Studying Dust for Clues to Respiratory Problems

To help determine possible links to increased respiratory problems associated with active duty service from troops deployed overseas, PNNL, the Institute for Systems Biology, and the Army are studying model samples exposed to dust taken from Afghanistan and Iraq. Some soldiers are returning from theaters of war with increased incidence of asthma and other related breathing problems. Researchers are employing mass spectrometry analyses to study time course models.

About EMSL

Since 1997, EMSL's distinctive focus on integrating computational and experimental capabilities as well as collaborating among disciplines yields a strong, synergistic scientific environment. EMSL has helped thousands of researchers use a multidisciplinary, collaborative approach to solve some of the most important national challenges in energy, environmental sciences, and human health. These challenges cover a wide range of research, including synthesis, characterization, theory and modeling, dynamical properties, and environmental testing.

EMSL supports more than 700 scientists annually who produce on average more than 350 peer-reviewed publications. Additionally, EMSL innovations have been recognized by more than 80 patents since 1997.

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Biomedical Clients, Partners, Collaborators, and Programs

- Air Force 59th Medical Wing
- Clinical Breast Care Project
- Congressionally Directed Medical Research Program
- Henry M. Jackson Foundation
- Institute for Systems Biology
- National Institutes of Health
- Proteomics Research for Integrative Biology
- University of Washington
- U.S. Army Medical Research Institute of Infectious Diseases
- U.S. Army's Logistics Innovation Agency
- Walter Reed Army Medical Center
- Windber Research Institute

About PNNL

Interdisciplinary teams at PNNL address many of America's most pressing issues in energy, environment, and national security through advances in basic and applied science. PNNL employs 4,700 staff, has an annual budget of nearly $1.1 billion, and has been managed for DOE by Ohio-based Battelle since the laboratory's inception in 1965.

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Serving Those Who Serve Us: Biomedical Science

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Genetics • Genomics • Proteomics

One size doesn't fit all; that's why scientists at the Pacific Northwest National Laboratory (PNNL) in Richland, Washington, continue to advance world class capabilities and research approaches enabling personalized and predictive care for crippling diseases, conditions, and disorders. With long-term U.S. military conflicts, predictive care for our nation's troops has never been more important.

Arduous battlefield conditions, rigorous training, and multiple deployments are resulting in complex physical and mental wounds for U.S. troops. Post-traumatic stress disorder, substance abuse, and toxic exposure are just some of the debilitating conditions that surface as a result of war. With a long history of applying systems biology methods to problems of interest to the U.S. Department of Energy (DOE) and the National Institutes of Health, PNNL is increasingly applying its science and technology base to the biomedical issues facing the military.

PNNL's focus is on basic human health studies for the clinical benefit of the warfighter, their dependents, and U.S. civilians. Additionally, PNNL is developing applied solutions to support the health and readiness of the military.

Equipping scientists and researchers with the best tools for world class science is a priority at PNNL. With new state-of-the-art facilities in biological and computational sciences, PNNL's research campus is among the most modern within DOE's national laboratory system.

Also located at PNNL is the Environmental Molecular Sciences Laboratory (EMSL), a national scientific user facility, featuring more than 150 pieces of research instrumentation directed at molecular research.

At EMSL, teams of scientists are accelerating research discoveries on some of the most pressing health issues facing the country, such as diabetes and Alzheimer's.

Leading 21st Century Biomedical Problem Sets of the Military with Potential Genomics-Based Solutions

Military Lifecycle

- cancer
- diabetes *(fastest growing disease in the nation)*
- obesity
- arthritis
- spinal cord injury
- substance abuse

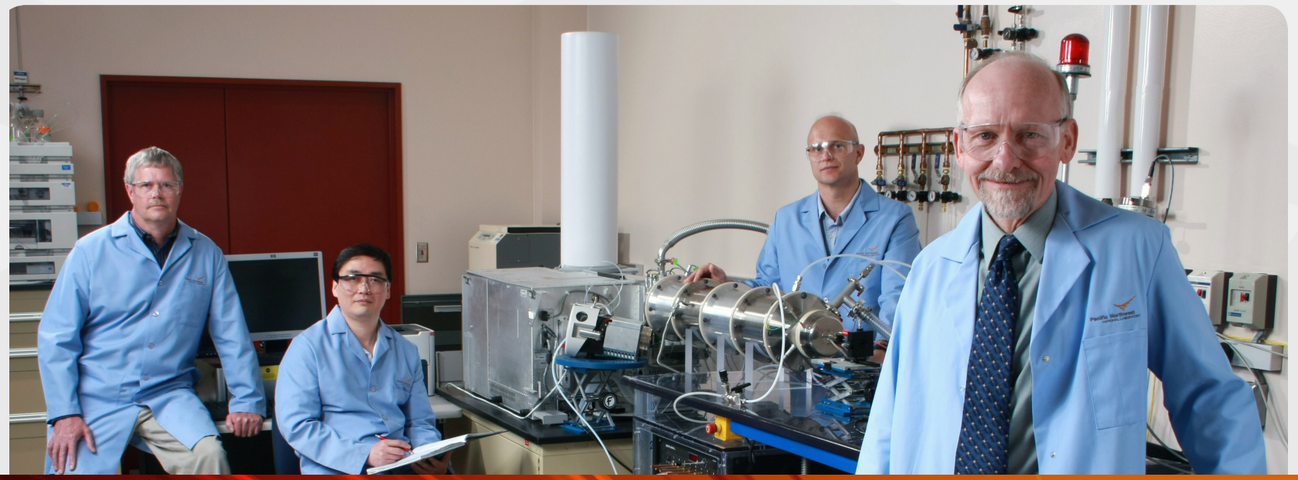
Deployment Related

- military workplace violence
- suicide
- post-traumatic stress disorder/mental health
- traumatic brain injury
- burns
- trainee health
- Gulf War Illness
- toxic exposure in theater

By using state-of-the-art mass spectrometers and other powerful scientific instruments, researchers are learning how proteins and other regulatory systems in the body signal the start of disease, accelerate healing, or respond to medications. The collection of mass spectrometers at EMSL are among the largest and powerful in the United States, with many being customized at PNNL for specialty processing of proteins expressed by cells under specific conditions. This capability enables high-quality, quantitative information on thousands of proteins from each experiment. As a world leader in global proteomics, PNNL research is contributing to predictive and personal care approaches that will benefit both military and civilian populations.

Flagship PNNL-EMSL Capabilities

- Molecular understanding of disease
- Visualization and decision support for larger, complex data sets
- Identification of molecular targets for therapy.



Predictive • Personal • Powerful

Researchers at PNNL with collaborators at the Walter Reed National Military Medical Center in Bethesda, Maryland, and the Windber Research Institute in Windber, Pennsylvania, are embarking on an aggressive, 20-month cancer research study to better understand and profile triple negative breast cancer, one of the most complex forms of cancer where no proven treatments currently exist.

The project takes advantage of one of the most comprehensive collections of breast cancer clinical samples located at Windber's tissue repository, Walter Reed's clinical patient studies, and advanced proteomics technology at PNNL. By profiling the tissue samples taken from Army volunteers both before and after a triple negative cancer diagnosis, researchers hope to find new cellular targets for drugs, as well as identify characteristics that indicate if the cancer will spread.

So why is the military interested in breast cancer?

- Incidence rates for breast cancer are significantly higher in the military among Caucasians and African Americans
- Of the total active duty force, 20 percent are women
- Breast cancer is the most common cancer in women.

"We need a better understanding of this disease," said PNNL biologist Dr. Karin Rodland. "And what's been holding that up has been getting enough samples. The Army's extensive tissue repository, with volunteers donating breast tissue samples pre- and post- cancer diagnosis, provides high quality samples for extensive analysis on triple negative breast cancer." The research team will be looking for proteins that the cancers share in common and any patterns that indicate progression of the disease. The U.S. Department of Defense is providing about $8.6 million for the study to be split between the organizations.

To obtain insight into the mechanisms of drug addiction for the powerful painkiller hydrocodone, PNNL and researchers at the Air Force's 59th Medical Wing are teaming on a proteomics-centered clinical drug study. The addictive properties of hydrocodone are especially concerning to the Armed Forces, whose members experience significant physical trauma—more than the average civilian—due to combat. Loss of limbs and blunt trauma assaults require the administration of powerful pain management medications, but in turn, there are alarming increases in substance abuse statistics within the military.

The aim of this study is to begin to understand genetic susceptibility to dependency, enabling new treatments that can help to mitigate addiction tendencies.

The 59th Medical Wing is performing the pharmacokinetic analyses on biological samples (blood and urine) from volunteers participating in the study. Samples are taken pre-drug exposure and at multiple time points after exposure, providing researchers with a baseline for determining the overall physiological response to hydrocodone.

At PNNL, the samples undergo a complex depletion process to remove common proteins. This allows researchers to observe proteins of lower abundance that might otherwise be obscured. Blood plasma samples are analyzed in duplicate by an LTQ Orbitrap Velos™ mass spectrometer. Even after depletion, hundreds of proteins remain. PNNL researchers are analyzing the protein patterns and "expression" that may reveal an insight into how addiction behavior begins. With 25 volunteers participating in the study, the pharmacokinetic and protein data collected is statistically significant and represents a large undertaking for mass spectrometry analysis of human samples.

PNNL science will enable predictive and adaptive care in support of the military lifecycle.