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Synchrotron Study Shows How Nitric Oxide Kills

Nitric oxide is a toxic pollutant, but the human body also creates it and uses it to attack invading microbes and parasites. A new study by researchers at UC Davis, the Massachusetts Institute of Technology and the Japan Synchrotron Radiation Research Institute (JASRI) shows how nitric oxide attacks an important group of proteins critical to cell survival.

A paper describing the work was published Dec. 6 in the Journal of the American Chemical Society.

“This information can be used to learn more about possible treatments for nitric oxide toxicity and to help design new and more powerful antimicrobial agents,” said Professor Stephen Cramer of the UC Davis Department of Applied Science. Cramer and Hongxin Wang, a project scientist in the same department, are co-authors on the paper.

Using X-rays from the SPring-8 synchrotron radiation facility at JASRI in Japan, the team studied how nitric oxide attacks Rieske proteins, a group of proteins that contain iron-sulfur clusters. These iron-sulfur clusters transfer electrons through the proteins, a vital process in all living organisms. The researchers found that iron-sulfur clusters can be broken up by nitric oxide, forming products with two irons, not the single iron form as was previously thought.

Understanding the structure of these products is important because it tells us exactly how the iron-sulfur clusters are broken down by nitric oxide? That helps researchers understand more about why it is toxic and could lead to new antimicrobials based on the same mechanism.

The SPring-8 machine produces X-rays that are very bright and extremely monochromatic, or of a very narrow range of wavelengths, Wang said. It is the largest synchrotron radiation facility in the world, but of a similar type to synchrotrons at the Argonne Advanced Photon Source in Illinois and the European Synchrotron Radiation Facility in Grenoble, France.

The other co-authors on the paper are: Professor Stephen Lippard, research assistant Christine Tinberg, postdoctoral fellow Zachary Tonzetich, and graduate student Lai Hung Do, all of MIT; and research scientist Yoshitaka Yoda of JASRI.

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