

# Ricin's deadly action revealed by glowing probes

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A new chemical probe can rapidly detect ricin, a deadly poison with no known antidote that is feared to be a potential weapon for terrorists and cannot quickly be identified with currently available tests.

The probe, developed by chemists at UC San Diego, glows when bound to a ricin-damaged part of the body's protein-making machinery, they report in the international edition of the journal *Angewandte Chemie*. Because the test pinpoints the specific injury underlying the poison's toxicity, it could also help to develop drugs to counteract the effect of ricin.

Ricin toxin is among the most deadly. Just 400 micrograms, about the size of a grain of salt, is enough to kill an adult, according to a report by the Congressional Research Service. Several other toxins including saporin and sarcin all cause harm in similar ways.

These poisons nick a crucial loop of RNA that is part of the cellular structure that synthesizes proteins called the ribosome. That small alteration, the loss of a single piece at the apex the loop, is enough to shut down the manufacture of proteins. Damage of this type is unusual in the absence of these specific toxins.

"We found a chemical reporter that detects a relatively rare event, one that is related to the action of the toxin," said Yitzhak Tor, a professor of chemistry and biochemistry at UCSD.

Tor, along with postdoctoral researcher Seergazhi Srivatsan and graduate student Nicholas Greco, created a short string of RNA building blocks, or nucleotides, that will attach to the loop. At one position, matching the site ricin damages, they substituted a synthetic nucleoside that glows when the piece that belongs there is missing. If the toxin has damaged the loop, ultraviolet light shone on the sample will fluoresce bright blue.

"Our reporter probe shows that the reaction is taking place," Tor said. "When there's no toxin, there will be no light emission."

Ricin worries security experts because the toxin, an extract of castor beans, is relatively easy to make and difficult to detect. Right now, tests rely on antibodies that recognize the ricin toxin protein itself, which take at least 48 hours to complete, according to the Centers for Disease Control and Prevention. The new test works quickly; it can reveal the presence of damaged ribosome loops in less than 30 minutes.

Tor's team has developed their probe using isolated RNA loops. These will be the basis for the future design of a sensitive chip that could be used in the field to detect quickly the presence of dangerous toxins.

And because their probe detects the action, rather than merely the presence of the toxin, it could be used to develop ways to help people who have been exposed, Tor said. "Now that we have an assay that senses the toxin's activity, we can try to discover inhibitors of the toxin or antidotes."

Source: University of California - San Diego

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