Scientists unlock key enzyme using newly created 'cool' method

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A team of Michigan State University scientists -- using a new cooling method they created -- have uncovered the inner workings of a key iron-containing enzyme, a discovery that could help researchers develop new medicines or understand how enzymes repair DNA.

Taurine/alpha-ketoglutarate dioxygenase, known as TauD, is a bacterial enzyme that is important in metabolism. Enzymes in this family repair DNA, sense oxygen and help produce antibiotics.

Specifically, the MSU team was interested in how iron and oxygen atoms reacted together in the enzyme. Understanding how TauD works, which serves as a model for many other proteins, has implications in the scientific and medical fields, said Robert Hausinger, MSU professor of microbiology and molecular genetics.

"This is a broad enzyme family with similar mechanisms," he said. "Understanding how TauD works sheds light on how many other enzymes function from bacteria to humans. This can be applicable to a wide variety of essential enzymes of medical and agricultural interest."

For example, Hausinger said, understanding how the enzyme works can help scientists design inhibitors to prevent it from doing its job, which is a key step in preventing diseases. Also, understanding how the iron inserts oxygen atoms into other molecules provides insight into how enzymes metabolize the majority of medical drugs or environmental pollutants in the human body.

As understanding how enzymes work can be very complicated — such reactions often are complex, fast and require multiple steps — the MSU team developed a new method to follow the TauD reaction. The difficult part for researchers was to slow down the reaction enough that the individual steps can be observed; one way to slow down an enzymatic reaction is to cool it.

The team used a stream of cold nitrogen gas to slow down the reaction at -36 C (-33 F). To prevent freezing and to keep the reaction going, the scientists used ethylene glycol - the same antifreeze that goes in vehicles.

Once the reaction started, the team used lasers - in an advanced method called Raman spectroscopy - to follow the vibrations of iron and oxygen atoms in TauD to determine how the reaction progressed. They found never seen before steps in the TauD reaction, overturning conventional thought.

The research was recently published in the *Proceedings of National Academy of Sciences Early Edition*.

Provided by Michigan State University