SOUTHWESTERN NEWS

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RESEARCHERS DISCOVER FAST, EFFICIENT, CONTROLLABLE WAY TO STUDY MOLECULAR INTERACTIONS

DALLAS–May 25, 1999–A molecule that is extremely sensitive to light has proved a highly efficient way of initiating bonding of two proteins. UT Southwestern Medical Center at Dallas researchers who designed this cross-linking reagent and technique said this will be an important tool in studying multiprotein complexes and may also help with drug development.

The study, in today's issue of *The Proceedings of the National Academy of Sciences,* reports the first protein cross-linking reagent that is activated by brief exposure to visible light, allowing observation of relationships between molecules in a time-controlled fashion.

"Our goal is to develop new methods to probe interaction between proteins in their native environment," said Dr. Thomas Kodadek, professor of internal medicine and biochemistry and lead author of the paper. "One problem with traditional methods of chemical cross-linking is lack of control over when the chemical reaction takes place. We wanted to invent something that was inert until you trigger it."

The investigators exposed ruthenium (II) tris-bipyridyl dication $Ru(II)bpy_3^{2+}$ in the presence of ammonium persulfate and interacting proteins to light from a high-intensity 150W lamp. They found that in only .5 seconds 60 percent of the molecules were coupled. Similar results occurred using a standard flashlight by just increasing the exposure time to five to 30

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seconds and holding the sample closer to the light. Thus, no specialized equipment is necessary to use this technique.

The technique, dubbed photo-induced cross-linking of unmodified proteins, is about 1,000 times more efficient than any previously used chemical methods.

The researchers picked Ru(II) because it absorbs light very efficiently and turns the energy into chemical reactions. Since this is a nonperturbing, light-triggered process, it doesn't corrupt concurrent biochemical processes. Using light as the activator also allows control over exactly when the bonding takes place.

Eventually, the scientists believe that this will aid in drug creation.

"Right now this is core technology for studying protein interactions," said Kodadek, a principal investigator for the Center for Biomedical Inventions at UT Southwestern. "The technological spinoff will be when we can use this cross-linking technique to determine a drug target within a cell."

The other researcher on this study was Dr. David Fancy, postdoctoral fellow in pharmacology and biochemistry.

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