha logrado un emocionante avance en la detección del cáncer. Dos nuevos biomarcadores presentes en el microbioma podrían ser clave para identificar lesiones precancerosas. Esta innovación promete una detección más temprana y un tratamiento más efectivo. Descubre más aquí: https://lnkd.in/d2e-GRYS #NormonInforma



Investigadores españoles identifican dos nuevos biomarcadores para detectar cáncer anal
elmundo.es

504 · 3 comentarios

Systems Biotechnology Group
160 seguidores
1 año

🌍 Exciting breakthrough in the fight against #MicroplasticPollution! Read our latest #research on "Sub-micro- and nano-sized polyethylene terephthalate deconstruction with engineered protein nanopores", published with @SpringerNature in @NatureCatalysis.
In collaboration with leading groups from Barcelona Supercomputing Center and @BBM_UCM, and with two other groups from Instituto de Catálisis y Petroleoquímica, https://lnkd.in/dHSuH9DW, and https://speicat.csic.es.
Great job done by Laura Fernandez-Lopez, José Luis González Alfonso, Víctor Alcolea-Rodriguez, David Almendral, Cristina Coscolín, Francisco Plou, Raquel Portela Rodríguez, Miguel A. Bañares and Manuel Ferrer.
👉 https://rdcu.be/doZ38
👉 https://lnkd.in/dvcUx5_t

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Recomendar Comentar Compartir

Estancias de personal en formación o durante colaboraciones con instituciones educativas

Otras


Behind the *PluriZyme* designs: the degradation of plastic particles as study case
Laura Fernandez-Lopez
Systems Biotechnology Group
Principal Investigator: Manuel Ferrer
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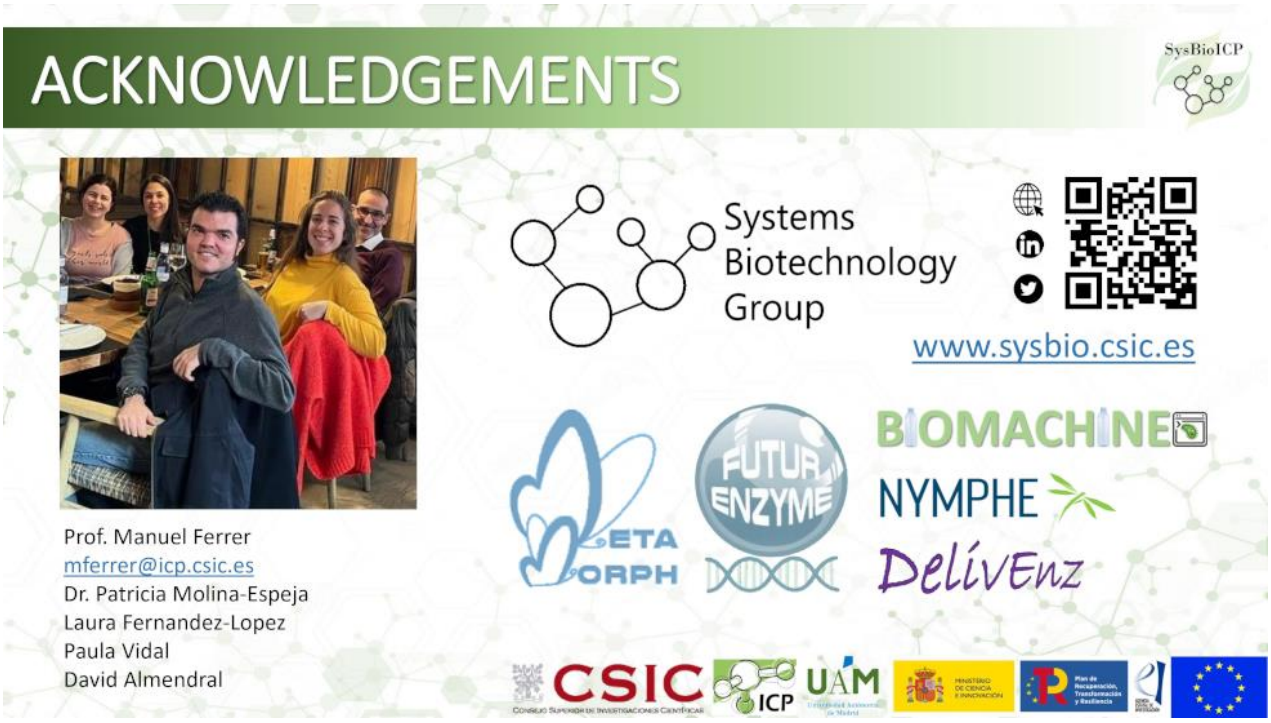
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MUJERES
CIENTÍFICAS:
EN LA SOMBRA
NUNCA MÁS!
Cristina Coscolín
Laura Fernández-López
Patricia Molina
Paula Vidal
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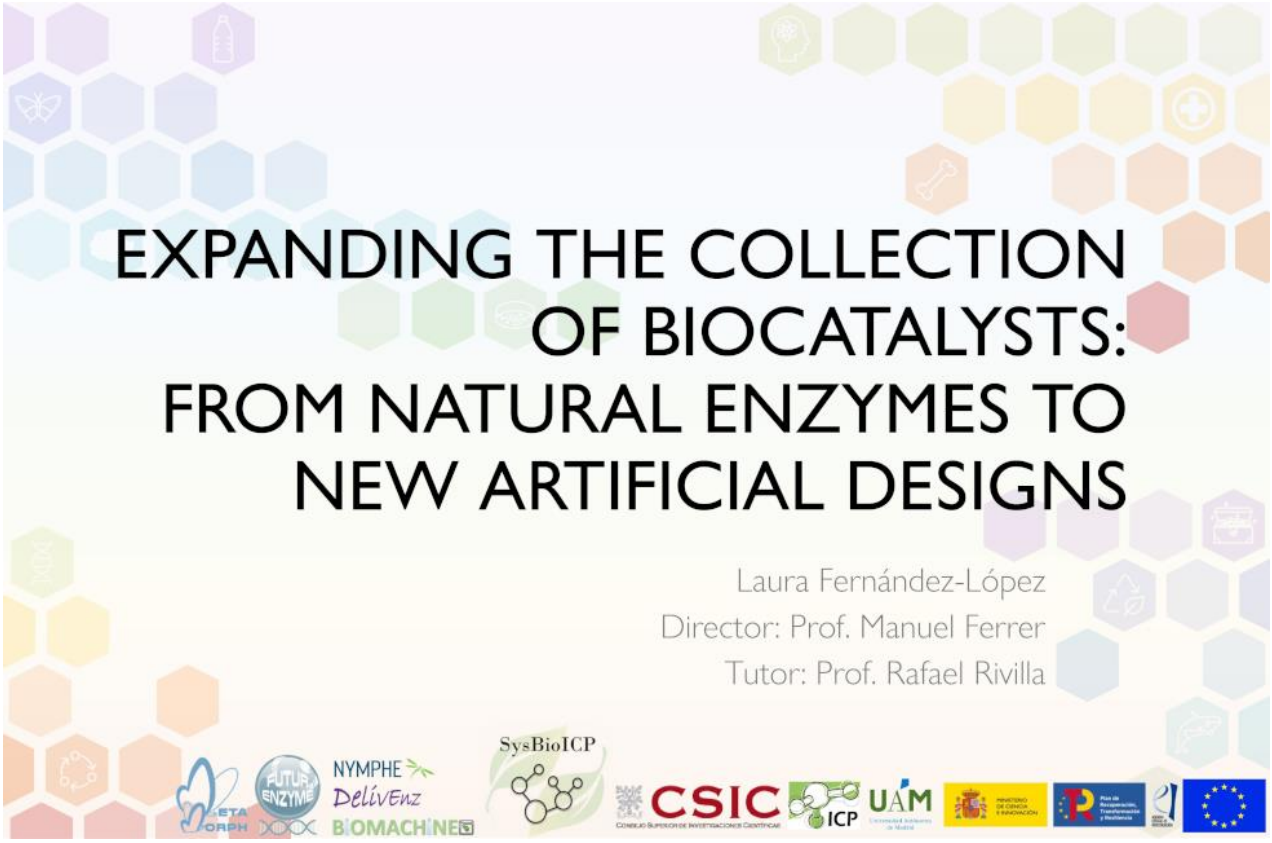
EXPANDING THE COLLECTION
OF BIOCATALYSTS:
FROM NATURAL ENZYMES TO
NEW ARTIFICIAL DESIGNS
Laura Fernández-López
Director: Prof. Manuel Ferrer
Tutor: Prof. Rafael Rivilla
NYMPHE
DelivEnz
BIOMACHINES
SysBioICP
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Desarrollo *de novo* de biocatalizadores con múltiples centros activos combinando diversidad natural, química avanzada y diseño computacional

Autora: **Laura Fernández-López**
Director: **Manuel Ferrer**
Tutor UAM: **Rafael Rivilla**

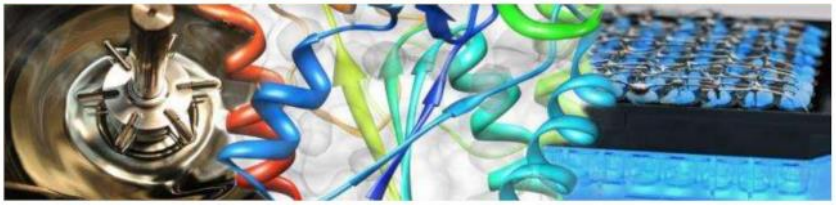
SYSTEMS BIOTECHNOLOGY GROUP · ICP · CSIC

Institute of Catalysis and Petroleochemistry - CSIC
Marie Curie 2, 28049 Madrid, SPAIN

CSIC

Enzymes in microbiomes and diseases: SARS-CoV-2, cancer, ageing and obesity as study cases

ESAB-SKB Webinar Biocatalysis and Molecular Medicine



Manuel Ferrer

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CNB CSIC
asociación española contra el cáncer
Instituto de Salud Carlos III
Plan de Recuperación, Transformación y Resiliencia
HORIZON 2020
www.sysbio.csic.es
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https://sysbio.csic.es/


FUTURENZYME
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YOUR IMPACT ON ENVIRONMENT AND SOCIETY: WORKSHOP ON RESPONSIBLE RESEARCH & INNOVATION
Scientific education, gender equality, open access, ethics and citizen's participation
21 June 2023 | h 10.00 - 12.30
Event organized also in collaboration with M. Ferrer (supported by MICINN and AEI (DOI 10.13039/501100011033) and the "NextGenerationEU/PRTR"; PID2020-112758RB-I00, PDC2021-121534-I00, TED2021-130544B-I00


FuturEnzyme
Technologies of the FUTURe for low-cost ENZYMEs for environment-friendly products
FUTUR ENZYME
Place: CEB, Bangor
Presentation: The FuturEnzyme project: enzymes, consumer products and climate neutrality
By: Manuel Ferrer
12 December 2022
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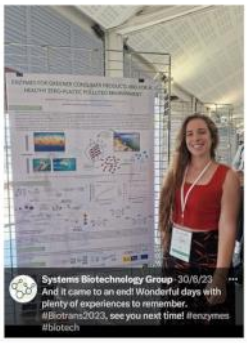
Systems Biotechnology Group · 7/9/23
Last week, our partner @BangorUni in @FuturEnzyme project hosted the 16th Thermophiles Congress! 🔥 A lot of talks and different activities to learn more about this am...


Systems Biotechnology Group · 30/6/23
And it came to an end! Wonderful days with plenty of experiences to remember.
#Biotrans2023, see you next time! #enzymes
#biotech


Systems Biotechnology Group · 9/6/23
How to obtain/manage/share your project's data? How important is it to obtain/share samples according to regulations? We have had an interesting internal webinar to discuss thes...


Systems Biotechnology Group · 20/6/23
-Boss, they called to invite you to an act in the Royal Palace with the Hashemite Kingdom of Jordan
-Is this a joke?
-If it is, they pranked us
After a while:
-I called back, it is true!
And so, our group leader @ManuelF_ICPCSIC, assisted to this act of the Aqaba Process meeting!
Casa de S.M. el Rey


Systems Biotechnology Group
@SystemsBiotech
We will participate in this interactive RRI workshop, join us!
Traducir post
FuturEnzyme @futurenzyme · 23/5/23
Don't miss the workshop on Responsible Research & Innovation organized by @clibcluster in the context of FuturEnzyme project. Experts in the matter will be involved and leading different groups. Register at the following link clib-cluster.de/en/veranstaltu...
YOUR IMPACT ON ENVIRONMENT AND SOCIETY: WORKSHOP ON RESPONSIBLE RESEARCH & INNOVATION
Scientific education, gender equality, open access, ethics and citizen's participation
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