ERA CoBioTech

BioTech Research & Innovation Hack

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ERA CoBioTech Funded Projects at A Glance: HOMBIOCAT

Fabrication of hierarchically organized multi-functional heterogeneous biocatalysts for the modular synthesis of ω-amino acids from renewable feedstocks

PART OF EUROPEAN BIOTECH WEEK

INNOVATION IS IN OUR GENES

HOMBIOCAT

Development of a tool-box for fabrication of efficient multifunctional biocatalysts

Researchers with the EU-funded HOMBIOCAT project are developing a tool-box for the fabrication of hierarchically organized heterogeneous multi-functional biocatalysts, for the generation of added value products from renewable raw materials.

Project coordinator:

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Consortium:

University of Nottingham - (United Kingdom)

Ruhr - Universität Bochum (Germany)

Bioassays (Spain)

Project duration:

01 May 2018 - 31 October 2021

Total budget: 1.1 €M

The potential of novel multi-functional heterogeneous biocatalysts as eco-efficient and competitive technology applicable to the available feedstocks

Chemical synthesis catalysed by enzymes is contributing to establish a modern chemistry supported on cleaner, faster and safer chemical reactions. In particular, cell-free metabolic engineering (or systems biocatalysis) in solution is currently emerging as an attractive alternative to synthetic biology using whole cells because isolated enzymes do not present regulation constraints at genomic level and the intensification of the chemical fluxes do negligible effect on the system subsistence. However, it presents major issues in terms of both process- and cost-efficiency because these soluble systems often reach low chemical yields, are notably unstable and their re-usability is rather limited. In order to overcome these limitations, HOMBIOCAT aimed to assemble multi-enzyme systems at the nanoscale of solid and porous materials aided by protein scaffolds that guarantee the hierarchical and spatial organization of the functional modules. This immobilized multi-enzyme cascade are utilised as heterogeneous multi-functional biocatalyst to transform renewable raw materials into ω-amino acids in one-pot and with in situ cofactor regeneration. The rational integration of different enzymes as functional modules with an engineered protein scaffold and a porous material as heterogeneous chassis has been addressed by combining protein engineering, surface chemistry and protein immobilization tools. The new technology and platforms developed by HOMBIOCAT open an innovative tool to build sustainable pathways for chemical manufacturing of high added value molecules using renewable raw materials. This will result not only on the creation of new market opportunities, also in more efficient, more environmentally friendly, sustainable, and less expensive competitive technology to generally access high added value products from renewable raw materials.

Combination of synthetic biology and biotechnological approaches

HOMBIOCAT convenes an international and multidisciplinary team of researchers from universities, research centres and companies around Europe (UK, Germany, and Spain), joining forces to make the main objective of the project come true: the development of a tool-box for fabrication of efficient multifunctional biocatalysts.
For this purpose, they combine synthetic biology and biotechnological approaches. They designed functional enzymatic modules with the required activities. In parallel, they designed scaffolding protein units with the objective of achieving the control assembly of the enzymatic modules. Once multienzymatic systems are achieved, they are further co-immobilized with other enzymatic modules on solid materials. These materials are the basis to obtain the desired synthesis of ω-amino acids from renewable sources (diols or bio-oils) catalysed by multi-functional heterogeneous biocatalysts. The system is tested in flow reactors under industrially relevant conditions for validation. Additionally, the project generated a genetic toolbox encoding different enzymes fused with distinct scaffolding units, and the scaffolding system for the application of the technology to the assembly of other interesting multi-enzymatic pathways for the production of other commercially relevant compounds in a sustainable manner.

Main results

The HOMBIOCAT project has already achieved breakthroughs in several critical fields. For example, researchers developed protocols for producing the components of 3 complete multienzymatic modules. They also successfully generated scaffolding systems based on engineered proteins. Among some of the main advances of HOMBIOCAT project is the successful scaffolding of multienzymatic systems. HOMBIOCAT researchers demonstrated the substrate channelling in these immobilized systems resulting in more efficient enzyme cascades for in vitro biocatalysis.

This project has received funding from the European Union´s Horizon 2020 research and innovation programme under grant agreement No [722361]

They also achieved the immobilization of the enzymatic systems on solid supports preserving the activity of the enzymes. The project accomplish the demonstration at lab-scale of the cell-free biosynthesis of omega-hydroxy acids catalysed by an immobilized 5-enzyme system without being scaffolded at the nano scale. This system will be the benchmark prototype to be compared with the scaffolded systems at the end of the project.
Finally, HOMBIOCAT project has generated a standardized genetic toolbox for the application of this powerful technology to other enzymatic systems. Those kits will be readily available in the near future for all potential users.

Future prospect

Many of these achievements have huge economic potential. The HOMBIOCAT project has achieved encouraging results, with the development of a technology and a tool-box for the fabrication of hierarchically organized heterogeneous multi-functional biocatalysts. This technology is sustainable, eco-efficient and competitive, and therefore will contribute to build an environmentally sustainable European economy and strengthening the competitiveness of European industry and SMEs.
Achievements of the HOMBIOCAT project will be further verified based on prototype bioreactors, in order to validate the scalability of the process and its potential industrial implementation using standard trials of industry in a bench-marking process, comparing with current gold standard technologies for enzyme immobilization. Not least, the project underlined its emphasis on sustainability since the case study used to validate the technology was focused on the generation of high added value products from renewable raw materials.
Up to date the scientific outcome of HOMBIOCAT project has resulted in 11 scientific publications in pear reviewed journals and one book chapter. Some of those publications are in collaboration between different partners within the project.
These publications cover different key aspects of the project development including:

1) the screening, selection and characterization of different enzymes for their application to the multi-enzymatic systems (DOI: 10.3389/fbioe.2019.00282; doi.org/10.1021/jacs.9b06823; DOI: 10.1021/acsami.0c17568);
2) the use of scaffolding proteins for enzyme stabilization (DOI: 10.1007/978-1-0716-0215-7_14; DOI: 10.1002/cbic.201900047);
3) the immobilization and characterization of the performance of enzymes on solid supports (DOI: 10.1002/cctc.201902404; DOI: 10.3390/catal9110896); and
4) the implementation of enzymatic systems in continuous flow and dialysis membrane reactors (DOI: 10.1039/D1GC01095F; DOI:10.3390/catal11040520).

Since the last stage of the project is the one in which all the input from the different partners merge, we expect to obtain additional collaborative high impact publications in the later stages, or even when the project is finalized.

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Figure 1: HOMBIOCAT consortium during their progress midterm meeting in Bern

Website: http://personal.cicbiomagune.es/alcortajarena/hombiocat/index.html
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