

Spring 2011

# UConn School of Medicine Dean's Newsletter, Spring 2011

Cato T. Laurencin

*University of Connecticut School of Medicine and Dentistry*

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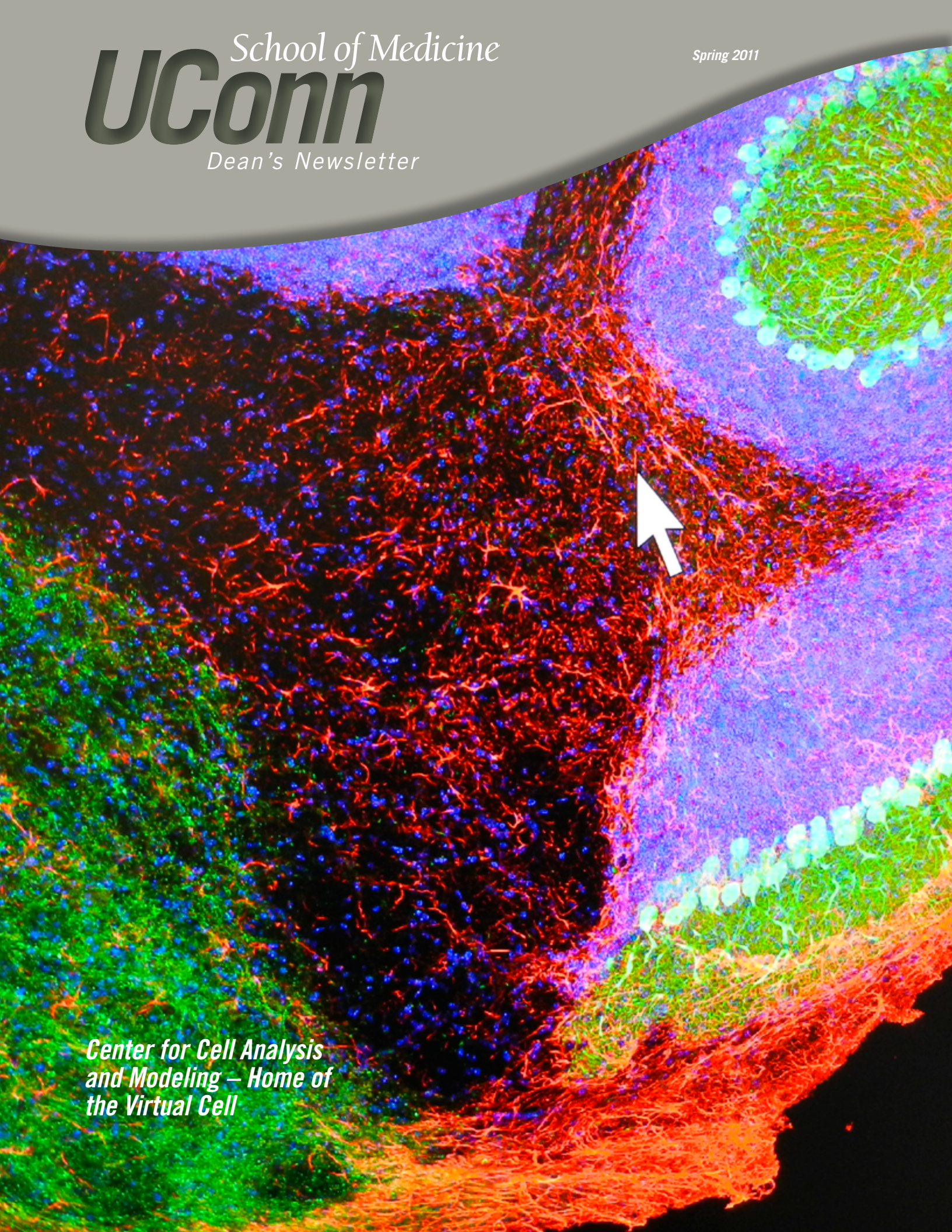
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*Center for Cell Analysis  
and Modeling – Home of  
the Virtual Cell*



## Dean's Message



**M**ore than 2,000 scientists from around the world – and counting – have utilized a computer software and database system created and housed at the UConn Health Center to construct computational models of cells. Called the Virtual Cell, it also performs simulations to analyze the results of those simulations to better understand cell physiology. In this issue, we will introduce you to Dr. Leslie Loew, director of the UConn Health Center's Richard D. Berlin Center for Cell Analysis and Modeling, and the impressive

work his multidisciplinary team is producing.

Dr. Loew, together with a cadre of elite researchers from several other bioscience departments, recently moved into the new, state-of-the-art Cell and Genome Sciences Building, adjacent to our campus. The building's award-winning design was created to encourage cross-disciplinary collaborations and innovations. Of note, the building also includes incubator space for emerging bioscience industries which was fully leased within the first year of occupancy.

The Cell and Genome Sciences Building was dedicated earlier this year (see photo on back page), heralding in a new era of growth in bioscience research and job creation. We look forward to sharing updates and exciting new advances in future issues!

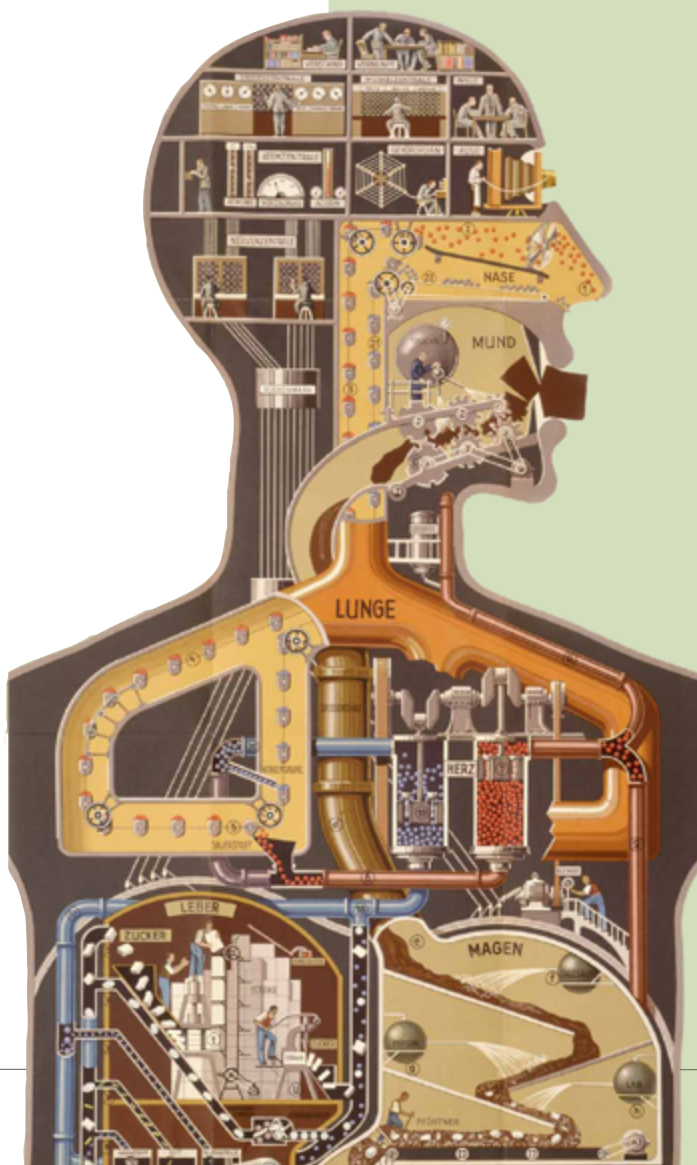
Sincerely,

Cato T. Laurencin, M.D., Ph.D.  
Vice President for Health Affairs  
Dean, UConn School of Medicine  
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## Education

### New Leader for Graduate School

**B**arbara E. Kream, Ph.D., has been appointed the associate dean of the Graduate School. A professor of Medicine and Genetics and Developmental Biology, she holds a joint appointment as professor in the Department of Orthopaedic Surgery. Kream has been active with student training and mentoring and is a long-standing member of the Biomedical Science and Dental Science Graduate faculty. She currently is the director of the M.D./Ph.D. program. ❄



### The 19<sup>th</sup> Century Goes Digital

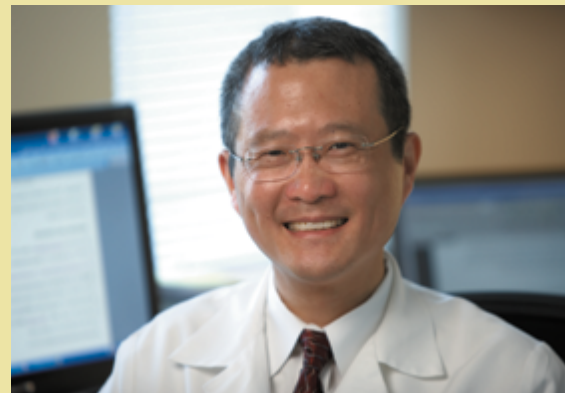
**T**he Hartford Medical Society Historical Library at the UConn Health Center has its first five titles digitized and available for viewing through the Internet Archive, a digital library found at [www.archive.org](http://www.archive.org) that offers free access to books and other materials. Touching on a range of unexpected topics, these newly digitized titles from the 19th century include such peculiar titles as *Human Monstrosities*, *Pathology of Drunkenness*, and *Observations on the Management of Madhouses*. To see the full list and access the digitized volumes visit <http://uchc.libguides.com/hms>. ❄

## UConn Cardiologists Uncover New Heart Attack Warning Sign

**H**ealth Center cardiologists, led by Bruce Liang, M.D., F.A.C.C., director of the Pat and Jim Calhoun Cardiology Center, have identified a protein fragment that when detected in the blood can be a predictor of heart attack. Their research was published in a recent issue of the *Journal of the American College of Cardiology*. It found that heart attack patients had elevated levels of the protein fragment known as Caspase-3 p17 in their blood.

"We've discovered a new biomarker for heart attack and showed that apoptosis is a cause of heart muscle damage," Liang says. "The ability to see a heart attack coming with a simple blood test and to develop new therapies to block apoptosis would enable us to get a head start on treatment and preserve crucial heart muscle and cardiac function."

"This test can work in patients but has not met regulatory requirements for clinical application in patients suspected of having a heart attack," Liang says. "If it is successfully applied one day, it would mean another way to diagnose heart attack and the possible development of new treatments."



Bruce Liang, M.D., F.A.C.C.

Co-investigators include Mariela Agosto, M.D., Michael Azrin, M.D., and Kanwar Singh, M.D., F.A.C.C., from the UConn Health Center and Allan Jaffe, M.D., from the Mayo Clinic and Mayo Medical School in Rochester, Minn. ✱

## Clinical Trials Favorable for Novel Breast Cancer Detection Device

**A** novel imaging device developed at the University of Connecticut is showing favorable results in an expanded clinical trial and could significantly reduce physicians' reliance on breast biopsies.

The device, which uses ultrasound-guided diffuse optical tomography (DOT) to locate and analyze suspicious tumors in breast tissue, was tested on 178 women over a four-year period from 2004 to 2008. The study was supported by the National Institutes of Health and the Donaghue Medical Research Foundation. Testing was conducted among patients between the ages of 21 and 89 at the UConn Health Center and Hartford Hospital.

The study showed that the device had a reliability rate of 92 percent in terms of sensitivity and 93 percent in terms of specificity when evaluating smaller cancers less than 2 centimeters in size. The results of the study have been published in the journal *Radiology*, published by the Radiological Society of North America.

"Based on our results, we believe DOT holds promise as an adjunct to diagnostic mammography and ultrasound for distinguishing early-stage invasive breast cancers from benign lesions," says Quing Zhu, Ph.D., a professor in the Department of Electrical and Computer Engineering. Zhu has been working with



graduate students in the School of Engineering and Health Center physicians over the past decade to refine and test the device.

"We expect this technology will be used to help radiologists evaluate small- to intermediate-sized lesions that are harder to diagnose with conventional imaging technologies," Zhu says. "We will not completely eliminate biopsies. No modality is perfect. But we want to improve existing imaging technology so a better diagnosis can be made."

In the UConn study, women who had suspicious lesions in their breasts were first analyzed with DOT and then given a needle biopsy. The results of each test were then correlated to judge the sensitivity and specificity of the DOT. Zhu says the DOT found both maximum and average total hemoglobin levels were significantly higher in the malignant groups than in the benign groups of tissue samples, proving the device's effectiveness. Laboratory examination of the tissue samples revealed two *in situ* carcinomas, 35 carcinomas that measured less than 2 centimeters, 24 carcinomas greater than 2 centimeters, and 114 benign lesions.

The DOT device has been patented. "The next step is to develop multi-institution prospective clinical trials to further evaluate the device's effectiveness," Zhu says. Collaborating with Zhu on the study were Poornima Hegde, M.D., Mark Kane, M.D., Susan Tannenbaum, M.D., Peter Deckers, M.D., and Scott Kurtzman, M.D., from the UConn Health Center and Edward Cronin, M.D., Andrew Ricci Jr., M.D., and Patricia DeFusco, M.D., from Hartford Hospital. ✱



## *Uncovering the Mysteries of Human Cells*

**“Our Center is unique in that we have chemists, physicists, mathematicians, biologists, and computer scientists all working together.”**

*Les Loew, Ph.D., director of CCAM*

Each of the 100 trillion cells in the human body is a tiny parcel of water and chemicals containing the entire human genome – all of the DNA that an individual possesses. For Leslie Loew, Ph.D., and his team of researchers, uncovering the mysteries of these cells and how they behave in the body is a mission, a fascination, a pursuit that can lead to a better understanding of diseases and how best to treat them.

Loew, a professor of cell biology as well as computer science and engineering, is the director of the UConn Health Center's Richard D. Berlin Center for Cell Analysis and Modeling (CCAM). Loew and fellow researchers at CCAM are developing new approaches to determine how cells work, interact, and respond – and how to organize this data so it can be applied to human health.

CCAM integrates state-of-the-art microscope technologies with computational tools that produce realistic models of cell dynamics. The innovative work performed at CCAM has received worldwide attention and millions in annual grant support since the Center was established in 1994.



Bringing together biomedical researchers from various disciplines, CCAM provides a setting that supports and reinforces the value of collaboration. "Our Center is unique in that we have chemists, physicists, mathematicians, biologists, and computer scientists all working together," Loew says. "We were far ahead of our time when we started these interdisciplinary groups."

It is also the home of the Virtual Cell, a computerized environment that allows scientists to simulate the inner workings of cells. With the Virtual Cell, investigators can build intricate models using a web-based interface in order to evaluate hypotheses, interpret data, or probe the predicted behavior of complex systems.

Designated and funded as a National Resource by the National Institutes of Health (NIH), the Virtual Cell is available for free via the Internet as a tool for scientists and other members of the scientific community.

"More than 2,000 labs around the world are using the Virtual Cell," Loew says. "The NIH grant mandates that we continue building software to support it and to make sure there is access to it."

## Research in Progress

Loew's team at CCAM is currently partnering on a project with the Mount Sinai School of Medicine and Columbia University to determine how human kidney cells are regulated to produce the delicate filtration system that allows the kidney to function. The project has been awarded a five-year, \$6 million grant from the NIH's Transformative Research Project Program, which supports innovative research with the potential for major impact on human health.

In this study, the Virtual Cell is being used to develop computational models of how cells interact within kidney tissues. Ultimately, its results could aid scientists in understanding disease processes and in screening for new drugs.

Another example of current Virtual Cell research is a study by M.D./Ph.D. candidate Sherry-Ann Brown that examines the way in which signals in the brain are transferred across synapses and neurons. Genetic defects in these biochemical pathways are linked to ataxia, which impacts an individual's motor coordination, speech, handwriting, and balance. Such research could lead to a better understanding of brain cell function – resulting in advances in prevention, diagnosis, and treatment.

CCAM provides a vast array of laboratory equipment that can be used for obtaining experimental data needed to create and enhance Virtual Cell models. Among CCAM's \$8 million in major equipment are confocal and laser optical microscopes, multiprocessor computers, and spectrometers that use light to study matter.

The Center recently moved to the new Cell and Genome Sciences Building, which was designed to promote interdisciplinary research in a wide range of projects. In addition to CCAM, the building also houses the UConn Stem Cell Institute, the Department of Genetics and Developmental Biology, and UConn's Office of Technology Commercialization (including the Technology Incubation Program – UConn's business incubator), enhancing the University's role as a leader in innovative research and technology in these areas.

CCAM, and especially the Virtual Cell, is the culmination of decades of work for Loew, who began his career in an academic chemistry department. "Some of the technology I was developing could be applied to asking questions about how cells behave," he says of his research. "It soon became clear to me that I was only going to enjoy developing these tools if I could use them myself." ❄

Ann Cowan, Ph.D., deputy director of CCAM.



## Cardiac Imaging Study Shows PROMISE

The Pat and Jim Calhoun Cardiology Center has been invited to be a test site for a groundbreaking clinical trial. The National Institutes of Health is studying the use of cardiac imaging to diagnose problems associated with chest pain, the most common clinical cardiology problem.

The PROspective Multicenter Imaging Study for the Evaluation of Chest Pain, or PROMISE, is the first randomized imaging trial in the history of cardiology. It seeks to enroll 10,000 patients at more than 200 sites throughout the U.S. The UConn Health Center was the first site in Connecticut to join the study, with Erick Avelar, M.D., director of noninvasive cardiac imaging, serving as principal investigator.

"Computed tomography of the coronary artery, also known as a cardiac CT, is hypothesized to yield better results than functional testing such as an EKG or stress test, but it is not the current standard of care and generally not covered by insurance," Avelar says.

The targeted study population consists of chest pain patients with low to intermediate probability of significant obstructive coronary artery disease, including men 55 and older and women 65 and older. Men as young as 45 and women as young as 50 also may be eligible, depending on their individual risk factors. ❄





*Front row, left to right: Title Sponsor Richard Lublin; Ray Neag; Carole Neag; Honoree Dr. Marja Hurley; Pat Calhoun; Honoree Dr. Ravi Nanda; Catherine Nanda.*  
*Back row, left to right: Dental School Dean Dr. Monty MacNeil; Lee MacNeil; Honoree Jim Calhoun; Vice President for Health Affairs Dr. Cato T. Laurencin; Cynthia Laurencin; John Hurley.*

## UConn Health Center Celebrates 50<sup>th</sup> Anniversary with White Coat Gala

**P**art of the yearlong celebration of the UConn Health Center's founding included the festive White Coat Gala this spring.

With more than 800 people in attendance, funds were raised to support faculty and researchers throughout the institution. During the event, three leaders who have played vital roles in the history of the Health Center were honored:

Marja Hurley, M.D., is an internationally prominent molecular biologist and endocrinologist who has served the Health Center for 25 years. She directs the Health Career Opportunity Programs, and is currently serving as the medical school's interim senior associate dean for education.

Ravindra Nanda, B.D.S., M.D.S., Ph.D., is a renowned leader in orthodontics who joined the Health Center in 1972. He is the UConn Orthodontic Alumni/Ravi Nanda Chair in Orthodontics and head of the Division of Orthodontics and the Department of Craniofacial Sciences.

Basketball Hall of Fame Coach Jim Calhoun is a long-standing and generous donor. All told, he and his wife Pat have helped raise nearly \$3 million to support the Health Center's cancer and cardiology programs. ❄



## Gift to Support Stem Cell Research

**I**n appreciation for committing \$700,000 to support stem cell research, the Edmund and Arlene Grossman

Auditorium was dedicated in their honor during the Cell and Genome Sciences Inaugural Symposium this past December.

"The University of Connecticut has been a national leader in the area of stem cell research, and the generous support of Edmund and Arlene Grossman will help us immeasurably to expand our work in this vital area," says University of Connecticut interim president Philip E. Austin. "Our faculty's research in this field is emblematic of the University's role in expanding the frontiers of knowledge in areas of critical importance to the people of Connecticut and far beyond."

The Grossmans, both cancer survivors, want to support research that has the greatest potential to treat and cure diseases such as Parkinson's and Alzheimer's, which have affected close friends of theirs, as well as cancer.

"This is such an incredible time in medical research that it behooves those of us who can to provide for the gains. The

implications are mind-boggling. The good that could be done with stem cell research far outstrips anything else we could do to help mankind," says Mr. Grossman.

"Ed and Arlene Grossman share our vision and believe in our promise to be a world leader in stem cell research. Their support will help us attract preeminent faculty and translate discoveries made in the lab into new therapies and cures," says Marc Lalande, Ph.D., director of the Stem Cell Institute and senior associate dean for research planning and coordination at the UConn Health Center. ❄



*Inside the Grossman Auditorium.*



## Cancer Center Director Appointed



**P**ramod K. Srivastava, Ph.D., M.D., an accomplished leader in basic and translational research, has been named the new director of the Carole and Ray Neag Comprehensive Cancer Center.

Srivastava is a professor and interim chair of the Department of Immunology, director of the Center for Immunotherapy of Cancer and Infectious Diseases, and part of the leadership team of the Connecticut Institute for Clinical and Translational

Science. He holds the Physicians Health Services Chair in Cancer Immunology.

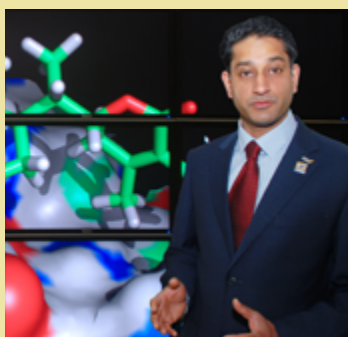
He has earned international acclaim for his groundbreaking work in the immunological function of heat shock proteins and in cancer immunology, is widely published in scholarly journals, and serves on editorial boards for several major journals in immunology. ❄

## New Academic Chair Announced

**R**oyce Mohan, Ph.D., a scientist and educator who specializes in tissue repair of the eye, has joined the UConn Health Center as the John A. and Florence Mattern Solomon Chair in Vision Biology and Eye Diseases.

Mohan, who has a Ph.D. in biochemistry from Ohio State University, was most recently an associate professor in the Department of Ophthalmology and Visual Sciences at the University of Kentucky. He won acclaim at Kentucky for a discovery that holds the potential for new treatments for diseases of the brain, spinal cord and eye.

Florence Solomon, one of the chair's donors, suffers from macular degeneration, a focus of Mohan's research. Mohan, mentored at Yale University in chemical genetics and inspired by pioneer Judah Folkman of Harvard Medical School, brings a distinctive mark to anti-angiogenesis and anti-fibrosis therapeutic research. ❄



## UConn Cardiologist 1<sup>st</sup> in New England with New Treatment

**K**anwar Singh, M.D., F.A.C.C., an interventional cardiologist in the Pat and Jim Calhoun Cardiology Center, is the first physician in the region to take an innovative, minimally invasive approach to treating peripheral arterial disease.

Using a new device called the Wildcat catheter, Singh was able to reopen a completely blocked artery in a patient's leg through a 2-millimeter skin incision.

Some blockages are severe and difficult to pass through with traditional catheters, forcing patients to undergo more invasive bypass surgery and subjecting them to higher risks and prolonged recovery. In those cases where the plaque deposits cannot be passed, patients face an increased possibility of losing a limb to amputation. This minimally invasive alternative to bypass surgery enables patients to leave the hospital within hours and return to normal activities within a few days.

"The Wildcat catheter was developed by Avinger, Inc., who approached us," Singh says. "They know we are doing truly advanced work here in vascular disease and wanted to partner with us early in the rollout of this new device. Amazingly, as advanced as the Wildcat catheter already is, the future generations of this tool will incorporate a forward-looking imaging component that may be the next quantum leap in vascular disease, so it's really exciting to be a part of this program." ❄



Dr. Kanwar Singh shows cardiology nurse Cathy Ingriselli the Wildcat catheter.

## Fast Fact

**1,264,919** Number of visits to the Health Center's Lyman Maynard Stowe Library – 1,057,474 virtual visits from homes or offices, and 197,445 in person





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## *Center of Innovation*

Connecticut Governor Dannel Malloy takes part in a ceremonial ribbon cutting with elected officials, University trustees and directors, and researchers at the newly renovated Cell and Genome Sciences Building. Equipped with the latest technologies, the nearly 120,000-square-foot research facility has united University scientists in accelerating discoveries that ultimately could lead to novel therapies treating a broad range of diseases.

