

Synthesis of peptide based [ni-fe] hydrogenase: a bottom-up approach for studying metalloenzymes

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In nature, utilization of hydrogen as an energy source or protons as terminal electron acceptors in different microorganisms is mediated by a unique class of metalloenzymes called hydrogenases through the reversible redox reaction $H_2 \leftrightarrow 2H^+ + 2e^-$. The main classes of these enzymes are [Ni-Fe] and [Fe-Fe] hydrogenases. Although the structures of these enzymes have been characterized, the catalytic mechanisms are still not very clear. In an attempt to elucidate the mechanisms of these enzymes, we have taken a bottom-up approach by constructing and characterizing artificial metallopeptides particularly designed to mimic structural and functional aspects of the larger enzymes. Our first goal is to synthesize structural or functional mimics of the [Ni-Fe] hydrogenase enzyme active site utilizing designed peptides as ligands for binding metals directly in a protein environment. We have synthesized the seven amino acid peptide SODA (ACDLPCG) which is known to coordinate Ni in an N_2S_2 environment (found in the Ni-superoxide dismutase enzyme) and are investigating reactions of this complex with water soluble $Ru(\eta^6-C_6Me_6)(H_2O)_3SO_4$. The biomimetic [Ni-Ru] metallocluster will then be anchored to different *de novo* designed protein maquettes. Analytical techniques such as NMR, EPR, CD, FTIR, UV-Visible spectroscopy and electrochemistry will be utilized to characterize the structural and functional aspects of these metal cluster bound maquettes, which are purely synthetic peptides with simple structures having protein flexibility that matches with variety of chemical, mechanical and electrical functions as displayed by natural proteins. The knowledge we gather from these experiments can help us to develop reusable, cheap and sustainable catalytic devices for the production of hydrogen, the fuel of the future, and these hydrogenase maquettes will also provide useful insights into the mechanism of oxidoreductase enzymes.

