

Study IDs first molecules that protect cells against deadly ricin poison

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The results of a high-throughput screen of thousands of chemicals in search of agents that could protect cells, and ultimately people, against the deadly ricin poison has turned up two contenders. Even better, the compounds also render cells immune to the effects of Shiga-like toxins that are produced by infectious strains of *E. coli* bacteria among other pathogens, suggesting they may be useful against other threats to public health and in fact any toxin that takes the same route to enter cells. The findings are reported in the April 16th issue of the journal *Cell*.

The discovery was made as part of a larger effort in France to address potential bioterror weapons following the 9/11 attacks in the United States, said Daniel Gillet of Commissariat a l'Energie Atomique et aux Energies Alternatives.

"There is a real need for countermeasures against ricin," one of the most [toxic chemicals](#) known to man, Gillet said. One of the reasons for concern is that ricin is not only deadly, but it can also be easy to come by. It is a natural ingredient in the seeds of castor oil plants, which are used in the industrial production of brake fluid, varnish, soap, ink and other products. "There are many plants growing and there is about one milligram of [toxin](#) per seed. Ricin is a byproduct of this industry."

Ricin first gained notoriety when it was used to assassinate the Bulgarian journalist Georgi Markov in 1978, notes Matthew Seaman and Andrew Peden in an accompanying commentary about the new findings. There are currently no known antidotes to ricin or Shiga toxins, and the

possibility that ricin might be used in a bioterror attack is a major concern.

Gillet said that other groups had looked for compounds to protect against ricin before without success. Some promising candidates didn't work consistently and others proved to be toxic in and of themselves.

In the new study, the researchers found two compounds that allowed [cells](#) to survive the assaults of ricin and Shiga-like toxins. The compounds work not by acting on the toxins themselves, but through their effects on the route the toxins follow as they travel through cells, they report. (Both ricin and Shiga-like toxins normally travel through cells by the so-called retrograde pathway. Ricin delivers its fatal blow after it escapes into the cytosol where it disrupts the ribosomal "factories" that produce all the proteins needed to do the work of the cell.)

The compounds, which they call Retro-1 and Retro-2, block the toxins' escape via a series of cellular components out into the cytosol after they've gained initial entry into cells, explained study coauthor Ludger Johannes of Institut Curie and Centre National de la Recherche Scientifique. Importantly, the

More information: Stechmann et al.: "Inhibition of Retrograde Transport Protects Mice from Lethal Ricin Challenge." Publishing in Cell 141, 231-242, April 16, 2010. [DOI:10.1016/j.cell.2010.01.043](https://doi.org/10.1016/j.cell.2010.01.043)

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