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For Immediate Release

Antibodies to detect nerve agents

San Diego, Calif., December 21, 2012 – Researchers at the Human BioMolecular Research Institute in San Diego, and the US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, Maryland, have created a number of monoclonal antibodies that detect biomarkers of nerve agent exposure. Writing November 28th in the online version of *Journal of Pharmacology and Experimental Therapeutics*, the team describes how they obtained and tested monoclonal antibodies that can be used to detect nerve agent exposure and nerve agent model compound exposure in biological samples from animals.

"Because, worldwide, 750,000-3 million individuals are intoxicated by organophosphates every year, we need an effective way to detect exposure," said John Cashman, Ph.D., director of the Human BioMolecular Research Institute and co-author of the study. "Using a highly sensitive antibody to selectively detect serum proteins modified by organophosphates is very appealing."

Immunobiology affords effective antibodies

In an earlier study, the team synthesized a number of small molecules to find ones that could elicit antibodies that recognized organophosphonates attached to proteins in the blood. Now, a team of medicinal chemists and immunologists at the Human BioMolecular Research Institute, led by John Cashman, Ph.D., obtained and refined the monoclonal antibodies. They also used test tube-based studies to further optimize the monoclonal antibodies. In collaboration with Lucille Lumley at the Aberdeen Proving Grounds, the monoclonal antibodies selectively

recognized nerve agent-modified proteins from blood of animals exposed to nerve agents.

"The monoclonal antibodies could become a powerful tool in immunodetection of nerve agent poisoning that overcomes the shortcomings of currently used detection technology" explained Sigeng Chen, Ph.D., a researcher in Cashman's lab and lead author of the paper.

Cashman, Chen and Zhang would like to further develop the monoclonal antibodies into a practical way of detecting organophosphate exposure.

How the monoclonal antibodies work

Monoclonal antibodies are useful because they do two novel things—selectively detect immunogens at exceedingly low levels and can be propagated from cells to obtain a large amount of the antibodies.

The monoclonal antibodies work by recognizing a specific region on a serum protein called albumin that attaches a portion of the nerve agent. This process is known as phosphonylation of serum albumin. Serum albumin is a very abundant protein in the blood and phosphonylation of serum albumin is stable and long-lived, thus providing a suitable biomarker of nerve agent exposure. Nerve agent bind to the outer surface of the albumin protein and the result is a modification that is readily detected by the antibody. The antibody can detect very low levels of nerve agent-modified serum albumin

The monoclonal antibody can be coupled with a number of analytical methods to produce a signal that indicates how much the serum albumin is modified with the nerve agent. With the signal turned on, the amount of nerve agent exposure can be quantified. The monoclonal antibodies are the first selective means of immunodetecting biomarkers of nerve agent exposure that indicates which nerve agent was present. The antibodies might also have applications in other processes involving nerve agent exposure.

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Media contacts: To arrange on-site, phone, or Skype interviews with the researchers involved in this study, please contact John Cashman at (858) 458-9305 / JCashman@hbri.org.

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The study was co-authored by Sigeng Chen, Human BioMolecular Research Institute; Jun Zhang, Human BioMolecular Research Institute; Lucille Lumley, US Army Medical Research

Institute of Chemical Defense, Aberdeen Proving Ground, and John Cashman, Human BioMolecular Research Institute.

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