Universität Basel

Research Project

Designed Evolution of Artificial Metalloenzymes Based on Streptavidin or Carbonic Anhydrase as Protein Scaffold.

Third-party funded project

Project title Designed Evolution of Artificial Metalloenzymes Based on Streptavidin or Carbonic Anhydrase as Protein Scaffold.
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Project Website http://www.chemie.unibas.ch/ward/
Project start 01.10.2009
Probable end 30.09.2012
Status Completed
In a catalytic cycle, a molecule, the catalyst, intimately participates to the reaction by accelerating the chemical transformation but is not consumed. Such catalysts have enormous societal impact, significantly decreasing the energy (and thus cost) required to produce various products, ranging from the delicate process of digestion, to fertilizers sustaining life on earth.

Natural enzymes have evolved over millions of years to orchestrate the ballet of life at a minimal energetic cost. A human being only requires 2000 Watts to sustain his daily activities. For this, we rely on 30'000 different proteins, most of which acting as enzymes.

To address the requirements for the production of various chemicals, ranging from paints, pharmaceuticals, fertilisers, foods etc., different types of catalysts are used: enzymes, homogeneous- and heterogeneous catalysts. All three types offer advantages and disadvantages.

With the aim of exploiting their most attractive and complementary features, it is proposed to merge homogeneous and enzymatic catalysis to yield artificial metalloenzymes. As we have demonstrated in the past, incorporation of an active metal moiety (the molecule) within a protein environment (the baseball glove) affords hybrid catalysts with very promising properties, including high activities and selectivities, reminiscent of both homogeneous and enzymatic catalysts.

Within this project, it is proposed to extend the concept of metalloenzymes towards i) other protein hosts and ii) more challenging oxidation reactions. For this purpose, we pursue a highly interdisciplinary and synergistic approach, including synthesis, molecular biology, enzymology, molecular modelling, X-ray crystallography etc. Oxidation reactions are central to addressing the grand energy challenge. Indeed, the selective catalyzed oxidation of i) abundant methane to methanol or ii) water to dioxygen would represent a big step towards solving both the energy crisis and the global warming.

Keywords artificial metalloenzyme, catalysis, biomimetic chemistry, directed evolution, enzyme design
Financed by
Swiss National Science Foundation (SNSF)

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