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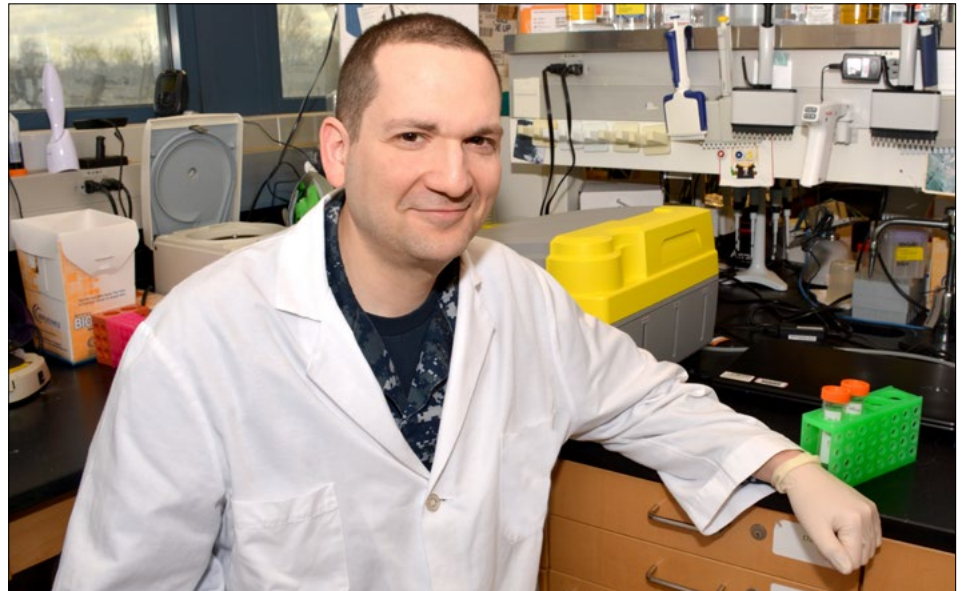
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## Navy Medicine Researchers Working on Dengue Vaccine

Story by Doris Ryan, Naval Medical Research Center Public Affairs



*Lt. Cmdr. Marvin Joel Sklar, a key researcher from Naval Medical Research Center (NMRC) Infectious Diseases Directorate (IDD), pictured in an IDD laboratory at NMRC in Silver Spring, Maryland. (Photo courtesy of Naval Medical Research Center Public Affairs)*

SILVER SPRING, Md. – The same mosquito that carries the Zika virus, carries the dengue virus. Dengue is caused by any one of four closely related viruses transmitted by the bite of an infected *Aedes aegypti* mosquito. About half of the world's population is now at risk.

Dengue is found in tropical and sub-tropical climates, mostly in urban and semi-urban areas. Military personnel are at risk when deployed or traveling in endemic areas.

There is currently no vaccine to prevent dengue infection, but progress is being made by researchers at the Naval Medical Research Center (NMRC).

“NMRC hopes to have a vaccine ready for testing (in volunteers) in the next

three to five years. Right now multiple vaccine candidates are being evaluated at different stages of preclinical testing,” said Lt. Cmdr. Marvin Joel Sklar, a key researcher from NMRC Infectious Diseases Directorate. “We have previously demonstrated the safety of a tetravalent DNA vaccine, and part of our testing involves combinations using that DNA vaccine with other types of vaccine products.”

According to Sklar there is strong evidence showing that infection with the different types of dengue virus increases the risk of complicated, severe and possibly life threatening illness. A vaccine for military use would need to generate sufficient immune response to multiple dengue virus types to help

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## NMRC Commanding Officer's Message



With recent media coverage of the Zika virus outbreak in Brazil and the spread of the disease in South and Central America, Zika has become a household word in the U.S. and around the world. Zika is a flavivirus that has recently been found in several countries within the Western hemisphere. The active transmission of Zika virus necessitates prudent preventive measures to minimize the risk of exposure, infection, and disease progression. No vaccine or drug is currently available to prevent Zika virus infection, and there is currently no specific anti-viral treatment for the disease. For NMRC, our priority is to make sure all NMRC team members, in the U.S. and overseas - military, civilian, contractors, local employees and their families - are well informed on current preventive measures. Even though our infectious disease researchers and other team members know very well the vector that transmits the disease and the standard preventive measures, it never hurts to be reminded. Infection risk is reduced by taking measures to avoid mosquito bites by wearing long sleeve and full length pants, using insect repellent; treating clothing with permethrin, and reducing mosquito breeding grounds such as standing water. If someone develops sudden fever, rash, joint aches, or conjunctivitis within two week of travelling to or living and working in

areas with ongoing Zika virus transmission, they should contact their healthcare provider immediately and report their symptoms and travel history. While we continue to increase our vigilance in the short-term to prevent infection and spread of the virus, these events emphasize the importance of our mission throughout the spectrum of emerging diseases. In the short term, our R&D mission is focused on the development and implementation of methods to detect Zika virus. Looking to the future, we are focused on better understanding the epidemiology of Zika virus and the threat that it represents to our U.S. military and determining how to mitigate that threat through the development of medical countermeasures. The challenge and uncertainty associated with emerging disease threats highlight our need to remain at the cutting edge in laboratory detection, field epidemiology, and medical countermeasure development throughout our NMR&D enterprise.

NMRC Commanding Officer sends,  
Jacqueline D. Rychnovsky, CAPT, NC, USN

## NHRC Commanding Officer's Message

February's Heart Health theme brings to mind the critical tie between basic and applied research, and the tremendous advances in medical care being provided to our service members. The cutting edge research, and development testing at NHRC and throughout the Navy Medicine enterprise, is the heart of military medicine. Research infuses "fresh blood" into medical systems every time we develop innovative solutions for optimizing health and performance, evaluating novel treatments and therapeutics, and streamlining medical logistics. Just as our hearts carry oxygen-poor blood to our lungs, research can reinvigorate our health system by ensuring current medical practices and procedures are safe and effective. Without research innovation, progress in health care stagnates.

At the start of World War II, many medical innovations were unheard of -- blood plasma, state-of-the-art amputee care and prostheses didn't exist. Each has significantly impacted the health and well-being of warfighters and exists today because of researchers' hard work and dedication. NHRC researchers are nearing the finish line of long projects to streamline and standardize AMALs throughout the fleet. They've also harnessed the power of databases they've created to develop advanced software enabling medical planners to ensure they have correct supplies, personnel to treat anticipated casualties and maximize life-saving efforts based on troop levels and operations. These tools are currently used by Navy Medicine for all medical logistics planning and have been accredited and adopted by the DoD. Other researchers collaborate with the CDC, AFHSB-GEIS, state health officials, and others in the detection, surveillance and response to outbreaks that could threaten the health of service members, their families and civilian populations.

We hosted training with scientists from Mexico's Instituto de Diagnostico y Referencia Epidemiologicos (InDRE) as part of joint effort to enhance infectious disease surveillance activities along the U.S.-Mexico border. NHRC continues to infuse Navy Medicine and DOD with products to support warfighter readiness and health. In the seven months since I assumed command, I have seen commitment to innovate, collaboration and excellence in research that translates into practical applications with the ultimate goal of improving our warfighters.

Truly, research is the heart of military medicine.

NHRC Commanding Officer sends,  
Rita Simmons, CAPT, MSC, USN





(continued from page 1)

reduce that risk.

“Dengue has a wide spectrum of presentations in infected people. Typical symptoms of classic dengue include headache, fever, muscle and bone aches and skin rash. The terms Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS) are descriptive and illustrate the severity of illness which can be debilitating, and sometimes fatal,” said Sklar.

Most people will resolve the symptoms of an infection within several days to a few weeks. In some patients the symptoms can be debilitating, and result in pain and malaise lasting weeks.

With appropriate care, the severe form of the disease can resolve but recovery can take weeks. Current treatment is supportive care meaning treating the symptoms and observing the person for worsening signs.

“A dengue outbreak can have a crippling effect on operational forces. For deployed Sailors and Marines who have no prior exposure to dengue the attack rate of infections can reach 50 – 75 percent,” said Sklar. “As such a fighting force entering an endemic region can be rapidly handicapped within days, with operational capacity reduced for weeks, and at the same time creating a sustained transmission that would put other groups at risk.”

The NMRC team is collaborating with other Navy Medicine researchers at the U.S. Naval Medical Research Unit No. 6 in Peru and the U.S. Naval Medical Research Center – Asia in Singapore



*Dengue is caused by any one of four closely related viruses transmitted by the bite of an infected Aedes aegypti mosquito. About half of the world's population is now at risk. (Photo courtesy of Navy Medicine West Public Affairs)*

along with other DoD and federal partners and partners in industry and academia.

According to Sklar, the NMRC laboratories are involved in robust surveillance efforts and that helps vaccine development in multiple ways, including tracking changes in dengue types, even within dengue types, which can affect vaccine targets.

Additionally tracking severe manifestations of the disease provides more information as to its causes and potential targets for study to develop better vaccines. Also, the research in vaccine development itself often leads to better surveillance tools.

“NMRC’s primary mission is focused on the operational health and medical readiness of Sailors and Marines, but our efforts are intimately linked with global health,” said Sklar. “While our focus is military personnel, our strategy is to sharing the best interventions and surveillance methods that ultimately improve the world’s ability to fight this and other infectious disease.”

Sklar added that until an effective vaccine is available, dengue will remain a public health threat around the world, with millions infected each year.

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Graphic illustration by Mikelle D. Smith, Naval Medical Research Center Public Affairs

# Deputy Command Surgeon AFRICOM Visits NAMRU-3 Ghana Detachment

Story courtesy of NAMRU-3 Public Affairs



(From left) Lt. Cmdr. Nehkonti Adams, Col. Jeff Gillen, Deputy Command Surgeon USAFRICOM, Colonel Timothy Robinette, Command Surgeon USAFE/AFAFRICA, Major Francis Obuseh and CMSgt Jayme Jackson. (Photo taken by Mr. Isaac Odoi)

Deputy Command Surgeon U.S. Africa Command (AFRICOM), Colonel Jeff Gillen, visited Naval Medical Research Unit No. 3 (NAMRU-3) detachment in Ghana, Dec. 10, 2015.

During his visit, Gillen received an overview of ongoing infectious disease projects undertaken by NAMRU-3 and collaborators in West Africa in Accra, Ghana.

The detachment was first established in 1997 and was developed as a site for testing vaccines to combat malaria. It is uniquely situated to benefit from its location in a politically stable country in West Africa and maintains strong science partnership with the University of Ghana. Ongoing projects encompass surveillance, diagnosis and characterization of the pathogens underlying infectious diseases.

Administratively based at the U.S. Embassy, Accra, the Detachment's scientific efforts are concentrated at the Noguchi Memorial Institute for Medical Research (NMIMR) where areas of study have included Sexually Transmitted Illnesses (STIs), respiratory infections, and control of disease vectors.

In addition to work in Ghana, the Detachment conducts regional studies in Nigeria and Liberia.

Colonel Gillen and Lt. Cmdr. Nehkonti Adams attended the Way Forward Meeting of the West African Disaster Preparedness Initiative (WADPI). The WADPI project was organized by The Economic Community of West African States (ECOWAS), Kofi Annan International Peacekeeping Training Centre (KAIPTC) and the Republic of Ghana National Disaster Management Organization (NADMO) and supported by AFRICOM through its Operation United Assistance (OUA) Transition Disaster Preparedness Project.

The primary objective of the meeting was to implement an all-encompassing approach to disaster preparedness and response management while promoting continued collaboration, communication and coordination. The recent Ebola Virus Disease outbreak in West Africa served as a model to compare responses among the partner nations.

This Way Forward meeting facilitated a dialog among WADPI participating nations and other key stakeholders to define long-term solutions for enhancement of national and regional disaster preparedness and response systems. Attendance at such meetings highlight the dual science and diplomatic mission that biomedical officers undertaken while serving OCONUS.

# NAMRU-6 Tracks Artesunate Resistance in Peru

Story by Lt. Craig Stoops, NAMRU-6 Public Affairs

LIMA, Peru - Human malaria is one of the most important vector-borne diseases worldwide and has had a significant impact on U.S. Naval Forces throughout history. During World War II the U.S. suffered 113,256 cases, 3,310,800 sick-days and 90 deaths due to malaria. The Vietnam War was no different with 24,606 cases, 391,965 sick-days and 46 deaths.

Artemisinin combination therapy (ACT) is the first-line treatment for *P. falciparum* (PF) malaria, as recommended by the World Health Organization. There is growing evidence of the emergence of PF resistance to Artesunate (AS) in Southeast Asia.

The delayed clearance of parasitemia for more than 24 hours has been taken as an early sign of resistance; a phenomenon seen at the Thai-Cambodian border. The emergence and spread of resistant strains would represent an alarming threat to the success of ACT in the region.

Researchers at the U.S. Naval Medical Research Unit – No. 6 (NAMRU-6) are looking for evidence of AS resistance in Peru. In late 2001, Peru became the first country in the Region of the Americas to adopt ACT with AS and Mefloquine (AS/MQ) as the first-line therapy for uncomplicated PF malaria.

“This is a real threat,” said Lt. Vince Gerbasi, Head of the NAMRU-6 Parasitology Department, “The lack of an effective malaria vaccine and the development of resistance to AS represent two of the biggest challenges for the control of malaria in U.S. Armed Forces performing operations in endemic areas.”

Subsequently, Bolivia, Brazil, Guyana and Ecuador also changed their first-

line treatment to AS/MQ. Given the current state of delayed parasitemia clearance in Southeast Asia and that ACT was first adopted in Peru, the NAMRU-6 Department of Parasitology considered it imperative to conduct a clinical trial in the Peruvian Amazon looking into early evidence of AS resistance in the region.

Lt. Cmdr. Sarah Ballard, Deputy Parasitology Department Head, one of the investigators said, “The main objective of this trial is to determine the rate of clearance of parasitemia in the first 72 hours after administration of AS. The clinical trial is being conducted in eight health facilities and one hospital in the Department of Loreto, where 59 volunteers with confirmed diagnosis of PF mono-infection will be enrolled and receive AS monotherapy.

“This clinical trial is being funded by the Global Emerging Infections Surveillance and Response Program. In order to better understand the current global state of AS resistance/tolerance, NAMRU-6 will compare their observed results with USAMRU-K [U.S. Army Medical Research Unit – Kenya] and AFRIMS [Armed Forces Research Institute of Medical Sciences], which will be performing the same parallel-designed clinical trial,” said Ballard who is optimistic about this study.

“This study will provide valuable information on the current state of resistance/tolerance to AS in Peru and take the necessary control measures to ensure that AS can be successfully used for treatment of PF malaria in the region, Ballard added.”

Thus far, results from the study suggest that there is no direct or indirect indication of parasite resistance/

tolerance to AS monotherapy during the first 72 hours.

Hosted by the Peruvian Navy and co-located at their flagship hospital in Lima, at the Naval Hospital in Iquitos, and in Puerto Maldonado; NAMRU-6 conducts research on and surveillance of a wide range of infectious diseases that are of military or public health significance in the region, including malaria and dengue fever, yellow fever, viral encephalitis, leishmaniasis, Chagas’ disease, and enteric diseases such as shigellosis and typhoid fever.

NAMRU-6 partners with the Peruvian Ministries of Defense and Health and works closely with prestigious universities like Cayetano-Heredia and San Marcos. NAMRU-6, also, enjoys a close and productive relationship with Ministries of Defense and Health universities throughout Latin America as well as with United States Agency for International Development (USAID), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Pan American Health Organization (PAHO), and a number of U.S. universities.

These partnerships yield a robust research agenda that includes work in prevention strategies, clinical management trials, immuno- and molecular rapid diagnostics, epidemiology, and ecology as well as projects measuring the social and economic impact of disease.



# Armed with Sleep: The Importance of Sleep on Warfighter Performance

Story by Rachel Markwald, Naval Health Research Center



SAN DIEGO – Sleep disruption is common among military personnel; often unavoidable during deployments, up-tempo operations, and other evolutions critical to mission success. Several studies indicate a large portion of military members do not routinely get the recommended seven or more hours of sleep each night. This increases the risk of developing insomnia and other sleep disorders.

Scientists at the Naval Health Research Center's (NHRC) Sleep and Fatigue Research Laboratory are studying the sleep concerns warfighters face. Their research addresses sleep throughout the continuum of military service; from

the new recruit to the transition back to civilian life.

There is currently no available ambulatory sleep monitoring device that is operationally-practical and capable of accurate, real-time auto-assessment and user feedback within operational settings.

This capability gap has been identified at military workshops and meetings as a major obstacle to identifying sleep issues and managing fatigue.

The availability of such a device would also allow for reliable at-home monitoring and the ability to gain awareness of how behaviors impact sleep quality before and after operational engagement.

To address this gap, the NHRC sleep research team is evaluating new consumer-available technologies in order to determine which, if any, perform well against the gold-standard methods of laboratory-based polysomnography and mobile wrist actigraphy for assessing sleep.

NHRC is also conducting studies with colleagues at the Naval Medical Center San Diego (NMCS) Sleep Clinic to determine if emerging sleep assessment technologies and smart phone applications can be used to help flag suspected sleep disorders and/or supplement the treatment of insomnia at clinics. It is important to test the effectiveness of these

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technology packages as stand-alone products, either as a prevention or screening tool or as a first-line intervention.

NHRC is also collaborating with the NMCSO OASIS program, a residential treatment facility for patients with combat-related PTSD, to test the effect of a brief, manualized behavioral treatment program for insomnia. Interventions that target behavioral change have been shown to be effective and long-lasting for many different patient populations experiencing poor sleep.

Overall research findings suggest that inadequate levels of sleep when sustained over time increase the risk of physiological disease (including metabolic diseases such as obesity and diabetes), may decrease testosterone levels, and lower immune system functioning, allowing greater susceptibility to illness. These are just some of the physiological effects poor sleep can have over time.



At the Naval Health Research Center (NHRC), scientists are evaluating new consumer-available technologies to determine if any of them perform well against the gold-standard methods of assessing sleep including mobile wrist actigraphy. (Photo courtesy of NHRC Public Affairs)

## TIPS FOR GETTING GOOD SLEEP

**A**void too much alcohol before bed. In general, alcohol may put you to sleep faster, but it will rob you of good quality sleep, leading to increased awakenings during the night and changes to the structure of your sleep stages.

**D**on't exercise intensely too close to your bedtime, it can delay your ability to fall asleep partly through increases in core body temperature. We feel tired and sleep best as our daily rhythm in core body temperature begins to naturally lower before habitual bedtime.

**A**void large meals within two-three hours of bedtime. The physiological process of digestion can interfere with sleep, especially after consuming foods high in fat, protein, and spice.

**I**f you're hungry, have a light snack. Intense hunger can keep you awake too. When your stomach is growling, a light snack can take care of the hunger pains without disrupting sleep.

**S**kip the caffeine six hours before bed. Caffeine taken too close to bedtime can also interfere with your body's ability to fall asleep and obtain restful sleep, more so if you are sensitive to the effects of it.

**C**reate a sleep environment that is quiet, dark, and not overly hot. Whenever possible, this includes limiting potential interruptions from pets, roommates, and street noise. Fans, white-noise generating machines and earplugs can help with unwanted noise interruptions.

**A**void exposure to bright light at night—this includes overhead lights and light exposure from TVs and handheld electronic devices. Light can impact your ability to fall asleep at your desired bedtime by delaying your body's internal clock and propensity to fall asleep until a later time.

**S**et a time for going to bed and waking up that is as consistent as possible from one day to the next.



# NAMRU-SA Announces the Publication of Three Journal Articles

Story from NAMRU-San Antonio Public Affairs

**PLOS ONE**

**Rapid Detection of Neutrophil Oxidative Burst Capacity is Predictive of Whole Blood Cytokine Responses**

Philip J. Vernon<sup>1</sup>, Leslie J. Schaub<sup>1</sup>, Jennifer J. Dallelucca<sup>1</sup>, Anthony E. Pusateri<sup>1</sup>, Forest R. Sheppard<sup>1\*</sup>

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**Abstract**

**Background**

Maladaptive immune responses, particularly cytokine and chemokine release, are a significant contributor to the deleterious inflammation present in many types of injury and infection. Widely available applications to rapidly assess individual inflammatory capacity could permit identification of patients at risk for exacerbated immune responses and guide therapy. Here we evaluate neutrophil oxidative burst (NOB) capacity measured by plate reader to immunologic Phasus Macoccus as an acute strategy to rapidly detect inflammatory capacity and predict maladaptive immune responses as assayed by cytokine array.

**Methods**

Whole blood was collected from anesthetized Rhesus Macaques (n = 25) and analyzed for plasma cytokine secretion (23-plex Luminex assay) and NOB capacity. For cytokine secretion, paired samples were either unstimulated or ex vivo lipopolysaccharide (LPS) stimulated (200 ng/ml, 10 min). NOB capacity was measured in adherent mononuclear cells (AMNC) following phorbol 12-myristate 13-acetate (PMA) ionomycin treatment. Pearson's test was utilized to correlate NOB capacity with cytokine secretion, and p < 0.05 considered significant.

**Results**

LPS stimulation induced secretion of the inflammatory molecules G-CSF, IL-1β, IL-1RA, IL-6, IL-10, IL-12(p70), IL-18, MIP-1α, MIP-1β, and TNFα. Although values were variable, several cytokines correlated with NOB capacity, p < 0.0001. Specifically, IL-1β (p = 0.0001, R = 0.49) and IL-12(p70) (p = 0.0001, R = 0.78) and TNFα (p = 0.0001, R = 0.78) were strongly associated with NOB.

**OPEN ACCESS**

Citation: Vernon PJ, Schaub LJ, Dallelucca JJ, Pusateri AE, Sheppard FR (2015) Rapid Detection of Neutrophil Oxidative Burst Capacity is Predictive of Whole Blood Cytokine Responses. PLoS ONE 10(12): e0146105. doi:10.1371/journal.pone.0146105

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Competing Interests: The authors have declared that no competing interests exist.

PLOS ONE | DOI:10.1371/journal.pone.0146105 December 30, 2015

**HSOA Journal of Clinical Immunology and Immunotherapy**

**Blast Overpressure Induced Pulmonary and Intestinal Damage is Ameliorated by Post-Injury Decay Accelerating Factor Injection**

James E. Campbell<sup>1</sup>, Thomas C. Chou<sup>1</sup>, Brady J. Sheppard<sup>1</sup>, Dale M. Sheppard<sup>1</sup>, Forest R. Sheppard<sup>1</sup>, and Jennifer J. Dallelucca<sup>1</sup>

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**Abstract**

Blast overpressure (BO) is a major cause of injury in military and civilian populations. BO causes pulmonary and intestinal damage, which can lead to death. The purpose of this study was to evaluate the effects of post-injury decay accelerating factor (DAF) injection on pulmonary and intestinal damage in a murine model of BO. Mice were exposed to a BO of 100 kPa and then injected with DAF or saline. Mice injected with DAF showed significantly less pulmonary and intestinal damage compared to saline-injected mice. DAF injection also significantly reduced the levels of inflammatory markers in the lungs and intestines. These results suggest that DAF injection may be a potential therapeutic approach to reduce BO-induced damage in humans.

**OPEN ACCESS**

Citation: Campbell JE, Chou TC, Sheppard BJ, Sheppard DM, Sheppard FR, Dallelucca JJ (2015) Blast Overpressure Induced Pulmonary and Intestinal Damage is Ameliorated by Post-Injury Decay Accelerating Factor Injection. HSOA Journal of Clinical Immunology and Immunotherapy 2: 007. doi:10.1371/journal.hsoa.007

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**International Journal of Nanomedicine**

**Photothermal killing of *Staphylococcus aureus* using antibody-targeted gold nanoparticles**

Nancy J. Millenbaugh<sup>1</sup>, Jonathan B. Baskin<sup>1</sup>, Mary N. DeSilva<sup>1</sup>, W. R. Glickman<sup>1</sup>, Randolph D. Glickman<sup>1</sup>

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**Abstract**

The continued emergence of multidrug-resistant bacterial infections and the decline in discovery of new antibiotics are major challenges for health care throughout the world. This situation has highlighted the need for novel antimicrobial therapies as alternatives to traditional antibiotics. The combination of nanotechnology and laser exposure has been proposed as a strategy to induce physical damage to bacteria, regardless of antibiotic sensitivity. The purpose of this study was to test the effectiveness of antibody-targeted gold nanoparticles combined with pulsed laser irradiation.

**Methods**

Gold nanoparticles conjugated with antibodies specific to *Staphylococcus aureus* surface antigens were incubated with suspensions of multidrug-resistant and methicillin-resistant *S. aureus* (MRSA and MRSE). Bacterial suspensions were then exposed to a pulsed laser irradiation at a wavelength of 532 nm and fluence ranging from 1 to 15 J/cm<sup>2</sup>. Viability of the bacteria following laser exposure was determined using colony forming assays. Scanning electron microscopy was used to confirm the binding of nanoparticles to the bacteria and the presence of cellular damage.

**Results**

The laser-activated nanoparticles treatment reduced the surviving population to 10% of control in the MRSA population, while the surviving in the MRSE population was reduced to 10% of control. Significant decreases in bacterial viability occurred when the laser fluence exceeded 1 J/cm<sup>2</sup>; antibiotic effect was more pronounced at 15 J/cm<sup>2</sup>. Significantly less bacteria were observed on the surface of the nanoparticles compared to the control.

**Conclusions**

Laser-activated nanoparticles targeted to *S. aureus* surface antigens significantly reduced the percentage of viable organisms and prevented a continuing immune response without the use of antibiotics.

**Keywords**

nanoparticles, bacteria, photothermal, immunotherapy, photodynamic

**Introduction**

The development of multidrug-resistant pathogens has become a significant public health risk across the world. Methicillin-resistant *Staphylococcus aureus* (MRSA) has become one of the pathogens of greatest concern due to its ability to cause a wide range of infections ranging from localized skin conditions to life-threatening pneumonia and sepsis and to high persistence in hospital and community-associated settings. Skin and soft tissue infections (SSTIs) are the most common manifestation of MRSA infection in the community setting. Recent studies found that MRSA now accounts for 10% of SSTIs presenting to emergency departments in the US, and the national cost associated with community-acquired MRSA SSTIs ranges from \$100 to \$143 million annually. The emergence of community-acquired MRSA infections over the last decade has been notable because these infections are typically young, healthy individuals without any apparent risk factors, the infections tend to be more

**OPEN ACCESS**

Citation: Millenbaugh NJ, Baskin JB, DeSilva MN, Elliott WR, Glickman RD, et al. (2015) Photothermal Killing of *Staphylococcus aureus* Using Antibody-Targeted Gold Nanoparticles. International Journal of Nanomedicine 2015:10. doi:10.1371/journal.ijnm.101010

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Original research, conducted by Navy scientists at Naval Medical Research Unit San Antonio is published in the journal Public Library of Science ONE (left), the journal Clinical Immunology and Immunotherapy (center), and the International Journal of Nanomedicine (right). (Graphics courtesy of NAMRU-SA Public Affairs)

SAN ANTONIO, Texas – Naval Medical Research Unit San Antonio (NAMRU-SA) announces the publication of three new journal articles describing studies conducted by Navy researchers at Joint Base San Antonio, Fort Sam Houston in San Antonio.

“Every NAMRU-SA project is directed toward the development of life-saving or health-improving technologies that will result in better outcomes for warfighters,” said Cmdr. Forest R. Sheppard, head of the Expeditionary and Operational Medicine Department at NAMRU-SA.

The capacity to quickly identify patients at risk for maladaptive immune responses and who may benefit from immune-modulatory therapies is described in a study published online Dec. 30, 2015 in the journal Public Library of Science ONE. The paper’s first author, Philip J. Vernon is a researcher in NAMRU-SA’s Immunodiagnostics and Bioassay Development Department. **Citation:** Vernon PJ, Schaub LJ, Dallelucca JJ, Pusateri AE, Sheppard FR (2015) Rapid Detection of Neutrophil Oxidative Burst Capacity is Predictive of Whole Blood Cytokine Responses. PLoS ONE 10(12): e0146105. Doi:10.1371/journal.pone.0146105

The capacity to quickly identify patients at risk for maladaptive immune responses and who may benefit from immune-modulatory therapies is described in a study published July 17, 2015, in the journal Clinical Immunology and Immunotherapy describes Blast Accelerating Factor or DAF as an attractive option for use by first-responders or emergency medical technicians for improved preservation of pulmonary and intestinal tissues and allow for patients arrival at a primary point of care in a lesser critical

condition. Co-author for this study, Cmdr. Forest R. Sheppard, U.S. Navy trauma surgeon, currently heads NAMRU-SA’s Expeditionary and Trauma Medicine Department, Combat Casualty Care and Operational Medicine Directorate. **Citation:** Campbell JE, Chou TC, Sheppard BJ, Sheppard DM, Sheppard FR, et al. (2015) Blast Overpressure Induced Pulmonary and Intestinal Damage is Ameliorated by Post-Injury Decay Accelerating Factor Injection. J Clin Immunol Immunother 2: 007.

Findings from a NAMRU-SA study published March 18, 2015, in the International Journal of Nanomedicine describes how laser-activated nanoparticles targeted to *Staphylococcus aureus* surface antigens significantly reduced the percentage of viable organisms and represents a promising new treatment modality that could be used either alone or as an adjunct to existing, conventional antibiotic therapy. The paper’s first author, Nancy J. Millenbaugh is a Principal Investigator in NAMRU-SA’s Maxillofacial Injury and Disease Department. **Citation:** Millenbaugh NJ, Baskin JB, DeSilva MN, Elliott WR, Glickman RD, et al. (2015) Photothermal Killing of *Staphylococcus aureus* Using Antibody-Targeted Gold Nanoparticles. International Journal of Nanomedicine 2015:10.

“NAMRU-SA is rigorously committed to publishing original research that supports the survivability of our warfighters and as we head into 2016, we already have three new papers accepted for publication,” Says NAMRU-SA Commanding Officer, Capt. Elizabeth Montcalm-Smith.



# NHRC Scientist Awarded for Work in Aviation Selection Research

Story Courtesy of NHRC Public Affairs

SAN DIEGO – Lt. Brennan Cox, aerospace experimental psychologist at the Naval Health Research Center (NHRC) was presented the Robert S. Kennedy Award for Excellence in Aviation Research, for his work in aviation selection and aircrew survivability, Jan. 14.

The award, which is given annually by the United States Naval Aerospace Experimental Psychology Society, was based on Cox's research in support of the Naval Aviation Selection Test Battery (ASTB), the primary tool for selecting pilots and flight officers for the Navy, Marine Corps, and Coast Guard.

Cox's research resulted in an updated version of the ASTB and the ASTB-E, which added new components to the battery, including computer adaptive testing framework, an adaptive forced-choice personality inventory and a series of performance-based measures for assessing candidates' psychomotor skills and abilities.

When translated into operational practice, the ASTB-E demonstrated improvements in predictive validity, test security, and administration efficiency, yielding an estimated \$42 million in cost savings annually.

"All test development and delivery decisions made by my research team were data-driven and supported by science," said Cox. "At face value, these tests resemble any number of basic flight simulator video games. An initial concern was whether experienced 'gamers' would over-perform on these ASTB-E tests and be incorrectly identified as fit for flight training – a false positive – but our research found that while individuals who self-report a history of flight simulator gaming experience tend to do well on the ASTB-E, they also tend to do better in flight training. Skills developed playing video games using stick and throttle devices at home translate to the ASTB-E as well as the cockpit."

Cox said his work reflects his interest in the study of individual difference variables, such as personality traits and cognitive abilities, and how they contribute to workplace



*Lt. Brennan Cox, aerospace experimental psychologist at the Naval Health Research Center (NHRC) was presented the Robert S. Kennedy Award for Excellence in Aviation Research, for his work in aviation selection and aircrew survivability. (Photo courtesy of NHRC Public Affairs)*

performance. During his research for the ASTB-E, Cox was able to systematically investigate the underlying constructs that predict a person's performance in a very complex environment like the cockpit.

"This research truly represents a team effort," said Cox. "I share the honor of this award with each of the colleagues who helped make it possible and I look forward to future opportunities to collaborate."

Cox joined the Navy in 2010, after being recruited while presenting his dissertation at a conference. Cox was still a student at Auburn University where he earned a Ph.D. in industrial and organizational psychology.

"I was unaware that the Navy had active duty positions for scientists," said Cox. "I chose this career path because it allows me to be a part of something bigger than myself, and I believe the work I do supports a greater good. Plus, I got to learn how to fly."

"I am extremely proud of the work done by Lt. Cox in support of our aviation community," said Capt. Rita Simmons, commanding officer of NHRC. "His commitment to excellence and innovation, his collaborative spirit, and his hard work and dedication are the qualities we need in our scientists in order to ensure we support the readiness of our warfighters. As a former aviator myself, I truly appreciate the work he is doing to keep our pilots safe."

As the DoD's premier deployment health research center, NHRC's cutting-edge research and development is used to optimize the operational health and readiness of the nation's armed forces. In proximity to more than 95,000 active duty service members, world-class universities, and industry partners, NHRC sets the standard in joint ventures, innovation, and translational research.

## R&D Chronicles

### Part II Behnke, Momsen, and the Advent of Submarine Rescue

By Andre B. Sobocinski, Historian, Bureau of Medicine and Surgery

(Continued from January 2016 Issue)



*USS Squalus and Diving Bell. Watercolor by John Groth, 1966. On the 4th rescue dive of the McCann diving bell, the steel wire used to raise the bell to the surface became fouled. The bell was lowered to the ocean floor and divers were sent down in an unsuccessful attempt to unfoul the wire. The bell was subsequently raised through the manipulation of buoyancy in the ballast tanks, and manual hauling to the surface. (Image courtesy of Navy Art Gallery)*

At 11:30 pm, May 23, 1939, a diving crew of 14 men and officers arrived from Portsmouth in cold and rainy conditions. Later, 25 divers arrived on the scene aboard the salvage vessel USS Falcon (ASR-2). Diving operations began at dawn, May 24. The divers from the Falcon made their first attempt at rescuing the crew from the Squalus with the ten-ton McCann rescue chamber.

The Falcon was moored above the Squalus. The first dives were conducted to attach the chamber's downhaul cable. By early afternoon, the rescue chamber was deployed, attached to the escape hatch and the first eight submariners were brought to the surface.

Behnke remarked at the time, "These men appeared calm and relaxed. There was no evidence of hysteria. All were cold and some were in a condition of mild shock. About one-third of the survivors suffered from headache[s], undoubtedly the result of increased carbon-dioxide concentration."

A major concern for the operation was the bends or

*"The atmosphere in the submarine was dark, cold and moist. The men suffered acutely from cold, which was only partially relieved by eating."*

*~Lt. Naquin, CO of Squalus, May 1939*

decompression sickness. The Squalus' crew had been submerged to an excess of 13 pounds of pressure for over 30 hours. The Navy had set up a recompression chamber in case the problem manifested.

However, the recompression chamber would mainly be used to supply warmth and oxygen therapy.

As Behnke later remarked, "Medical treatment was directed toward maintaining absolute rest, and supplying heat and fluids, consisting of coffee and malted milk, to which liberal amounts of sugar were added."

Follow-up medical care was provided at the nearby Naval Hospital Portsmouth, Portsmouth, New Hampshire. Carbon dioxide poisoning, effects of oxygen depletion, pneumonia, fatigue, and shock were among the chief medical concerns.

Some 15 hours after the start of the operation fatigue began setting in among the rescuers. On its fourth deployment the rescue chamber became stuck on its ascent with eight men aboard. Divers were sent down to sever the downhaul cable and attach a new one. A safety cable held the rescue chamber in place.

Throughout the operation conditions were less than ideal for the divers. Water temperature hovered around 39 degrees Fahrenheit and the rescue was conducted in near complete blackness.

By May 25, 33 surviving crewmembers were rescued marking the first time in history that a successful rescue took place 100 feet below the surface. Some would call it the greatest submarine rescue in history. But the mission was not yet over. May 25, the Navy would lead the salvage operation and retrieval of the 26 deceased Sailors.

(Will continue in March 2016 Issue)



# NHRC Scientists Receive Outstanding Achievement Award

Story courtesy Naval Health Research Center Public Affairs



The National Training and Simulation Association presented its annual Modeling & Simulation Awards during a banquet Dec. 1, 2015, Orlando, Florida. The Naval Health Research Center's PhyCORE team was recognized in the category of "Cross-Function," for work done to expand and enhance a virtual reality walking and balance tool for injured warfighters into one that can also promote injury prevention and resilience. (Photo courtesy of NHRC Public Affairs)

SAN DIEGO – Scientists from the Naval Health Research Center (NHRC) recently received the Outstanding Achievement in Modeling and Simulation (Cross-Function) award at the National Training and Simulation Association's (NTSA), Dec. 1, 2015.

NHRC's Physiological and Cognitive Operational Research Environment (PhyCORE) team was honored for their work in expanding a virtual reality walking and balance-based rehabilitation tool for injured warfighters into one now capable of promoting injury prevention and resilience.

"This award is well-deserved," said Capt. Rita Simmons, commanding officer of NHRC. "The PhyCORE team embodies the professionalism, expertise, and collaborative spirit that can be found in each of our researchers. This recognition also spotlights the type of innovative work that goes on every day at NHRC and how we are uniquely positioned with cutting-edge tools and seasoned experts to do some exciting and ground-breaking work."

The tool, the Computer Assisted Rehabilitation Environment (CAREN),

was installed at NHRC in 2008 and originally used for rehabilitation research to support the recovery of combat-injured service members, particularly those with lower-limb amputations and traumatic brain injuries (TBI).

The CAREN's initial configuration incorporated a 6-degree of freedom motion platform with integrated instrumented treadmill, multiple motion capture cameras, and a large curved screen with 180-degree projection creating a virtual environment mirroring real-world situations.

"Over the last three years, my team has enhanced the CAREN's capabilities with a programmable scent system, 3-dimensional projection and environments, improved surround sound system, accurate laser shooting system, and a high performance treadmill capable of high accelerations for simulating trips," said Pinata Sessoms, Ph.D., senior biomedical engineer with NHRC's PhyCORE team.

Additional improvements include a unique driving cab developed in-house by NHRC scientists that can be placed on

the CAREN platform. Service members are challenged as they drive through customizable simulated driving scenarios to assess awareness, speed infractions, driving violations, and other errors.

The PhyCORE team designed additional performance measurement tools and incorporated them into the CAREN allowing researchers and clinicians a host of different quantitative physiological measures to support the recovery and rehabilitation of injured service members. These include surface electromyography (sEMG) for measuring muscle activation and fatigue, eye-tracking and gaze-tracking for attention and symptom measurement in patients with TBI, and mobile electroencephalography (EEG) systems to measure increased cognitive workload and differences in brain activity while service members perform different tasks.

"The PhyCORE team has invested over 1,000 hours of clinical investigation and therapy, treating over 100 patients within the virtual environment," said Sessoms. "We work closely with our collaborators at the Naval Medical Center San Diego to treat our wounded warriors and our research has led to improved therapies and capabilities such as walking, balancing, and cognitive performance that allow injured service members to return to their daily activities and, in many cases, full function. The work we've done to expand the CAREN system beyond its original configuration was actually the genesis of what we now call the Physiological and Cognitive Operational Research Environment, or PhyCORE."

Part of what led to the PhyCORE team's success in expanding the CAREN's capabilities and furthering of their research is the interdisciplinary nature of the team. The group of researchers and clinicians includes physical therapists, kinesiologists, biomechanists, biomedical engineers, software and hardware engineers, sleep physiologists, an aerospace experimental psychologist, and a neuropsychologist.

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# Teaching Teachers: STEM Careers in Navy Medicine Research

Story courtesy of NHRC public affairs

SAN DIEGO - High school science, technology, engineering, and math (STEM) teachers from Washington, Oregon, California, and Idaho toured the Naval Health Research Center (NHRC) Jan. 15, to see a working research lab in action and gain insight from researchers actively working in STEM professions.

The 31 teachers who visited NHRC were participants in the M. J. Murdock Charitable Trust "Partners in Science" program, which held its annual meeting in San Diego this January. The program helps high school science teachers expand their knowledge about cutting-edge research so they can take that information back into their high school science classrooms, promote hands-on science education, and get their students excited about science.

"We really enjoyed hosting the teachers and opening up new possibilities they can share with their students who are interested in future STEM careers," said Capt. Rita Simmons, NHRC's commanding officer. "For many students, combining a science education with a military career can be a great way to do some incredibly innovative research, be of service, and pay for a college education. There are many paths to a career in science, and serving as a military scientist conducting health research can be very rewarding and offer experiences you can't find anywhere else."

As part of the tour, teachers visited the

molecular and microbiology labs to learn more about the infectious diseases research being conducted at NHRC. They also had an opportunity to visit the Warfighter Performance Lab that focuses on research in sleep, environmental physiology, injury recovery, and human performance optimization.

A highlight of the tour was a visit to the Computer Assisted Rehabilitation Environment (CAREN), which is used in the Warfighter Performance Lab for research to support the recovery and rehabilitation of wounded warriors to prevent injuries and promote resilience.

During the tour, the teachers had an opportunity to talk with military and civilian scientists, learn what they do on a day-to-day basis, and find out how they went from student to scientist.

One teacher who particularly enjoyed the tour was Cynthia McIntyre, an honors and advanced placement biology teacher at Everett High School in Washington state.

"Everett is home to a military base and we have the Navy right there, so this provided an opportunity for me to learn more and be able to talk to my students who are interested in the science field about what you can do in the Navy," said McIntyre.

When asked what her favorite part of the tour was, McIntyre had a hard time choosing one thing.

"I could live in a lab and never come out," said McIntyre. "I'm a molecular biologist and a microbiologist, but I loved the [Warfighter Performance] lab. That was really cool. Just thinking about all the ways you can monitor and quantify sleep and movement, and learning about the CAREN was amazing."

According to McIntyre, an important insight gained from the tour was that STEM career opportunities are continually expanding and that there is something for everyone.

"When we were learning about the CAREN, I thought about all the different support staff that is needed, from computer coders to the people who design the equipment itself to the scientists, and realized there is a place in STEM careers for every single kid," said McIntyre. "Even if you love science, but don't want to do the science, there's still a place in the field so you can be around it and still enjoy it."

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## BLACK HISTORY MONTH

The Naval Medical Research Center (NMRC) and Walter Reed Army Institute of Research (WRAIR) Joint Multicultural Committee held a ceremony in recognition of black history month in the Albert Behnke Auditorium, Feb. 18. The event theme "Hallowed Grounds: Sites of African American Memories," featured a guest speaker that touched on the history of African Americans who lived during the time of enslavement in the state of Maryland, as well as the singing of the black national anthem.



Naval Medical Research Center (NMRC) Commanding Officer, Capt. Jacqueline D. Rychnovsky congratulates the winner of the Find Your Freedom challenge for Black History Month observance. (Photo courtesy of Naval Medical Research Center Public Affairs)





## TrEAT TD and COBRA GOLD 2016

Story by Army 2nd Lt. Amanda Case, USUHS

THAILAND - The Trial Evaluating Ambulatory Treatment of Travelers' Diarrhea (TrEAT TD) and Cobra Gold 2016 have officially started throughout Thailand! TrEAT TD is one of the largest collaborative studies funded by the Navy's Bureau of Medicine and Surgery and involves multiple partners including the Uniformed Services University of the Health Sciences Infectious Disease Clinical Research Program, multiple U.S. Naval Medical Research Units, all four military services, and the Armed Forces Research Institute of Medical Sciences (AFRIMS).

The study initiated in early February includes investigators from San Antonio to Singapore joining the study team coordinated by Navy Capt. Mark S. Riddle from the Naval Medical Research Center, and Army Maj. Brett Swierczewski from AFRIMS.

At its core, TrEAT TD is a cutting edge clinical trial aimed at developing more efficacious treatment protocols for the optimal management of dysentery and watery diarrhea frequently experienced by military personnel overseas. Dysentery and watery diarrhea are the number one cause of lost duty days in deployed troops and current defined treatment protocols have not been established thus current management has been found in repeated studies to be sub-optimal.

The study results from the TrEAT TD study will be used to develop Clinical Practice Guidance with the aim of reducing lost duty days from dysentery and watery diarrhea by defining and standardizing the most efficacious treatment protocols for use by all levels of medical providers. Prior to starting in Thailand this year, TrEAT TD was executed at other sites around the world, including Afghanistan, Djibouti, Honduras and Kenya and has included service members acutely ill with travelers' diarrhea from both U.S. and United Kingdom deployed forces.

In Thailand, TrEAT TD is being conducted during Cobra Gold 2016, an Asia-Pacific military exercise ongoing since 1982



TrEAT TD study team at Cobra Gold 2016 in Thailand. L to R: HM2 Jason Ramirez, Maj. Bett Swierczewski, Capt. Shauma Butler, Cpl. Mathew Timlin, 2nd Lt. Amanda Case, Capt. Mark Riddle, Cmdr. Chris Duplessis, Dr. Rober Deiss, and immunologist Mrs. Nuanpan Klemn. (Photo courtesy of USUHS)

between the United States, Thailand, and multiple other Asia-Pacific countries. The Cobra Gold 2016 exercise is used to improve coordination between the United States and Thailand in both military and humanitarian efforts, as well as strengthen ties between the United States and our Asia-Pacific allies.

TrEAT TD is being conducted at three separate Cobra Gold 2016 sites. Investigators are working with the U.S. Army, Navy and Marine Corps units to identify and enroll cases of dysentery and watery diarrhea in American troops.

Investigators are also collaborating closely with the Royal Thai Army to optimize laboratory resources. Providers have already seen cases of both dysentery and watery diarrhea that will contribute to the TrEAT TD study. The good news: TrEAT TD and Cobra Gold 2016 are both well underway.

## NHRC Scientists Receive Outstanding Achievement Award

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Due to the enhancements the team developed for the CAREN, it is now much more than a rehabilitation tool—it can also measure the physical performance of service members using operator-specific tasks. The CAREN is now ideal for testing the effects of new protective gear, carriage loads, and equipment on warfighter performance.

“The use of one system for so many different capacities maximizes the resources of the Navy and has led to the creation of a multi-faceted team of experts who can study multiple performance metrics at one time, in one place,” said Sessoms. “For example, instead of just measuring cognitive load, fatigue, or movement, we

can measure the correlation between each of these factors. We’ve created a tool that isn’t just for rehabilitation—it’s now capable of promoting injury prevention and resilience.”

The PhyCORE team shares information with other Department of Defense CAREN sites to promote best practices, collaboration, and cost savings.

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