清华工业生物催化论坛

Tsinghua Forum on Industrial Biocatalysis

Engineering the local environment for enhanced enzyme and pathway biocatalysis

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报告摘要：

Traditional enzyme engineering, by rational design or directed evolution, often targets point mutations in and around the active site to enhance catalysis. These methods have been successful in developing enzymes for chemical synthesis, biosensors and therapeutics. In our work, we seek to develop new architecture-based enzyme engineering strategies that can work in parallel with traditional approaches to enhance desired properties. The architectural component is nanoscale scaffolds that introduce new chemical and physical features outside of the active site and in close proximity to the enzyme. The scaffolds modulate the local environment and allow for operation in changing and unfavorable conditions in the bulk environment. The first example uses DNA scaffolds with designed binding affinity to organophosphate nerve agents to increase detoxification rates by phosphotriesterase. Such a strategy is needed because organophosphates chemical weapons are highly toxic at very low concentration and an effective enzyme therapy requires high catalytic turnover in vivo. The second example uses synthetic protein scaffolds to create intracellular multienzyme complexes in yeast. The scaffolds re-localize the enzymes of yeast ester biosynthesis and create a local environment that promotes substrate channeling and increases flux down the pathway. The protein scaffold strategy doubled ester biosynthesis rates in yeast fermentations. Together, these examples show that molecular scaffolds can be used to control the local environment and improve enzyme catalysis in useful and beneficial ways.

报告人简介：

Dr. Wheeldon is an Associate Professor of Chemical and Environmental Engineering at the University of California, Riverside. He received his PhD in Chemical Engineering from Columbia University, and completed two years of postdoctoral training at Harvard Medical School and the Wyss Institute for Biologically Inspired Engineering at Harvard University. Dr. Wheeldon received a Master's of Applied Science from the Royal Military College of Canada, and a Bachelor's of Applied Science from Queen's University, Canada.　His research is focused on protein engineeing and synthetic biology.

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