***Bradley/Herzfeld Catalyst Phase 5 Awards ($231,000 awarded in the summer 2012)***

The Research Foundation has selected five new projects for funding in the fifth round of the Bradley Catalyst Grant Program. This is being funded by $200,000 from the Lynde and Harry Bradley Foundation and an additional $31,000 from the Richard and Ethel Herzfeld Foundation in their third round of support for the program. A total of $231,000 will be awarded to support these projects in the summer of 2012

## *Catalyst Award Recommendations:*

### Vitamin D Receptor Targeting for Ovarian Cancer

**Alexander Arnold**, Ph.D., Assistant Professor, Department of Chemistry and Biological Science

Alexander Arnold has worked in the field of nuclear receptor biology for more than ten years. Nuclear receptors are key to the protein-protein interactions that are essential for signaling in all living organisms. Arnold's work focuses on the vitamin D receptor which is one of 48 nuclear receptors identified in the human genome. He joined UWM as an Assistant Professor in 2009 after work at previous institutions that included St. Judes Children's Research Hospital.

**High-Throughput Screening Identified Promising Compounds for Cancer.** Dr. Arnold is developing a high-throughput screening capability at UWM which allows Arnold and colleagues at UWM, the Medical College of Wisconsin and other institutions to quickly test tens of thousands of compounds and identify those that are promising for further research.

This capability helped Arnold discover molecules that can disrupt interactions between the Vitamin D receptor and other proteins; this discovery has the potential for treating a variety of metabolic disorders, including ovarian cancer. In the United States, ovarian cancer is the most common cause of gynecologic cancer death. Current treatments involving surgery and chemotherapy have limited efficacy due to tumor resistance, recurence and serious side effects, and they offer only a five year survival rate for 47% of treated ovarian cancer patients. According to the American Cancer Society there are 22,280 new cases of epithelial ovarian cancer annually in the U.S. and 15,500 related deaths.

**Project Objective – Obtain Key Animal Data.** In this project, "*In Vivo* Evaluation of Selective Inhibitors of the Vitamin D Receptor-Coregulator Interaction," Arnold and his colleagues hope to address this unmet clinical need; they will test a group of compounds that he developed which showed strong promise in initial screening. This project will take an important next step by moving from *in vitro* testing to *in vivo* testing conducted in a mouse model for ovarian cancer.

**Important Steps Toward Commercialization.** The research proposed here is a critical step along the commerical development pathway for a new drug. The work will provide the *in vivo* efficacy and druggability data needed to a) demonstrate pharmacological proof-of-concept and b) support strong patent claims covering novel compositions and therapeutic uses for cancer treatment. The expected data will be included in a full patent application in 2012 and related applications thereafter to strengthen the IP portfolio. The performance data and patents will be the foundation for transitioning the academic research to commercial development. Market research data show that cancer programs are the most active areas of pharmaceutical partnering and M&A activity in the U.S. Dr. Arnold, in close collaboration with the UWM-Research Foundation and the Milwaukee Institute for Drug Discovery, expects to play an

High-throughput screening equipment helped Arnold to identify promising compounds for treatment of cancer. With this capability, Arnold is helping other researchers find promising new targets for a variety of diseases.

active role in marketing the technology to relevant biopharma companies to license the technology and conduct collaborative research. Arnold may also participate in organizing a commercial venture to fund (via SBIR and/or private equity) and pursue development of lead cancer drugs.

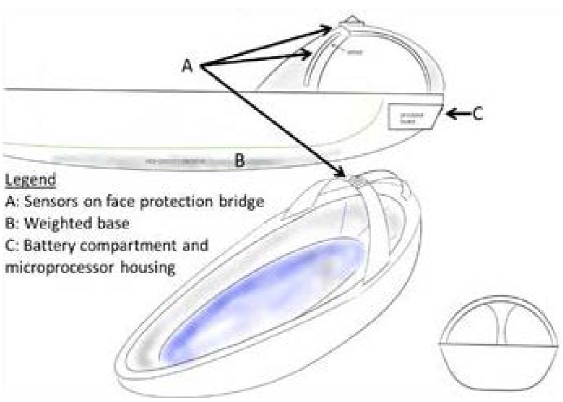
## Protective I-SleepPod for Young Infants

**Jennifer Doering**, Ph.D. R.N., Associate Professor, College of Nursing

Jennifer Doering is an Associate Professor at the University of Wisconsin-Milwaukee College of Nursing. She studies how sleep deprivation affects depression in urban women after childbirth. In the past six years, Dr. Doering has conducted five studies in impoverished areas of Milwaukee County that have qualitatively and quantitatively investigated maternal sleep, fatigue, and depression in family's homes over the first six months. Her efforts have included the development and implementation of a community-based depression screening program within an early intervention program.

**Community Health Need – Addressing Sudden Infant Death Syndrome.** Innovative approaches are needed to reduce infants deaths related to unsafe sleep environments. In 1992, the Back to Sleep Campaign, which encourages parents to place their infants to sleep in a supine position rather than prone or side-lying, was implemented, and the program has saved many lives. However, since 2001 Sudden Infant Death Syndrome (SIDS) rates have leveled off at 0.56 deaths per 1000 live births despite increases in supine sleep behavior and continued refinement of the American Academy of Pediatrics (AAP) policy statement discouraging bedsharing. Researchers and parents alike are calling for innovative harm-reduction strategies to make adult sleep environments safer for infants, since 20 to 50 percent of infants will continue to sleep on adult beds, couches, and recliners in spite of heightened public health efforts to end these practices. Commercially available co-sleeper products are an unsafe choice for parents, because they do not utilize design or safety mechanisms that reduce risk of harm from the common causes of death within unsafe sleep environments

**Prototype Device Intended to Make Sleeping Environment Safer.** The goal of this project is to build and pilot the usability and feasibility of a prototype device – the Infant Sleep Pod (I-SleepPod) – that will provide a dedicated, portable, and protective sleep environment for an infant up to 6 months of age. A shared sleep surface (e.g., bed, couch, recliner) with an adult caregiver is a major factor in approximately half of infants who die of SIDS with greatest risk in infants less than 4 months of age. These deaths are preventable tragedies. This project brings together an interdisciplinary team that includes researchers in nursing and engineering to create an infant sleep system that mitigates the risk of asphyxia, mechanical airway obstruction, and overlay and can function in a variety of sleep environments.




Concept drawing of Infant Sleep Pod Device that is intended to make the sleeping environment safer and address community health issue of Sudden Infant Death Syndrome.

**Proof of Concept Will Help Develop Commercial Partnerships.** This proof-of-concept demonstration, including a prototype device and demonstration study will help lead to commercial partnerships that can address the $8.9 billion market in the United States for infant consumer products. The UWM Research Foundation, working with Dr. Doering's team will approach major infant product manufacturers such as American Baby Company, Graco, and The First Years and seek to bring this important idea to the broadest possible audience.

## New Treatements for Neuropathic Pain

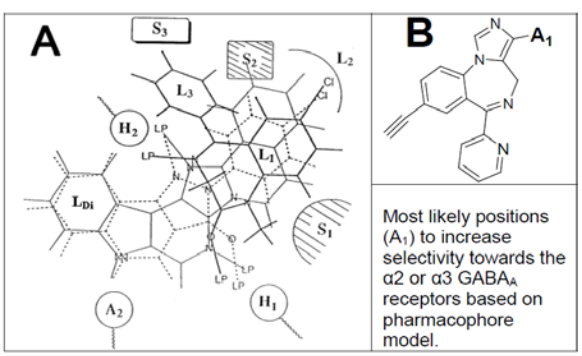
**James Cook**, Ph.D., Professor, Department of Chemistry and Biological Science

**The GABA System – Importance to Pain and Addiction.** The GABA system refers to a group of chemical receptors in the brain that are important to pain, anxiety, depression and addiction. The system includes several major receptors. By targeting specific receptors and avoiding other receptors, scientists strive to design drugs that can address things like pain and anxiety without giving rise to negative side effects like addiction and drowsiness (effectively turning on and off individual receptors like circuit breakers). James Cook has built his career around understanding this important system and working to design compounds that attack this tricky problem of hitting the right "circuit breakers" while avoiding the others. To do this, he relies on his knowledge of chemical structures and how they have reacted as well as increasingly sophisticated tools that model the positions of molecules and predict how they will interact with what is known about the structure of the receptors.

**Unmet Clinical Need in Neuropathic Pain Treatment.** Neuropathic pain encompasses a range of painful conditions of diverse origins including fibromyalgia, diabetic neuropathy, ghost limb pain, post-herpetic neuralgia and nerve injuries after surgery. Back pain, cancer pain and AIDS associated pain also qualify as neuropathic pain. Currently, prescribed drugs for neuropathic pain are often addictive, are not effective for all patients, and have various side effects including tolerance, addiction, sedation, and liver toxicity. The financial burden from the loss of productivity in the US alone numbers in the billions of dollars, notwithstanding the misery these patients suffer.

**Targeted Receptor Activity Makes New Compounds Superior.** Recently, Cook and his research team discovered a series of compounds that are active against neuropathic pain as well as anxiety disorders and convulsions. These new compounds do not develop tolerance and are comprised of a chemical structure which is less likely to be toxic. Because these compounds target selective receptors but are not active for other key receptors they will exhibit very little or no abuse potential.

**Obtaining Important Data for Potential Partners.** This project, "New Treatments for Fibromyalgia, Diabetic Neuropathy, Ghost Limb Pain and other Pain Disorders," centers on the modification of these new agents to prolong the duration of action *in vivo* and to provide better subtype selectivity (targeting desired receptors while avoiding the undesirable receptors). This will make them less likely to give rise to undesirable side effects including sedation, ataxia, amnesia, tolerance and abuse potential. Cook's collaborators will help him test the new compounds in animal models giving him important data which may lead to licensing agreements with major pharmaceutical companies or one of several Wisconsin-based startup companies that has expressed interest in the work.




Cook's knowledge of the GABA receptors help build a model for the system (shown in A). Based on this model he is able to predict where to attach key elements to target molecules (shown in B) that will increase the likelihood of producing the desired effects.

## Blue Light Device for Bacterial Eradication

**Chukuka Enwemeka**, Ph.D., Professor, College of Health Sciences

Chukuka Enwemeka is a Professor in the College of Health Sciences and was recently appointed UWM Distinguished Professor, the most prestigious title that can be bestowed on a faculty member at UWM. He is also Dean of the college and maintains an active research program. Enwemeka is one of the world's foremost authorities in the area of photo-engineering of tissue repair process with visible and near infrared light and lasers. He has authored more than 85 research papers, monographs and book chapters, and has presented more than 300 papers, seminars, symposia and workshops nationally and internationally.

**Unmet Clinical Need in Controlling MRSA.** Bacterial resistance to drugs is a major problem in health care. Despite the emergence of stronger antibiotics, outbreaks of Methicillin resistant *Staphylococcus aureus* (MRSA) infection are rampant and are of major concern worldwide. Bacteria have developed a range of adaptive mechanisms which make the quest for stronger and effective antibiotics even more challenging. The Centers for Disease Control (CDC) indicates that reducing MRSA in both healthcare and community settings continues to be a high priority.

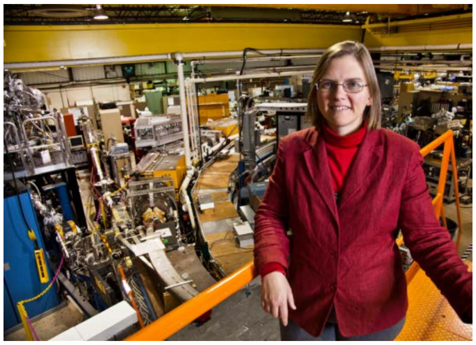
**A Different Approach to Controlling MRSA – Blue Light.** Enwemeka and his collegues made a departure from the efforts to develop stronger antibiotics and turned to the use of blue light to eradicate MRSA. They have been able to show that blue light at wavelenghts of 405 nm and 470 nm can kill as much as 94% of bacterial colonies in their *in vitro* assay. Their work so far has shown that use of these wavelengths is equally effective against two genetic variants of MRSA, hospital acquired strain (HA-MRSA) and community acquired strain (CA-MRSA), indicating that, unlike antibiotics to which the bacteria continue to develop resistance, photo-eradication may be effective in killing both current and future variants of the bacteria.

These results are promsing, but challenges remain. Their results show that the bacteria must be irradiated repeatedly at high dosages in order to attain 100% clearance. The denser the bacterial culture, the higher the dose and the greater the number of treatments needed to achieve 100% eradication. These findings suggest that, although the superficial layers of bacteria are readily killed by 405nm or 470nm light, colonies below them in the Petri dish are less susceptible to photo-eradication because of the limited depth of penetration of blue light. If the properties of either 405nm or 470nm light were altered to improve irradiance and depth of penetration, then more MRSA colonies could be effectively eradicated at clinically desirable lower, safer doses.

**Project Objective – Building an Effective Device.** The goal of this project, "Development of a Light Delivery System That Optimizes Bacterial Eradication," is to enhance the depth of penetration of 470nm light in order to optimize its bactericidal effect. Enwemeka and his collaborators will construct an optical system that will maximize the depth of penetration by controlling the phase of the wave front using various optical components including a "phase mask" which would make the device commercially practical. They will then determine the dose-response performance of the system by irradiating MRSA cultures in vitro and explore clinical safety concerns by examining the effects of various doses on human cell viability. If they are successful, these will be important steps to making a practical and safe device that could be commercially viable.

## Graphene Monoxide Advanced Material for Lithium-Ion Batteries

**Carol Hirschmugl**, Ph.D., Professor, Department of Physics



Carol Hirschmugl is a physicist who studies matter in its most fundamental form. She has developed innovative tools to study human cells using infared radiation from a synchrotron – a device that accelerates electrons to the speed of light. She also collaborates with colleagues in physics and engineering using advanced microscopy tools to study intriguing new materials such as graphene – a single atomic layer sheet of carbon atoms linked together in a regular structure. The astounding properties of graphene have made this material an exciting and versatile new candidate for novel electronic technologies, but viable large-scale production methods for graphene have yet to be found.

**Study of Graphene Leads to a Surprising Discovery – Graphene Monoxide.** In searching for a practical method to make graphene on a large-scale, Hirschmugl, and her co-investigators, Marija Gadjardziska-Josifovska, Junhong Chen, and Mike Weinert made a surprising discovery. While heating graphene in a vacuum, they discovered that films of graphene oxide undergo a previously unreported phase transition during thermal reduction. The new phase is a layered, mixed nanocrystalline phase of graphene and a new material – Graphene Monoxide (GMO) with an unusual ratio of C:O of 1:1. These results have recently been published in a nano-technology journal, *ACS Nano,* and have been generating significant interest.

**Graphene Monoxide Properties Make it Promsing Material for Lithium-Ion Batteries.** This new material has a theoretical band gap of ~0.9 eV. Band gap is a property of semiconductor materials; it refers to the energy needed to promote electrons from one energy state to a higher discrete state within the material. Having the right band gap makes it possible that graphene monoxide can act as a semi-conductor. Carbon is a common material; if it can be made to act as a semi-conductor in practical devices, it could be employed in a host of applications including Lithium-ion batteries.

**Exploring a New Material.** Despite having found a new material, the researchers still face the initial challenge that led them to the discovery – making it in large quantities. The goal of this project, "Graphene Monoxide (GMO)/Graphene Nanocrystalline Films for Lithium-Ion Batteries," is to identify strategies to produce large quantities of GMO and characterize the resulting material. If successful, they will explore complementary optical and transport measurements to obtain more information about the electronic properties of GMO and compare these results with theoretical predictions. They will then go on to demonstrate the use of the material in Li-ion batteries designed to use GMO as the anode.


Physics Professor Michael Weinert (right) and engineering graduate student Haihui Pu display the atomic structure of Graphene Monoxide (GMO).

The UWM Research Foundation is pursing patent protection on this new material. They are also exploring partnerships with materials companies and leading companies such as Johnson Controls who might be the first to bring practical devices based on this discovery.