BRC Science Highlight
September 2018

A Designed Heme-[4Fe-4S] Metalloenzyme Catalyzes Sulfite Reduction Like the Native Enzyme

Background/objective

Researchers designed a synthetic metalloenzyme capable of achieving the same catalytic efficiency as the natural enzyme sulfite reductase (SiR), which occurs in anaerobic respiration and has an unusual metal cofactor that catalyzes the complex sulfite reduction to sulfide, requiring six electrons and seven protons. This type of synthetic enzyme could play an important role in the bioremediation of sulfites and other oxyanions such as perchlorate and nitrate.

Approach

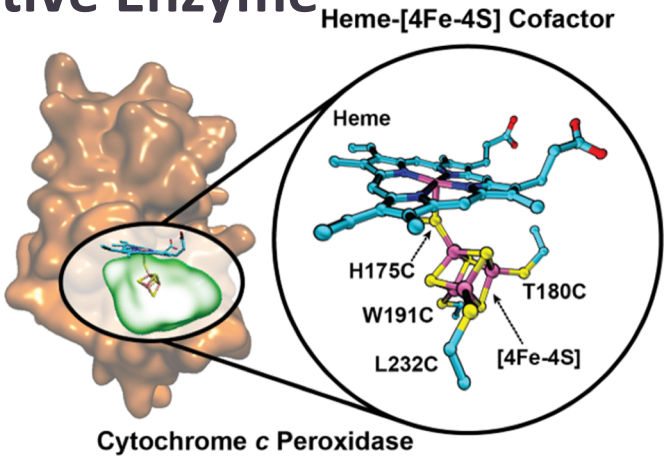
- A cytochrome *c* peroxidase (C*c*P) scaffold was modified to include both a [4Fe-4S] cluster and heme-*b* cofactor.
- Further modification of key amino acids in the C*c*P scaffold was guided by the native SiR structure to increase enzyme activity.

Results

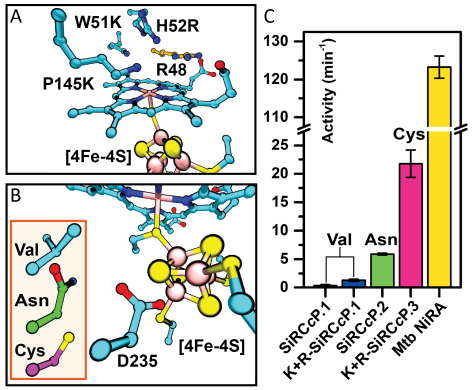
- Activity of the synthetic enzyme (SiRC*c*P) was similar to that of SiR.
- The iterative testing of multiple intermediate enzyme structures during the development of SiRC*c*P led to increased understanding of the influence of structural motifs on enzyme function.

Significance

- The demonstrated ability to produce a metalloenzyme capable of catalyzing complex multi-electron/proton reactions in a simple scaffold might serve as a foundation for designing highly active catalysts for other challenging reactions in bioproduct/biofuel production.



The designed [4-Fe-4S] binding site in the synthetic metalloenzyme CcP.



Iterative testing of different amino acids within the designed binding site yielded increased enzymatic activity.

*EN Mirts et al. 2018. "*A Designed Heme-[4Fe-4S] Metalloenzyme Catalyzes Sulfite Reduction Like the Native Enzyme." **Science**. 361. 1098-1101, DOI:10.1126/science.aat8474

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