Synthetic protein mimics structure, function of metalloprotein in nature

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Scientists led by chemist Yi Lu have designed a synthetic protein that is both a structural model and a functional model of a native protein, nitric-oxide reductase. Photo by L. Brian Stauffer

Scientists have designed a synthetic protein that is both a structural model and a functional model of a native protein, nitric-oxide reductase.

The designed protein "provides an excellent model system for studying nitric-oxide reductase, and for creating biocatalysts for biotechnological, environmental and pharmaceutical applications," said University of Illinois chemistry professor Yi Lu, who directed the work.

"Through rational design, we can better understand native proteins, and maybe make one that is more efficient, more stable or more functional," Lu said.

While considerable progress has been made in designing proteins that

mimic the structure of native proteins, the goal of reproducing both the structure and the function of native proteins - especially metal-containing proteins called metalloproteins - has been elusive.

Lu's research group, including lead author Natasha Yeung, and collaborators at the University of Illinois and at Brookhaven National Laboratory, are among the first to design a protein that mimics both the structure and the function of a metalloprotein. The researchers described their work in the journal *Nature*, published online on Nov. 25.

Nitric-oxide reductase is a key enzyme in the nitrogen cycle that is critical for life. Nitric oxide plays a key role in cell signaling and host-pathogen responses. Therefore, study of nitric-oxide reductase is an important step toward understanding these physiological and pathological processes.

It has been difficult to study nitric-oxide reductase, however, as it is a membrane protein that is not water soluble.

To mimic the structure and function of nitric-oxide reductase, the researchers began with myoglobin, a small muscle protein. Although smaller than nitric-oxide reductase and water soluble, myoglobin can reproduce key features of the native system. Into this scaffold protein the researchers engineered a new iron binding site consisting of three histidines and one glutamate.

In addition to their structural roles, the histidines and glutamate in the active site may also provide the two protons required for nitric oxide reduction.

"The designed protein models both the structure and the function of nitric-oxide reductase, and offers additional insight that the active site glutamate is required for both iron binding and reduction activity," Lu

said. "The designed protein also serves as an excellent model for further mechanistic studies of nitric-oxide reductase."

Source: University of Illinois at Urbana-Champaign (news : web)