October 7, 2009

FOR IMMEDIATE RELEASE

Contact:

Carrie James
Human BioMolecular
Research Institute
San Diego, CA 92121
(858) 458-9305 x 106
cjames@hbri.org

Scientists Study Model Compounds that Mimic Neurodegenerative Agents

San Diego, Calif. (October 7, 2009) – Scientists at the Human BioMolecular Research Institute in San Diego, in collaboration with scientists from The Ohio State University and The University of Nebraska Medical Center are researching model compounds that mimic nerve agents that will allow scientists to create enzymes that prevent the effects of nerve agents.

Pesticides and nerve agents are composed of organophosphate compounds that can irreversibly inactivate acetylcholinesterase (AChE). Inactivation of AChE leads to neuronal damage and neurodegenerative disease. Efforts to mitigate the effects of these agents have focused on developing enzymes that can act as scavengers that bind to and react with the organophosphate compounds thereby preventing inhibition of AChE. Nerve agents are currently unavailable for testing, which has forced scientists to use alternate model compounds to study their effects on different aspects of neurodegeneration.

Two papers recently published in Chemical Research and Toxicology[1,2] outline significant research to create alternate organophosphate model compounds and study their mechanism of action. In one study (Gilley et al., 2009), the goal was to test model compounds of soman, sarin, tabun, and cyclosarin for their suitability as substitutes of true nerve agents in enzyme mechanism studies. Some of these 14 model compounds were found to be suitable substitutes for nerve agents that allowed scientists to research their effects on specific enzymes relevant to neurodegeneration.

The second article (Barakat et al., 2009) described studies done to compare the effects of different types of nerve agents and pesticide model agents on key human enzymes. The work identified a useful panel of compounds to use in place of the real nerve agents and pesticides when studying their effects on human enzymes. These model compounds have great utility in studying enzymes that render organophosphate compounds nontoxic.

The development of organophosphate model compounds has provided useful tools to understand the interaction of organophosphates with many target enzymes. The potential for using these model compounds in the development of biological therapeutics against the toxic effects of nerve agents and pesticides is significant.

About HBRI: The Human BioMolecular Research Institute is a non-profit research institute conducting basic research focused on unlocking biological and chemical principles related to diseases of the human brain, cardiovascular disease and cancer. The institute conducts fundamental studies of central nervous system disorders, heart disease and cancer and translates findings into new drug development to address human illness. In addition, the institute promotes scientific learning through community service and public access by disseminating information and sharing research with collaborators, colleagues and the public. For more information, visit www.HBRI.org.

About the University of Nebraska: The University of Nebraska–Lincoln is a member of the Association of American Universities since 1909. Nebraska is recognized by the Carnegie Foundation as a Doctoral/Research Extensive university. UNL is a land-grant university and a member of the National Association of State Universities and Land-Grant Colleges (NASULGC). Today, the University of Nebraska–Lincoln is one of the nation's leading teaching institutions, and a research leader with a wide array of grant-funded projects aimed at broadening knowledge in the sciences and humanities.

About The Ohio State University: The Ohio State University is a world-class public research university and the leading comprehensive teaching and research institution in the state. Ohio State provides a distinctive educational experience for students and pursues cutting-edge interdisciplinary research that brings together scholars from diverse disciplines to solve key

problems in society. Ohio State now ranks seventh among the nation's public research universities and 11th among all universities in research expenditures. Ohio State University leads the nation in having the most faculty chosen as "fellows" of the American Association for the Advancement of Sciences, the world's largest scientific organization.

[1]Gilley C, MacDonald M, Nachon F, Schopfer LM, Zhang J, Cashman JR, Lockridge O (2009) Nerve Agent Analogues that Produce Authentic Soman, Sarin, Tabun, and Cyclohexyl Methylphosphonate-Modified Human Butyrylcholinesterase. *Chem. Res. Toxicol.* Aug 31 (Epub ahead of print).

[2]Barakat NH, Zheng X, Gilley CB, MacDonald M, Okolotowicz K, Cashman JR, Vyas S, Beck JM, Hadad CM, Zhang J (2009) Chemical Synthesis of Two Series of Nerve Agent Model Compounds and their Stereoselective Interaction with Human Acetylcholinesterase and Human Butyrylcholinesterase. *Chem. Res. Toxicol.* Aug 31 (Epub ahead of print).