Exploring the Chemical Biology of Sequence Space via Picoliter Droplets

Fact Sheet

Project Information

PicoCB

Grant agreement ID: 695669

Project website

DOI
10.3030/695669

Project closed

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6 June 2016

Start date
1 October 2016

End date
30 September 2022

Funded under
EXCELLENT SCIENCE - European Research Council (ERC)

Total cost
€ 2 308 221,00

EU contribution
€ 2 308 221,00

Coordinated by
THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE
United Kingdom

Objective

Directed evolution of functional proteins has arguably emerged as an approach to protein engineering that can complement or better design-led approaches to protein function. However, as a random process, enormous numbers of variants have to be screened and selected to have a chance to identify successful catalysts. This process is costly and cumbersome: Industrial screening facilities require investment of tens to hundred millions of dollars. My group has implemented key steps towards conducting quantitative biological experiments in a much cheaper format. Screening

of individual library members in monodisperse oil-in-water compartments ('microdroplets') that are generated at kHz frequencies in microfluidic devices has been shown to be possible. The droplet compartment constitutes a link between a given phenotype and its encoding genotype, by capturing reaction product, and thus providing a unique system to screen for catalysis.In this way quantitative fitness landscapes for interconversion of members of enzyme superfamilies along the lines of catalytic promiscuity, understanding the factors governing specificity and the mechanistic interpretation of the observed evolutionary pathways can be made. We now apply this screening system of unprecedented capacity for directed evolution and metagenomic screening of enzymes in in vivo and in vitro formats. We plan to apply this system to do experiments that would not be possible with conventional, lower throughput approaches: (i) screening of metagenomic libraries for rare and promiscuous activities that characterise environmental gene collections for their reactivity and potential for applied biocatalysis; (ii) developing a fundamental understanding of and strategic guidelines for enzyme evolution based on fitness landscapes that record data on multiple, promiscuous activities in response to Indel mutations; and (iii) evolution of gene networks to build up signalling networks in vitro.

Fields of science (EuroSciVoc)

natural sciences > biological sciences > genetics > **mutation**

natural sciences > chemical sciences > catalysis > **biocatalysis**

natural sciences > biological sciences > biochemistry > biomolecules > proteins > **enzymes**

Keywords

directed evolution | protein engineering | enzyme mechanism | chemical biology | sequence space | fitness pandscape | ultrahigh-throughput screening | theory of evolution

Programme(s)

H2020-EU.1.1. - EXCELLENT SCIENCE - European Research Council (ERC) MAIN PROGRAMME

Topic(s)

ERC-ADG-2015 - ERC Advanced Grant

Call for proposal

ERC-2015-AdG

See other projects for this call

Funding Scheme

ERC-ADG - Advanced Grant

Host institution

THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE

Net EU contribution

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Address

TRINITY LANE THE OLD SCHOOLS
CB2 1TN Cambridge
United Kingdom

Region

East of England > East Anglia > Cambridgeshire CC

Activity type

Higher or Secondary Education Establishments

Links

Contact the organisation Website
Participation in EU R&I programmes
HORIZON collaboration network

Beneficiaries (1)

THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE

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