

U.S. Navy, Virginia Tech Announce Agreement to Benefit Students and Navy Technology Programs

By Lynn A. Nystrom, Contributing Editor | tansy@vt.edu | (540) 231-4371

DAHLGREN, Va., November 25, 2008 – Virginia Tech and the Naval Surface Warfare Center Dahlgren Division (NSWCDD) signed a memorandum of understanding in Dahlgren, Va., Nov. 25, designed to develop and expand a framework of cooperation that will benefit the university’s students and faculty in addition to Navy technology programs.

The agreement will enable a framework of cooperation between Virginia Tech and NSWCDD to develop mutually beneficial innovative research projects and activities.

“Virginia Tech is one of the state’s premier research and development institutions,” said NSWCDD Cmdr. Capt. Sheila Patterson. “Our ongoing relationship with the university’s engineering department has already bolstered the development of crucial programs from Electromagnetic Railgun to Nano Technology and we hope that this new agreement will further enhance our relationship with young scientists and engineers to better support the Navy.”

According to rankings provided by the National Science Foundation, “Virginia Tech is the Commonwealth’s leading research university and is one of the preeminent leaders in technological research in the country. Our researchers are pushing the envelope of science, and their outstanding work has led to the creation of Virginia Tech’s Institute for Critical Technology and Applied Science (ICTAS),” said Robert Walters, vice president for research at Virginia Tech.

Christopher Cornelius, the associate director for research, ICTAS, will lead the university’s work with the Navy.

(continued on back cover)



Left to right: Front row - Michael Wood, Technical Partnering Office, NSWCDD; Captain Sheila Patterson, NSWCDD; Dr. Robert Walters, Research Division, VT; Dr. Richard Benson, College of Engineering, VT;

Back row: Dr. Roop Mahajan, ICTAS, VT; Dr. Chris Cornelius, ICTAS, VT; Albert Riedl, Technical Partnering Office, NSWCDD; Ann Craig, ICTAS, VT; June Drake, Technical Partnering Office, NSWCDD; Roger Burnett, Research Division, VT; Rodd Hall, Research Division, VT

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DEAN'S CORNER

Interdisciplinary Graduate Education and Research



Karen P. DePauw, Vice President and Dean for Graduate Education

Graduate education and research/scholarship are inextricably connected; especially so at research universities with an interdisciplinary perspective. Interdisciplinary research continues to be a focus of academic dialogue and graduate education must respond to the challenge of better preparing our graduate students for careers in the 21st century.

"Graduate programs must not only educate future scientists to be experts in the methods, techniques, and knowledge of their chosen disciplines but to have the broader problem-solving skills that require learning, unlearning and relearning across the disciplines" (Rhoten, 2004). These future scientists need to have both depth of training and education in a discipline (I-educated individuals) and the training/education and ability to work across disciplinary lines (T-educated individuals) or "Pi shaped (π) individual," having breadth and depth in several areas. Known as adaptive innovators, these highly educated future scholars and professors are needed for the 21st century. This is our challenge and our opportunity.

In order to address this challenge, an interdisciplinary summit was convened in the Graduate Life Center on August 11, 2008 for the purpose of "establishing an action agenda for interdisciplinary graduate education at Virginia Tech". The summit, supported by the Vice President and Dean for Graduate Education and the Senior Vice President for Academic Affairs and Provost, involved faculty members, senior administrators, college deans, Institute Directors (ICTAS, Fralin, ISCE) and IGERT faculty. The agenda was focused on identification of challenges and opportunities for interdisciplinary graduate education and research in four specific

areas: teaching interdisciplinary classes, advising and mentoring interdisciplinary graduate students, facilitating interdisciplinary research, and academic policies and university structure. As a result of the summit, a vision of interdisciplinary graduate education and research at Virginia Tech was articulated that included:

- *Faculty and administrators who embrace and actively promote an interdisciplinary approach to discovery, learning and engagement.*
- *An environment through which faculty and graduate students are actively encouraged and acknowledged for their interdisciplinary efforts in graduate coursework, mentoring, research, scholarship, civic engagement, and more. Existing programs would be nurtured, new opportunities be easily created, and barriers to such endeavors be minimized if not eliminated.*

ICTAS serves as a fine example of interdisciplinary research and graduate education in action. The four research focus areas - nanotechnology, cellular and molecular biology, cognition and communication, and sustainable technology - provide fertile ground where faculty and graduate students work together to solve the complex problems of today's society and tomorrow's future. And the ICTAS doctoral scholars program offers outstanding graduate students the opportunity to engage fully in research efforts during their doctoral studies. Much has already been accomplished but a sustained effort will still be needed to advance interdisciplinary research and graduate education for Virginia Tech. Progress will continue through the leadership of ICTAS and the efforts of ICTAS faculty and graduate students.

DIRECTOR'S CORNER

The Big Move



*Roop Mahajan
Director, ICTAS*

On March 2, 2009, we moved from our temporary offices in the Corporate Research Center to our new building at the corner of Stanger and Old Turner Streets on campus. With hundreds of boxes unpacked and initial move-in glitches resolved, the building is now bustling with activity and creative energy. The excitement among its occupants is palpable, together with the deeply-felt comfort of “home at last.” This ~100,000 sq ft building will indeed serve as a home to the School of Biomedical and Engineering Sciences (SBES) and the ICTAS headquarters administration. In addition, it will provide much-needed

laboratory space in support of teams engaged in cutting-edge research in Sustainable Water Infrastructure Management, Renewable Materials, Nanoscience and Technology of the Environment, Targeted Delivery of Nanomedicine, Sustainable Energy, and Carbonaceous Nanomaterials, among others.

As majestic as this structure of brick and mortar, or more precisely of “hokie” stone and glass may appear to a casual observer on the street, it is the people who reside and the research that is conducted within the confines of its walls that will define this building. It is my sincere hope that the well-equipped laboratories

and break-out rooms designed to promote interdisciplinary research will provide our talented innovators with an environment to conduct creative research and experiment with ‘blue skies’ thinking.

Building on a proud record of accomplishment over the last few years, ICTAS promises to continue to develop innovative technologies and pursue the advancement of knowledge to inspire researchers to build a sustainable future for our planet. With the “Big Move” under our belt, the Institute is indeed poised to move on to the next frontier in research.



POST-DOC SPOTLIGHT

New Drugs for Bad Bugs

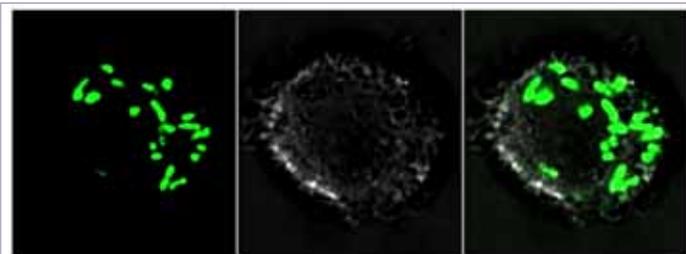
By Mohamed Seleem | naguieb@vt.edu | (540) 231-4002



Intracellular pathogens (bad bugs) like Mycobacterium, Brucella, Salmonella and Listeria have developed various mechanisms to evade host defenses and can establish chronic infections. Treatment and eradication are difficult since these bacterial pathogens are living within phagocytic cells and most antibiotics, although highly active in-vitro, do not actively pass through host cellular membranes. Our research is focused on using nanoparticles as carriers for site-specific targeted drug delivery and increased bioavailability of antimicrobials/drugs.

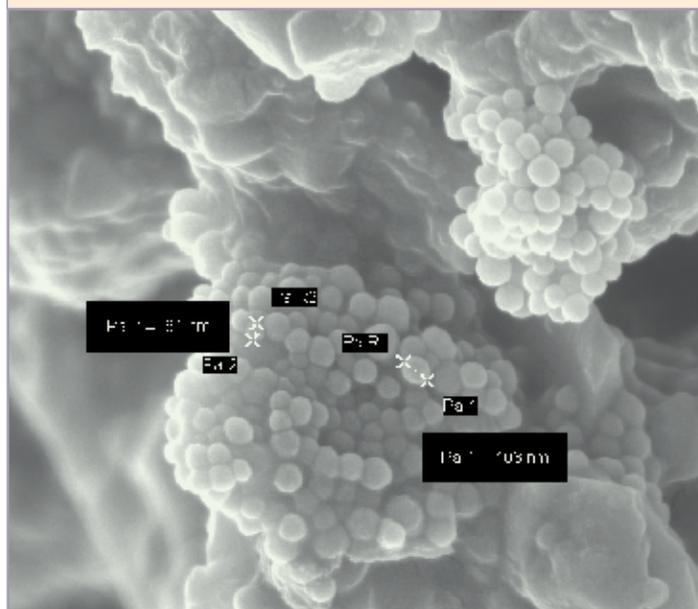
Seleem relocated in July 2007 from Cornell University to ICTAS to lead this project that uses an interdisciplinary team approach to problem solving. The team (Drs. Sriranganathan, Riffle and Pickrell) combines expertise in microbiology and veterinary medicine with nanomaterial synthesis and material science to design and test therapeutic nanomaterials that have the targeting and bioavailability characteristics. We are using Mycobacterium, Brucella and Salmonella as models for the most significant intracellular pathogens that reside in macrophages, Seleem explains.

This project addresses several of the most critical issues impacting the targeting of intracellular pathogens like M. tuberculosis that causes tuberculosis (TB), a leading cause of mortality worldwide. Recent implementation of the World Health Organization's strategy of short course therapeutics has been problematic and



Confocal Image of J774A.1 murine macrophage cell line infected with bioterrorism agent Brucella

SEM image of silica gel xerogels nanoparticles loaded with antibiotic.

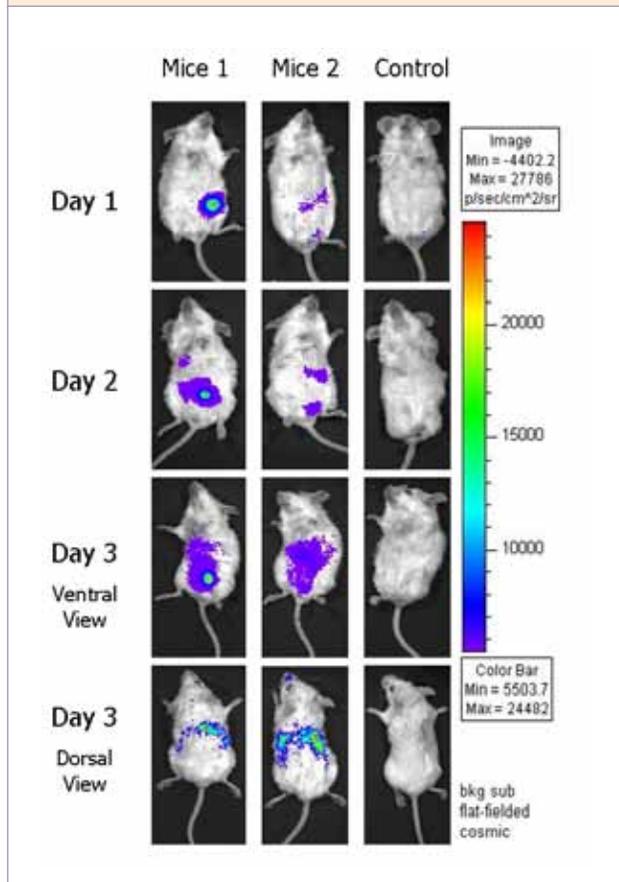


TB remains a major burden in many countries. “One of the major problems is noncompliance to prescribed therapeutic regimens, primarily because TB treatment involves continuous, frequent multiple-drug dosing” Seleem said. Adherence to treatment and therapeutic outcome could be improved with the introduction of long-duration drug formulations that release the antimicrobial agents such as nanoparticles into the site of infection. “Our targeting efforts have only begun to scratch the surface of drug delivery to intracellular pathogens; we have some very promising results”, Seleem said.

Seleem and his team are currently developing a second-generation biodegradable nanoparticles with higher loading capacity and slower sustained release. “Such sustained release would allow reduction in frequency and dosing numbers”, Seleem explains.

Seleem and the team utilized a highly sensitive noninvasive real time imaging system to assess the distribution and clearance of intracellular pathogens (in-vivo bioluminescence imaging). The ability to track disease progression temporally and spatially within the same infected mouse will provide an opportunity to test antimicrobial effectiveness and will provide a clearer understanding of the bacterial pathogenic events and host interactions with the nanoparticle drug delivery system,” Seleem explains.

Monitoring mice infected with bioluminescent bacteria.



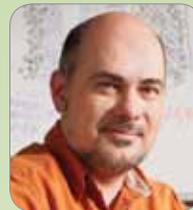
ICTAS SEMINAR SERIES: LOOKING FORWARD



Friday, April 3,
ICTAS Room 310,
1:30 - 3:00 pm

GEM*STAR Green Energy-Multiplier: Subcritical Technology for Alternative Reactors

with **Bruce Vogelaar**,
Professor of Physics, Virginia Tech



Friday, April 17,
ICTAS Room 310,
1:30 - 3:00 pm

Hierarchical Structures in Fuel Cell Electrocatalysts: Applications of Nanoscience and Nanotechnology for Power Generation

with **Plamen Atanassov**,
Chemical and Nuclear Engineering,
University of New Mexico



Friday, April 24,
ICTAS Room 310,
1:30 - 3:00 pm

Non-Equilibrium Statistical Mechanics: a Growing Frontier of "Pure and Applied" Theoretical Physics

with **Royce Zia**,
Professor of Physics, Virginia Tech



Tuesday, May 5,
ICTAS Room 310,
10:30 - 11:30 am

Research Developments in Germany: Opportunities for US Research

with **Cathleen S. Fisher**, Executive Director of American Friends of the Alexander von Humboldt Foundation, and **Deirdre Kelly**, Senior Program Director at American Friends of the Alexander von Humboldt



ICTAS IN THE NEWS

Engineers Have Created ICE in Order to SWIM

By Lynn A. Nystrom, Contributing Editor | tansy@vt.edu | (540) 231-4371

A few years ago, America's drinking water and collection system earned a "D" on its report card, as issued by the American Society of Civil Engineers (ASCE).

With that "D" came an estimated five-year investment in excess of \$1.3 trillion needed to repair the drinking water and collection systems owned by U.S. municipalities.

Most of the water infrastructure systems are over 100 years old, and many "have not received adequate upgrades, maintenance, repair and rehabilitation over time," said **Sunil Sinha**, a 2007 National Science Foundation (NSF) CAREER Award recipient and an associate professor of civil and environmental engineering (CEE) at Virginia Tech.

Sinha and **Marc Edwards**, who holds CEE's Charles P. Lunsford Professorship of CEE and who received an NSF Presidential Faculty Fellowship, have teamed to establish the Virginia Tech Institute for Critical Technology and Applied Science (ICTAS) Center of Excellence (ICE) in Sustainable Water Infrastructure Management (SWIM).

"Today, municipal governments are facing an infrastructure crisis requiring costly renewal beyond their capacity," Sinha said. "There has been a steady decline in the state of our water infrastructure over the past two decades and a growing concern is that these facilities



Sunil Sinha



Marc Edwards

may be inadequate both for current requirements and projected future growth, according to Environmental Protection Agency (EPA) statistics."

Funding for these municipal needs is limited, and a "deferred maintenance, out-of-sight, out-of-mind philosophy still prevails in many regions," Sinha added. Outdated, but most recent ASCE estimates from 2000 on the cost of replacing all potable water mains in the United States at \$348 billion.

Also, "the net present replacement value of water infrastructure in homes and buildings is on the order of a trillion dollars," according to Edwards. "In the last few years, many consumers have been startled to discover that the utilities and health agencies have been assuming that the consumer is completely responsible for complex decisions regarding materials selection, maintenance and replacement, often without any sound research guidance or public outreach."

Several examples of water quality problems have appeared in the popular press and on the evening news. For instance, Edwards' research team discovered that EPA regulations encouraging chloramine use in drinking water inadvertently triggered problems with lead leaching from home plumbing in Washington D.C. Other work he led examined plumbing devices installed in homes, certified as "safe" in the marketplace, but which leached harmful amounts of lead to drinking water when installed in practice. Several subsequent congressional investigations examined flaws in the system that could cause such troubling outcomes, and Edwards was called to Washington D.C. to serve as one of the expert witnesses.

He also examined outbreaks of pinhole leaks in copper tubing in many regions of the United States, which have cost consumers billions of dollars, and discovered that

ICTAS IN THE NEWS

a key contributing factor was changes in water chemistry resulting from EPA regulations. The moisture from these leaky pipes contributed to mold growth in homes, which in turn contributed to billions of dollars of losses in the home insurance sector, sky-rocketing premiums or cancelled insurance, and “as is” home sales.

Edwards and Sinha have also learned that well-intentioned home housing trends are causing potentially serious problems with bacterial growth. Specifically, the temperature in new water heaters is often too low to kill harmful micro-organisms, including legionella, mycobacterium avium and pseudomonads. The maximum temperature is often limited to prevent scalding of young children and to save energy, yet this temperature is not high enough to kill the microorganisms. Likewise, new plumbing construction with water saving devices means that water is sitting in home plumbing longer, which can also contribute to the bacteria problem.

In some cases residents using this water for showering complained of breathing difficulties, rashes, dizziness and other maladies, although no definitive links between the bacteria and these problems have yet been established. But testing did reveal “very worrisome levels of indicator micro-organisms and positive detection of pathogens including mycobacterium and pseudomonas, organisms that can cause a form of tuberculosis in residents breathing in their shower, or severe skin rashes,” Edwards asserts. An analogy would be with the use of hot tubs that are poorly maintained, in which some patrons obtain “hot tub rash” and “hot tub lung” due to the same microorganisms.

(ICTAS Center for Excellence) ICE

Sustainable Water Infrastructure Management (SWIM) will focus its research on the sustainable water infrastructure management systems. This includes a multiple number of areas such as water chemistry, sensor technology, nanotechnology, information technology, material science, construction technology, green engineering, sustainable and innovative technologies, renewal engineering, and infrastructure asset management.

Edwards, dubbed the “Plumbing Professor” by Time

magazine for his internationally recognized expertise on drinking water, concentrates in environmental and water resources engineering. Sinha, who specializes in construction engineering and management, is now focusing his research on developing a sustainable water infrastructure management system.

Sinha has several ongoing research projects, funded by the Environmental Protection Agency (EPA), Water Environment Research Foundation (WERF), and American Water Works Association Research Foundation (AWWARF) and all related to the water infrastructure system. He is also working closely with international research institutions working in the areas of water infrastructure such as Commonwealth Scientific and Industrial Research Organization (CSIRO), Australia, University of Birmingham, U.K., and The Foundation for Scientific and Industrial Research of the Norwegian Institute of Technology, Norway (SINTEF). His research includes the development of an integrated water and wastewater pipe management system with recent sensor technologies and non-destructive testing tools. This research has the potential to change the utilities’ ability to rate the condition and performance of their pipeline infrastructure system and to develop a rational repair, rehabilitation and replacement program.

Together, they will be able to lead the ICE–SWIM efforts to develop new generations of installation, repair and rehabilitation systems; new sensors to track obstacles and deterioration of water systems; advanced, integrated asset management approaches; and to educate a new breed of engineers for research and application of new technologies. Edwards will act as the first director, and Sinha will be the co-director.



2009 Awards Announced

Congratulations to 2009 Research Award recipients:

Team Leader	Title
Moen, Cris	A Design Framework for Thin-Walled Concrete Structures
Schmittmann, Beatte	A New Paradigm for Non-Equilibrium Dynamics
Pereira, Andy	Algal Biodiesel Production: Breaking Barriers via Functional Genomics
Sultan, Cornel	Bio-inspired Energy Harvesting
Martin, Stephen	Challenges in the Fabrication of PEM Fuel Cell Membranes: Phase Separation Kinetics in Block Copolymer Systems During Solvent Removal
Moglen, Glenn	Climate Change and Urban Growth: Development of a Sustainable and Resilient Water Management System Portfolio for the Greater Washington, DC Metropolitan Area
Bose, Tamal	Cognitive Radio Network
Hochella, Mike	Critical Programmatic Expansion of the ICTAS Environmental Nanosciences and Technology Research Theme: Nanoparticle/Cell Interactions and Nanotechnology-Enabled Sensor Development
Scott, Durelle	Development and Incorporation of a River-floodplain Metric into Regional Water Quality Models
Davalos, Rafael	Dielectrophoretic Microweaving: New Technology Platform for Biofabrication of Advanced Nanomaterials
Gabbard, Joseph	Enabling Sustainable Agriculture and Natural Resource Research and Education by Integrating Emerging Engineering Technology into Sustainable Practices
Heflin, J. Randy	Enhanced Performance in Bulk Heterojunction Solar cells via Endohedral Metallofullerenes and Morphological Control
Xu, Yong	Holey Scaffolds
Lattimer, Brian	ICE - Advanced Fuel Gasification: A Coupled Experimental Computational Program
Wi, Sungsool	In-Situ NMR Investigation of Gas Hydrates-the Future Energy Source and Storage
Santos, Webster	Inhibiting HIV-1 TAR RNA Function Using Nanoparticle-Delivered Branched Peptides
Abiade, Jeremiah	Magnetic and Optical Properties of Au Core/Oxide Shell Nanoparticles using Pulsed Laser Ablation
Lu, Kathy	Nanopatterning and Quantitative Characterization of Nanostructured Materials
Morgan, Abby	Nanostructured Biomaterial Meshes with Gradient Properties for Tissue Engineering
Martin, James	Near Real-time Monitoring and Adaptive Risk Assessment of the US National Levee System Using Satellite-based Remote Sensing
Robinson, Hans	Selective Functionalization and Guided Assembly of Nanoparticle Molecules
Boroyevich, Dushan	Sustainable Building Design Initiative
Novak, John	Sustainable Water Development: Water and Wastewater Treatment, Infrastructure Assessment and Repair, and Urban Watershed Management
Shaumont, Patrick	Unique and Unclonable On-Chip Identifiers
Dietrich, Andrea	Water for Health ICTAS Center of Excellence

Photos of “The Big Move”



Movers wheel a vibration-proof table into a 4th floor lab.



A desk comes off the moving truck on the way to the freight elevator.



Unloaded boxes wait in the hallway for transport to the ground floor.



Break rooms serve faculty, staff, and students.

New building at a glance:

- **4 Floors and 99,411 gross square feet** housing research laboratories, offices, and workspaces.
- **Notice to proceed: May 15, 2006**
- **Occupancy: March 2, 2009**
- **Project Manager: Van Coble, Capital Project Manager, Virginia Tech Capital Design & Construction**
- **Architect/Engineer: Burt Hill Kosar Rittleman Associates, Washington, DC**
- **General Contractor: Branch & Associates, Inc. Roanoke, VA**

TECHNOLOGY FOCUS

Cancer Research at Virginia Tech:

Understanding the Fundamentals of Cancer and Developing Appropriate Drugs

By Carla Finkielstein and Tom Campbell

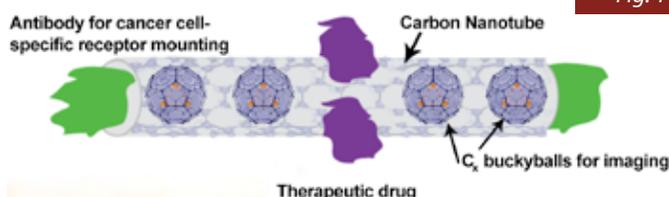
Cancer treatment today continues to be based primarily on treatment approaches developed more than a quarter-century ago. Non-specific and highly toxic chemotherapy treatment, aggressive radiation therapy, and invasive surgical resection are a patient's primary means of recourse against this deadly disease. Consequently, patients must survive not only the cancer, but also the treatment protocols themselves. Simultaneously, the number of cancer cases is on the rise, with 1.4 million new cases estimated for 2007 alone in just the Western world. As an alternative, more efficacious treatment protocols are desperately needed for cancer. A better fundamental understanding of the biology of cancer is critically needed to advance all forms of cancer research. ICTAS, along with partners in VT departments and industry, is working in these areas to ensure this knowledge is gained— an essential step toward a better future for cancer patients.

Targeted therapeutics for prostate cancer

In collaboration with ADA Technologies, Inc. (Littleton, CO), a recently funded Phase I Small Business Technology Transfer (STTR), 2-year, \$400,000 project from the National Institutes of Health (NIH) is focusing on synthesizing a novel nanomaterial construct and validating its effectiveness in treating prostate cancer. This new construct will offer a multimodal therapeutic advantage by acting simultaneously as an image contrast enhancement agent, a targeted drug-delivery vehicle, a thermal sensitizer, and a generator of singlet oxygen. The proposed research is to apply a novel class of nanostructures as dual imaging and therapeutic agents for prostate cancer treatment. Because of their shape, their capacity for multiple encapsulants, and their chemical functionalizability, nanomaterials are ideal nanoconstructs for next-generation diagnostic and therapeutic nanoprobes. Moreover, they have an inherent advantage

as a nanoplatform in medical applications because of their high chemical stability and resistance to metabolic cage-opening processes. Thus, the release of toxic metal ions used as imaging agents into surrounding tissue, serum, and other biologic components is prevented. Prostate cancer is specifically chosen as the initial model because of the already proven treatment efficacy of a primitive version of the nanostructure against prostate cancer cells.

The novel nanostructure being researched is presented



Proposed $Gd_3N@C_{80}@CNT$ peapod nanostructures for imaging and drug delivery. Inside the carbon nanotube are C_x buckyballs that contain Gd_3N imaging agents. Therapeutic drugs and tumor-specific antibodies are bonded to the exterior of the carbon nanotube.

in Figure 1. Trimetallic nitride template endohedral metallofullerene (TNT EMF) molecules are contained within a carbon nanotube (CNT) peapod nanostructure. The ability of TNT EMFs to serve as magnetic resonance imaging (MRI) contrast enhancement agents when containing the chemical elements of gadolinium and other paramagnetic lanthanides is well-documented. Working in collaboration with Dr. Harry Dorn of the Chemistry Department, it is feasible to achieve a 40-fold improvement in magnetic resonance imaging (MRI) contrast enhancement using TNT EMFs. Furthermore, this multi-modal nanostructure offers a powerful new opportunity for photodynamic therapy. In collaboration

TECHNOLOGY FOCUS

with Prof. M. Nichole Rylander of the Mechanical Engineering Department, using *ex vivo*, near-infrared irradiation, hyperthermia treatment is being developed to eradicate tumor cells preferentially by leveraging the carbon nanotube's high thermal conductivity. Following infrared excitation, these carbonaceous nanomaterials can induce reactive oxygen species [i.e., singlet oxygen (1O_2), superoxide (O_2^-), and hydroxyl radical ($\cdot OH$)] in living tissue. Singlet oxygen permits targeted cell cytotoxicity, and thus diseased cell apoptosis can be enhanced. It has previously been shown that hyperthermia treatment with the chosen nanomaterial does not damage the surrounding, non-cancerous living tissue.

Moreover, the carbon nanotube offers a ready platform for targeted drug delivery. Chemotherapy drugs specifically selected for the tumor of interest drugs such as Taxol® and Doxorubicin® can be either covalently or non-covalently bonded to the exterior of the carbon nanotube. Release of these drug agents either during or after infrared radiation treatment can further ensure diseased cell apoptosis. It has been shown that therapeutic action of chemotherapy drugs is enhanced during hyperthermia treatment. Lastly, antibodies mounted externally on the nanostructure will allow targeted delivery preferentially to tumor cell receptors.

The next stage for targeted therapeutics

An extension of this funded work is already in the planning stages. Working under a recently awarded no-cost access grant with the Center for Nanophase Materials Sciences (CNMS) at Oak Ridge National Laboratory (ORNL), we will be assessing another form of carbonaceous nanomaterial called a carbon nanohorn.

Single-walled carbon nanohorn (SWNH) agglomerates are comprised of thousands of nanotubes with individual diameters of 2-5 nm arranged as an agglomerate structure possessing overall diameters of 50-100 nm (e.g., Figure 2). Each individual SWNH has an open and a closed end where all the open ends are oriented toward the center of the structure and closed ends point out toward the periphery. Based on their morphology, SWNH are classified

by analogies to flowers into dahlia, bud, or seed types. SWNH are typically produced by laser ablation of pure graphite target samples; therefore, toxicity associated with the presence of metal catalysts is not an issue. This is a significant advantage when comparing to other nanomaterials such as nanotubes, which require a metal catalyst thereby increasing likelihood of toxicity. SWNHs are non-irritants and non-dermal sensitizers through skin conjunctival irritation tests, nontoxic to lung tissue following inhalation and non-carcinogenic through negative mutagenic and clastogenic potentials. SWNHs can be chemically modified with considerable ease, providing a versatile platform for investigating the effects of different surface characteristics, such as surface charge and functional groups on toxic responses.

The extensive surface area and multitude of interstices inherent to SWNHs permit the opportunity for addition of guest molecules, making SWNHs an exceptional nanopatform for drug delivery. SWNH surface area can be further increased by oxidation, which causes formation of nanowindows in the SWNH walls to permit infiltration of a variety of small molecules [e.g., N_2 , Ar, and fullerenes (C_{60})] into their inner space, thereby nearly quadrupling the adsorptive surface areas. Pore size can also be controlled by altering the oxidation conditions, leading to a series of oxidized SWNHs (ox-SWNHs) with distinct molecular sieving effects. Effective drug delivery systems development, careful selection of shell materials, targeting molecules, and drugs are critical to achieving stability, targeting efficiency, and high drug efficacy.

But how can the advantages of SWNHs be fully harnessed? In collaboration with ORNL, we will be applying SWNHs in concert with another biomedical therapeutic approach - Irreversible Electroporation (IRE). Prof. Rafael Davalos of the Department of Biomedical Engineering has shown strong progress in treating cancerous tumors using IRE, a new, minimally invasive tissue ablation technique.

(continued on next page)

TECHNOLOGY FOCUS

Cancer Research at Virginia Tech: Understanding the Fundamentals of Cancer and Developing Appropriate Drugs (continued)

This procedure delivers a series of low energy (intense, but short) electric pulses to the targeted tissue for approximately one minute. These pulses permanently destabilize the cell membranes of the targeted tissue, inducing cell death without causing thermal damage. IRE has the ability to create complete and predictable cell ablation with sharp transition between normal and necrotic tissue, while sparing neighboring blood vessels, connective tissue, and nerves. IRE is a relatively simple process, involving the application of minimally invasive electrodes similar to those used in radio-frequency ablation, but it is much faster (microseconds-milliseconds compared to minutes-hours), it is more precise (no dependence on blood flow), it does not induce any thermal damage (no scarring), it promotes a positive immune response, and it can be monitored in real-time using ultrasound. Nevertheless, focal ablation techniques such as IRE are not selective and thus cannot distinguish between healthy and cancerous cells. SWNHs will be used as an insertable nanomaterial to focus the energy of the IRE therapy directly to the tumor. Working with ORNL, Virginia Tech will optimize the properties of SWNHs through advanced synthesis approaches at ORNL, and validate their properties using nanometrology instrumentation at both VT and ORNL.

Life Style Factors in Cancer Development and Progression

Cancer is a collection of diseases where its etiology is primarily unknown. Statistics are alarming: every minute of every day an American is expected to die of cancer this year (American Cancer Society, Cancer Facts & Figures 2008). Interestingly, epidemiological studies suggest this proportion rises more dramatically in western societies suggesting that disturbance in our daily physiology (i.e.,

shift-work, chronic jet lag), named “circadian disruption”, significantly impacts cancer incidence. Circadian rhythms are mechanisms that adjust our physiology to a 24 h cycle. In mammals, the circadian system is organized in a hierarchy of multiple circadian oscillators, with a master circadian clock (pacemaker) located within the neurons of the suprachiasmatic nucleus (SCN) in the anterior hypothalamus of the brain. The oscillatory mechanism of the clock can function autonomously, without any external input or time cues, although environmental signals can reset (“entrain”) the pacemaker and therefore, synchronize the daily rhythms in peripheral oscillators.

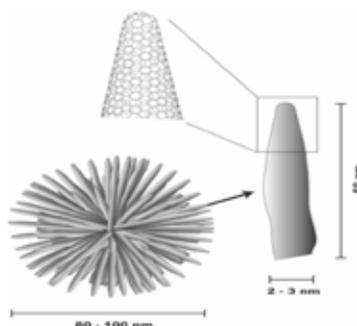


Figure 2: Schematic Representation of SWNH agglomerate

The basic oscillatory mechanism is formed by a set of conserved genes that are present in organisms as diverse as bacteria

and eukaryotes, although species-dependent functional variations were described for some core oscillator components. Interestingly, large-scale gene array screens have shown that about 7% of all genes controlled by circadian components regulate cell division or death processes, suggesting that these mechanisms might be interlocked at the molecular level.

Accordingly, increasing evidence points to functional links between the two major biological rhythms, namely the cell division cycle and circadian rhythms within living organisms. Their molecular architecture is essentially similar since both biological processes rely on the function of autoregulatory

TECHNOLOGY FOCUS

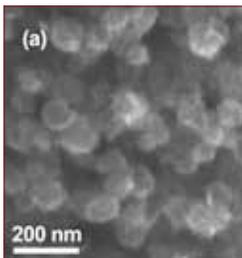
loops generated by sequential phases of transcription/translation, protein modification and degradation.

A great deal of effort has been extended over the past decade to identify the genetic basis for breast and ovarian cancer susceptibility. Families with high incidence of breast cancer were found to carry germ-line mutations in two genes, named BRCA1 and BRCA2. Loss-of-function mutations in BRCA1 are quantified by penetrance values, defined as the risk of developing breast or ovarian cancer before the age of 70 years, of about 80% and 54% respectively, whereas BRCA2 mutations encounter for up to 20% of all ovarian cancers and have high incidence in male breast cancer. Although these numbers appear remarkably significant, they only account for an estimated 10% of all cases diagnosed in the United States each year. The majority of both breast and ovarian cancers (~90%) are still sporadic forms that are caused by changes that occur during woman's life, rather than an inherited genetic mutation. Interestingly, epidemiological studies and clinical data show that women exposed to irregular circadian cycles due to night-shift work or constant exposure to light exhibit increased mammary and ovarian tumorigenesis. For example, a large cohort study revealed an increased breast cancer risk of 23% for flight attendants, nurses, telegraph operators and women working night-shifts. Thus, we hypothesize that factors in the environment that disrupt the endogenous rhythm may account for a higher predisposition to acquire sporadic cancer.

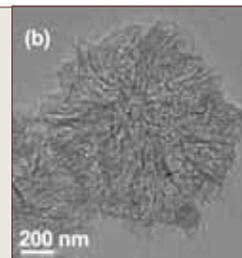
Research in the Integrated Cellular Responses Laboratory in the Department of Biological Sciences aims to

identify the regulatory mechanisms by which circadian components directly control cell cycle transitions and death processes. Our team brings modelers and experimentalists together to tackle one of the most challenging problems in the rising era of cell biology: whether uncontrolled cell proliferation, and thereby cancer, could actually result from an imbalanced circadian homeostasis. We envision a multidisciplinary approach that will result in a comprehensive analysis of circadian regulation of cell division and death processes from the atomic to the cellular level. Our team combines the expertise of Dr. C. Finkielstein in cell signaling, the vast experience of Drs. D. Capelluto and D. Bevan in multidimensional NMR spectroscopy and computational molecular modeling, and Dr. I. Lazar's background in cancer proteomics and biomarker discovery. As result, we have been able to elucidate novel regulatory networks, crosstalk mechanisms, unsuspected associations between molecules as well as specific protein profiles of prognostic value. Our team has now added an experienced tumor pathologist (Dr. Schmechel, Univ. of Minnesota) to further correlate the functional status of specific signaling pathways to their clinical significance, thus accelerating the translation of our discoveries into new medical treatments.

The project described was supported by Award Number R41EB008907 from the National Institute Of Biomedical Imaging And Bioengineering. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute Of Biomedical Imaging And Bioengineering or the National Institutes of Health.



(a) SEM and (b) TEM micrographs showing CNHs synthesized by laser ablation at Oak Ridge National Laboratories, with Dahlia flower for comparison.



FACULTY FOCUS: GE WANG

500nm-resolution Nano-CT Enables New Projects at Virginia Tech

Over past decades, x-ray CT has revolutionized many aspects of our society especially biomedical imaging. Recently, advances in x-ray optics have enabled x-ray nano-CT with 50-500nm resolution and a wide range of applications. Among modern $\mu\text{m}/\text{nm}$ -scale imaging tools, nano-CT fills in an important gap in image resolution, contrast mechanism, penetration depth, sample preparation and application territory. From biomedical perspective, nano-CT is advantageous in screening of small animals, imaging of physiological and pathological features, and monitoring of disease progression and response to therapy.

Recently, a team of researchers led by Dr. Ge Wang received a National Institutes of Health Sharing Instrumentation Grant to acquire a state-of-the-art nano-CT scanner that resolves features down to 500nm, as compared to medical CT scanners and typical micro-CT scanners with a 0.3mm and 5 μm resolution, respectively. This nano-CT capability enables imaging studies of small organs and biological tissue samples at a cellular level, and will significantly benefit many leading investigators on the Virginia Tech and Wake Forest campuses. Specifically in inflammation, a field of study of increasing importance at Virginia Tech and the newly-formed VT Carilion Research Institute, the new nano-CT scan system will

allow researchers to visualize the inflamed tissues in the micron/sub-micron domain, and determine the molecular pathogenesis of inflammatory diseases in mice models. In nano-medicine research, the requested system will provide a capability to image deeply-embedded μm -sized features of samples non-invasively to maintain specimen integrity and hydration, minimize radiation damage, and reduce operation time and system cost. The system will also provide support to many NIH-funded projects involving vasculature modeling and analysis, and cellular imaging of biomarkers for skeletal developmental and other studies. Furthermore, the technical development "interior tomography" based on the requested system will expand our portfolio of biomedical applications.

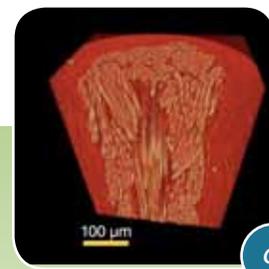
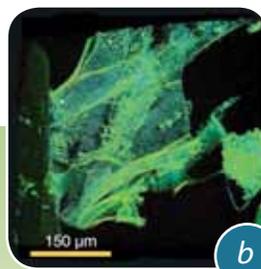
The requested system is made by the leading nano-CT company Xradia. This product was awarded the prestigious R&D100 Prize in 2003. The specifications include 90kV micro-focus source, 2kx2k CCD camera, multiple resolution modes, phase-enhanced optics, and up to 50mm diameter samples. It will be highly complementary and synergic with a variety of the micro-/nano-scale imaging equipment in Virginia Tech. Also, it will be the first nano-CT system on the East Coast, and will most likely serve the entire eastern United States.



a. 3D X-ray of a whole mouse

b. 3D cellular distribution on polymer scaffold in tissue regeneration research

c. CT of human laryngeal nerve fiber bundle



images courtesy of Xradia

FACILITIES NEWS

Developments with ICTAS Buildings

ICTAS

(Headquarters location on campus at Stanger Street)



The long anticipated move into the new campus facility, originally slated for October 2008, was delayed due to discovery of an infrastructure complication only days before the move was to begin. Move-in was rescheduled and began on March 2, 2009, now

complete in many areas. Operational staff are now settled into their new offices, while other tenants continue to unpack in other areas of the building.

ICTAS – CRC

(Corporate Research Center location)



In addition to the state-of-the-art Nanoscale Characterization and Fabrication Laboratory (NCFL), ICTAS-CRC houses the following research facilities:

- Nano CT (Room 1003): Contact - Ge Wang (wangg@vt.edu)
- X-ray Imaging Lab (Room 1005): Contact - Ge Wang
- Nanophotonics (Room 1020): Contact - Yong Xu (yong@vt.edu)
- Bio-AFM (Room 1024): Contact - Randy Heflin (rheflin@vt.edu)
- Bio-AFM (Room 1019): Contact - Maren Roman (maren.roman@vt.edu)
- Nano Biomaterials (Room 1025): Contact - Paul Gatenholm (pgatenho@vt.edu)
- EXTREME LAB (Room 2008): Contacts – Scott Case/ Brian Lattimer (lattimer@vt.edu)
- Sensors and Structural Health Monitoring (Room 2007): Contact - Rakesh Kapania (rkapania@vt.edu)
- Disaster and Risk Management Lab (Room 2003): Contact - James Martin (jrm@vt.edu)

- E-SITE Lab (Room 2002): Contact – Antonio Nieto (anieto@vt.edu)
- Nano CMOS Lab (Room 2001): Contact – Mariusz Orlowski (m.orlowski@vt.edu)
- SuperDARN Lab (Room 2019): Contacts – Jo Baker (jo.baker@vt.edu) / Mike Ruohoniemi (mikeruo@vt.edu)

A special welcome is extended to the newest tenant, the Nuclear Magnetic Resonance (NMR) Lab (Room 1027): Contact - Geno Iannaccone (genoi@vt.edu)

ICTAS-LSC

(Life Sciences Corridor location on campus)



Also known as the ICTAS II construction project, ICTAS-LSC is in final design stage. The site work is scheduled to begin in spring 2009 in space near the Virginia BioInformation Institute that is currently designated for parking. Construction completion is slated for spring 2011.



ICTAS-NCR (National Capital Region location)

The ICTAS facility in the Ballston location is under design. A contractor is to be named in the spring 2009. ICTAS is committed to approximately 6,000 square feet in the Virginia Tech Ballston facility. The anticipated construction completion date is 2011.

Virginia Tech does not discriminate against employees, students, or applicants on the basis of race, color, sex, sexual orientation, disability, age, veteran status, national origin, religion, or political affiliation. Anyone having questions concerning discrimination or accessibility should contact the Office for Equal Opportunity, 540/231-7500.

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U.S. Navy, Virginia Tech Announce Agreement to Benefit Students and Navy Technology Programs

(continued from front cover)

Cornelius joined the Virginia Tech engineering faculty after an eight year stint at Sandia National Laboratories (SNL), a national facility operated for the U.S. Department of Energy by Sandia Corp.

“Dr. Cornelius has achieved recognition and respect from industry and academic communities. His research has been supported by more than \$16 million in competitive research awards, and he has three patents, with an additional two pending, all in the past seven years,” Walters added. “He is an excellent choice to lead our pioneering efforts with the Navy.”

In today’s information rich environment, it is critical that the Navy stay abreast of technology and understand the realm of the possible for the future. Today’s academic institutions are key in being able to do this.

Moreover, in the current fiscally constrained environments, it is important for the Navy and academic institutions to look for more synergistic ways to continue providing cutting edge technology to the warfighter with less funding using progressive relationships and agreements.

This Virginia Tech – NSWCDD memorandum of understanding is supported by a variety of longstanding partnership programs, comprising the Educational Partnership Agreement, Naval Research Enterprise Intern Program, Summer Faculty Research Program, Work for Others, Cooperative Research and Development Agreements, as well as other contracts and

grants.

Collaboration and efforts to meet objectives in the performance of mutual innovative research and activities may include:

- Collaboration and management of innovative research projects.
- Evaluation of existing technologies for innovative uses in the Naval environment.
- Access to and use of each party’s unique laboratories and facilities.
- Joint publication of studies, evaluations and lessons learned.
- Acceleration and expansion of promising technologies for warfighter benefit.
- Joint innovative research in programs related to NSWCDD technical capabilities in dozens of areas from Chemical, Biological, and Radiological Warfare Defense Systems and Directed Energy Systems to Human Systems Integration and National Response Missions that include Homeland Security and Defense Physical and Non-Physical Vulnerability Analysis.

For more information, visit the NSWCDD website, the Virginia Tech website, and the ICTAS website.

In the months following the MOU signing, Virginia Tech submitted a proposal in response to an NSWC contract solicitation. If awarded, the resulting contract will provide the basis for a long-range partnership between NSWC and Virginia Tech.



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