

New Graduates Honored at Class Day 2004

Under skies as bright as the graduates' futures, Dartmouth Medical School's class of 2004 received their hoods with some sage advice at this year's Class Day. DMS Dean Stephen P. Spielberg, leading the ceremony for the first time, welcomed the students' family, friends and faculty before introducing the keynote speaker, Dr. Judah Folkman of Harvard Medical School and Boston Children's Hospital.

After touching on Folkman's extensive body of research, Spielberg introduced him as a "model physician, scientist, teacher and true contributor to the cause of medicine in our country."

Folkman told the students to "find a good mentor early so that you can become a good mentor later," and urged them to acknowledge the education they will receive from their patients, whom he referred to as the ultimate teachers.

He discussed several new technologies and therapies in health care, pointing out that this class will be the first medical class in history to prescribe drugs to inhibit angiogenesis, a field he established that investigates the formation of blood vessels and holds promise in the fight against tumors and cancer. Folkman also advised the master's and doctoral researchers "to continue to persist and persevere, because it is you who will arm your fellow clinicians with new ways to relieve suffering and with an increased understanding of the scientific basis of medicine."

Gary Maslow spoke on behalf of his fellow graduating medical students. Discussing the appropriate attire for a medical professional, he pointed out, "It is what is inside the white coat that counts – namely ourselves, all of our experiences, what we have learned here on these hallowed grounds."

ence on which our methods are founded." She also voiced her conviction that, despite the several challenges that include an aging population, pressure to reduce the cost of medical care, and shrinking federal budgets to fund research, DMS has prepared them to meet and overcome these obstacles.

Student class marshals Ian Pitha-Rowe, Alexander Thorngren and Andrew Smith then led classmates to the stage to receive their hoods. Thirty-two students received a Master of Public Health. In life sciences, 27 received a PhD and two earned a master's. In the evaluative clinical sciences, 23 students obtained degrees: one PhD and 22 master's. Forty-nine students earned an MD and an additional 14 Brown-Dartmouth students received degrees in May at Brown University. From here, the Dartmouth medical students will continue their training in generalist and specialty areas across the nation; eight of them will remain in New Hampshire to train at Dartmouth-Hitchcock Medical Center.

In a celebration filled with allusions to the future of medicine and the technological breakthroughs advancing practice, the medical students concluded the 2004 Class Day ceremony by reciting the Hippocratic Oath. The 2,500 year-old vow symbolizes that while the technology of medicine continues to evolve, the physicians' commitment to their patients will never change.



Dr. Judah Folkman (center) delivers an insightful keynote address as DMS master's, doctoral and medical students take part in the Class Day festivities with their families.

He also praised his classmates by quoting a letter he received from a former patient's family, encouraging them to "continue on – you're doing a great job!"

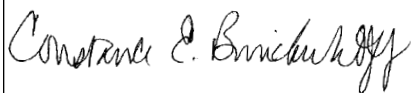
Addressing the audience that included her father, children and grandchildren, graduate student speaker Mardi Crane-Godreau discussed the pride she felt in her fellow graduates and referred to this as "an exciting time to be involved in medicine and the sci-

Deans Column

It has been another successful year for the MD/PhD program, as our students continue to push scientific research at DMS to the forefront of medicine. In addition to their hard work and vision, the accomplishments of our medical and PhD students are a result of time spent with top faculty members, who treat them as colleagues, not simply as students. The MD/PhD candidates are also indebted to Dean Stephen Spielberg and the rest of the administration who have placed this program high on their list of priorities.

There are several aspects that make the DMS MD/PhD program exceptional, including ready access to faculty and the Upper Valley pristine surroundings. This program is truly distinct because it connects DMS students to the incredible resources available at Dartmouth College and the Thayer School of Engineering. By discussing the MD/PhD projects with each other and their other students, faculty from these Dartmouth institutions are connecting on a number of issues that may set foundations for future collaborations.

Our students are building bridges of their own to enhance the relationship between science and medicine. One project being discussed is a student initiative to help patients understand their role in a clinical trial. Once patients have completed their therapy, this program would enable them to see the results of the trial and offer their insight. Bringing these trial patients back into the fold will improve our researchers' understanding of patient care and promote communication between the medical and graduate students. I think this is an inspired idea and hope that this program can serve as a model for future efforts between students as well as faculty in the spirit of collegiality and higher learning.



Constance E. Brinckerhoff, PhD
Nathan Smith Professor of Medicine
and of Biochemistry
Associate Dean for Science



Jon Gilbert Fox

2004 Dartmouth Medical School Awards

Student Awards

<i>The Dean's Medal</i>	Symeon Missios
<i>John W. Strohbehn Medal for Excellence in Biomedical Research</i>	Sergio Andres Quezad
<i>The Good Physician Award</i>	Leigh Perry Strauss
<i>Saul Blatman Award for Excellence in Maternal and Child Health</i>	Sarah Alden Boynton Pitts
<i>Harte C. Crow Award in Radiology</i>	Leila Khorashadi
<i>Dartmouth-Mosenthal Surgical Society Department of Anesthesiology Outstanding Graduating Student Award</i>	Danielle Mercedes Adams, Todd Eric Burdette, Jason Alan Kemp, Symeon Missios
<i>French Distinguished Student Award in Pathology</i>	Kirsten Erica Redborg
<i>Dr. Freddie Fu Orthopaedic Surgery Medical Student Award</i>	Joren Brent Keylock
<i>AMWA's Glasgow-Rubin Achievement Citations</i>	James Barr Ames
<i>Hitchcock Foundation Student Research Prize</i>	Sarah Alden Boynton Pitts, Fremonta Lee Meyer, Danielle Mercedes Adams
<i>Julian and Melba Jarrett Memorial Prize</i>	Gary Ross Maslow
<i>Frederic P. Lord Award in Anatomy</i>	Wendy Lee Osterling
<i>Department of Medicine Award</i>	Joren Brent Keylock
<i>Merck Manual Awards</i>	Emily Wood Demetriou
<i>Arthur Naitove Surgical Scholar Award</i>	Todd Eric Burdette, Angela Dee Sanchez
<i>American Academy of Neurology Medical Student Prize for Excellence in Neurology</i>	Danielle Mercedes Adams
<i>New England Pediatric Society Award</i>	Fremonta Lee Meyer
<i>Department of Psychiatry Award for Excellence in Clinical Psychiatry</i>	Gary Ross Maslow
<i>John F. Radebaugh Community Service Award</i>	Andrew Joseph Smith
<i>Rural Health Scholar Awards</i>	Jason Alan Kemp, Victoria Jane Martin, Gary Ross Maslow
<i>Hilda Weyl Sokol Award</i>	Leigh Perry Strauss
<i>Rolf C. Syvertsen Scholars</i>	Danielle Mercedes Adams, Joren Brent Keylock, Fremonta Lee Meyer, Symeon Missios, Sarah Alden Boynton Pitts
<i>Leonard Tow Humanism in Medicine Award Presented by the Arnold P. Gold Foundation</i>	Gary Ross Maslow
<i>John and Sophia Zaslow Prize</i>	Jason Alan Kemp
<i>Douglas P. Zipes, MD Research Prize in Medicine</i>	Robert Cresson Nutt

Faculty Awards

<i>Thomas P. Almy Housestaff Teaching Award</i>	Christopher M. Alessi, MD, Chief Resident in General Surgery
<i>Basic Science Teaching Award</i>	Matthew B. Heintzelman, PhD, Assistant Professor of Anatomy
<i>Clinical Science Teaching Award</i>	Roshini Pinto-Powell, MD, Assistant Professor of Medicine
<i>Leonard Tow Humanism in Medicine Award Presented by the Arnold P. Gold Foundation</i>	Paul D. Manganiello, MD, Professor of Obstetrics and Gynecology
<i>Dartmouth-Mosenthal Surgical Society</i>	Brian Catlin, MD, Assistant Professor of Anatomy

Pancreatic Tumor Growth Reduced

Two Dartmouth medical studies offer promise against pancreatic cancer, one of the most deadly and aggressive cancers, and may lead to the development of new, highly targeted therapies to manage previously untreatable tumors. Pinpointing some of the most challenging traits of pancreatic cancer cell growth, two trials demonstrated success in slowing and preventing tumor development. Norris Cotton Cancer Center researchers led by Dr. Murray Korc, professor and chair of medicine, reported their studies in the May 15 issues of the journals *Clinical Cancer Research* and *Cancer*.



Dr. Murray Korc

Mark Washburn

The fourth leading cause of cancer deaths in US adults, pancreatic cancer spreads rapidly while becoming increasingly resilient to traditional chemotherapy, and kills more than 30,000 Americans yearly. "That is why we are excited about this research and hope that it will lead to more advances in the treatment of pancreatic cancer," said Korc. "Our research has focused

on determining what factors enable the cells to grow at such a fast rate and then how to slow that rate down and actually suppress pancreatic tumor growth."

Korc likens the disease to speeding in a car with an accelerator stuck to the floor. "Naturally, you apply the brakes but they don't work, so you begin pumping the brakes to slow the car down. The brakes are broken in pancreatic cancer and in addition, we found that the brake has been converted into an accelerator by the cancer cells. In essence, pumping the brakes gives you two accelerators."

In *Clinical Cancer Research*, Korc and Dr. Mitsuharu Fukasawa, a research associate in medicine, report a new, effective anti-angiogenic approach for treating pancreatic cancer. They focused on VEGF, a molecule responsible for angiogenesis, or blood vessel formation, that hampers chemotherapy in pancreatic cancer cells, which have much higher than normal levels of VEGF so cancer cells grow and metastasize quickly and efficiently.

The researchers injected a protein sponge, VEGF-Trap, into mice bearing pan-

creatic tumors to absorb most of the angiogenic VEGF molecules, thereby slowing the blood vessel proliferation and curbing tumor progression. "The protein sponge completely suppressed pancreatic tumor growth. In all the tumors tested, there was a marked decrease in blood vessel formation," said Korc.

In *Cancer Research*, Korc's team, with lead author Dr. Nicole Boyer Arnold, a post-doctoral fellow, describe a novel mechanism for chemoresistance, a hallmark of aggressive tumors such as pancreatic cancer. The team identified pathways that give the cancer cells a growth advantage and make them resistant to chemotherapeutic drugs.

Many pancreatic tumors contain high levels of two molecules, Smad7 and thioredoxin, that make signaling pathways abnormal, allowing cancer cells to resist tumor-suppressing drugs and continue growing. "Now that we know this pathway exists, it will allow us and other investigators to try to figure out ways to interfere with this pathway to design new therapies for pancreatic cancer," said Korc. The researchers will also investigate the potential of a molecular sponge to absorb molecules that promote Smad7 and thioredoxin expression to render the cancer cells more responsive to therapy.

Novel Vitamin Discovered Offers Clues for Cancer Chemotherapy

In a fusion of biochemistry and genetics, Dartmouth Medical School cancer researchers have discovered a new vitamin in a molecular pathway central to such processes as gene regulation, metabolism and aging. And, they found, milk contains this nutrient.

Their study defines another metabolic route to a compound called NAD (nicotinamide adenine dinucleotide) one of the cell's essential small molecules, and suggests that therapeutic approaches for cancer or heart disease may depend on the enzyme pathways identified. The research was published in the May 14 issue of *Cell* by Drs. Charles Brenner, associate professor of genetics and of biochemistry, and Pawel Bieganski, a postdoctoral fellow.

NAD, vital for all organisms, from bacteria to humans, is versatile, working both as a partner that helps enzymes and as an ingredient that other enzymes consume.

Niacin, or vitamin B3, a mixture of the NAD precursors nicotinic acid and nicotinamide, prevents pellagra and can help control cholesterol. Anti-cancer drugs including tiazofurin and benzamide riboside are converted to toxic NAD analogs; proteins dependent on NAD prolong lifespan in experimental systems.

Enzyme studies in Brenner's laboratory at the Norris Cotton Cancer Center revealed a novel twist. Yeast cells where every known NAD biosynthetic pathway was shut down, did not die, yet no vitamins or supplements were known to keep the cells alive. The researchers discovered that an NAD precursor, nicotinamide riboside (NR), known as a vitamin only in certain bacteria, also served as a vitamin in yeast and could prevent death. Using what Brenner termed a "biochemical genomics approach," they zeroed in on the gene for a novel kinase enzyme in yeast and humans responsible for this vita-

min conversion pathway. Then they found the vitamin in milk.

Their findings upend some decades-old assumptions underlying biosynthetic schemes for NAD and refocus the pharmacology of cancer drugs that look like nicotinamide riboside. As a nutrient, NR may be an alternative to niacin, which helps lower cholesterol but has uncomfortable flushing effects. And, while tiazofurin-related drugs have potential against cancer, they are unpredictable so kinase screening may benefit patients. "Certain tumors respond, while others don't, so if we can select the right patients we will have a more effective treatment strategy," Brenner said. "In the future, testing for nicotinamide riboside kinase expression might be used to identify the patients that are likely to respond to this class of drugs."

Calcium Supplements Can Lower Risk of Large Colon Polyps

While taking calcium supplements can decrease the risk of all types of colorectal polyps, research led by Dartmouth Medical School shows calcium had the greatest effect on advanced colorectal lesions, considered most strongly associated with invasive colorectal cancer.

The multi-center study, reported in the June 16 issue of the *Journal of the National Cancer Institute*, builds on prior Dartmouth research and provides more evidence that calcium supplementation appears to be a relatively safe and inexpensive way to reduce the risk of the most serious types of colorectal polyps, or adenomas.

“Our results suggest that calcium supplementation may have a more protective effect on advanced adenomas than on other types of colorectal polyps,” said Kristin Wallace, a Dartmouth Medical School graduate student who was the lead author on the study. “These findings highlight the need to consider ‘polyp type’ when assessing the efficacy of a given treatment.”

John Baron, MD, professor of medicine and of community and family medicine and an investigator at Norris Cotton Cancer Center at Dartmouth-Hitchcock Medical Center, has done numerous studies on the

effects of aspirin and calcium on colon cancer and led the project. “Previous studies have demonstrated an association between calcium intake and moderate decreases in the



Dr. John Baron

risk of precancerous colorectal tumors, but this is the first randomized trial to evaluate the effect of calcium on different types of colorectal lesions,” he said.

Colorectal polyps, are bumps or fleshy tumors that occur on the inside lining of the colon and may become cancerous over time. By decreasing the size of the polyps and their number, there is less potential for colorectal cancer.

Researchers analyzed data from 913 patients enrolled in the Calcium Polyp

Prevention Study, a randomized, double-blind, placebo-controlled trial — meaning that neither the patient nor those following them knew which treatment they were receiving. Patients took either a 1,200-milligram calcium supplement or a placebo and had a follow-up colonoscopy one and four years after enrolling in the trial.

The results showed that supplemental calcium slightly decreased the risk of all types of colorectal polyps, but effect was greatest for the most advanced colorectal lesions. There was also some evidence that a diet high in fiber and low in fat increased the preventive effect of calcium, but these results were not statistically definitive.

The research was supported by the National Cancer Institute. Other Dartmouth Medical School researchers who contributed to this study include Drs. Bernard Cole, Margaret Karagas, Michael Beach, Richard Rothstein, and Loretta Pearson.

In addition to Dartmouth-Hitchcock Medical Center, the other participating centers were the Cleveland Clinic Foundation, the University of Southern California School of Medicine, the University of Minnesota, the University of North Carolina School of Medicine and Emory University.

Paintings of DMS Historical Achievements Unveiled



Artists Joseph Dwaihy, DMS II, and Sara Dykstra pose next to “The First X-ray,” one of three of their masterpieces, at the unveiling ceremony on June 11. Dykstra and Dwaihy volunteered for over a year to complete the three mural-sized paintings, each depicting a defining moment in the history of DMS. The mural above shows Dr. William Mosenthal and the first intensive care unit in the country, which he established at Dartmouth in 1955. The paintings, part of a student-led effort to beautify the campus of DMS, will be hung in Chilcott auditorium and in the Rubin section of DHMC.

Dartmouth Medical School Awarded \$9 Million Grant for Genomics Research

Dartmouth Medical School has received \$9 million from the National Institutes of Health to lead a national collaboration in functional genomics that could shape future medical studies, including the development of antibiotics and treatments. The five-year award, from the National Institute of General Medical Sciences, will fund one of the most comprehensive studies to date on the roles and functions of genes in filamentous fungi.

"We're truly excited about this project, and the fact that it will be centered at Dartmouth Medical School," said Drs. Jay Dunlap and Jennifer Loros, both professors of genetics and of biochemistry, who will lead two of the four collaborative projects, "Filamentous fungi, for which *Neurospora* is perhaps the best understood model organism...include a number of sig-

nificant animal, human and plant pathogens, as well as a large number of strains used in industrial manufacture. This study will provide a foundation for a great deal of further work," said Dunlap.

Fungi allied to *Neurospora*, better known as bread mold, have been manipulated to produce antibiotics and pharmaceuticals.

While about 60 percent of the *Neurospora* genes enable functions shared by other organisms including people, the rest of the more than 10,000

Neurospora genes are apparently novel and activate biochemical functions that will be new, suggesting that

examination of these genes will be informative and wide ranging.

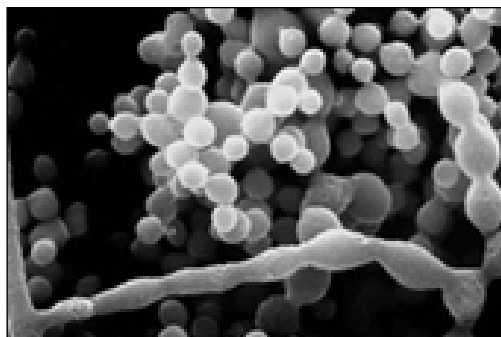
"*Neurospora* is a fascinating fungus," said DMS Dean Stephen P. Spielberg. "It is an

enormously helpful model system; organisms like it cause disease, manufacture medicine and most biomass turnover on the planet requires filamentous fungi. This grant represents a wealth of promising research opportunities and we look forward to understanding the gene expression of this potentially groundbreaking genetic model. The results of this study will probably change our thinking about how we look at humans and gene expression."

Four interconnected studies will be conducted among UC Berkeley, UCLA, MIT, University of New Mexico, UC Riverside University of Missouri and Oregon Health Sciences University in addition to DMS.

The projects will:

- pursue the systematic disruption of genes through targeted gene replacements;
- produce a platform for electronically capturing community feedback and data about the existing annotation;
- provide a baseline analysis of gene expression under various growth conditions;
- generate cDNA libraries and a single nucleotide polymorphism map from wild type and related strains.



A scanning electron micrograph shows the filamentous fungus *Neurospora crassa* that will be the focus of the work.

Matt Springer and the Fungal Genetics Stock Center

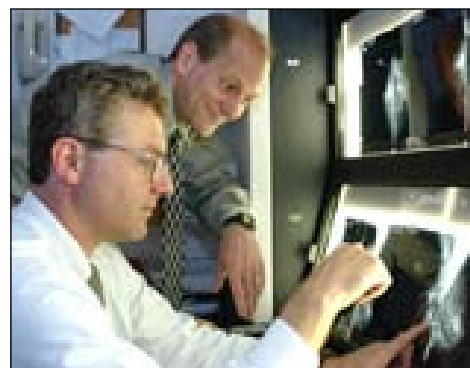
Alternative/Supplemental Breast Imaging Methods Tested

Dartmouth physicians and engineers collaborating to test three new imaging techniques to find breast abnormalities, including cancer, report the first stage of their research, information about the electro-magnetic characteristics of healthy breast tissue, in the May issue of Radiology.

"This study offers the foundation for future research and clinical trials," said lead author Dr. Steven Poplack, associate professor of radiology and obstetrics. "We're establishing normal ranges for healthy breast tissue characteristics in order to more easily recognize the abnormalities." The methods are not invasive or particularly uncomfortable for participants, and they all provide detailed information about different properties of breast tissue.

An interdisciplinary team, which includes researchers from Dartmouth Medical School and the Thayer School of Engineering, the Norris Cotton Cancer

Center and Dartmouth-Hitchcock Medical Center, is developing and testing imaging techniques to learn about breast tissue structure and behavior. The techniques are electrical impedance spectral imaging (EIS),



Drs. Steven Poplack and Keith Paulsen

microwave imaging spectroscopy (MIS) and near infrared (NIR) spectral imaging.

- EIS, a painless test, uses a low voltage electrode system to examine how breast tissue

conducts and stores electricity. Living cell membranes carry an electric potential that affects the way a current flows, and different cancer cells have different electrical characteristics.

- MIS involves the propagation of low microwave energy levels through breast tissue to measure electrical properties. This technique is particularly sensitive to water. Generally, tumors have more water and blood than regular tissue.
- NIR utilizes infrared light, which is sensitive to blood, so sending infrared light through breast tissue with a fiber optic array can locate and quantify regions of oxygenated and deoxygenated hemoglobin.

Other authors of the Radiology report include Dr. Keith D. Paulsen, professor of engineering, who heads the research program, and Drs. Alexander Hartov, Paul Meaney, Brian Pogue, Tor Tosteson, Wendy Wells, Margaret Grove and Sandra Soho, all of DMS or Thayer School.

Joseph Melling, '09

Improving Health Care for Children with Special Needs

Health care delivered close to home is very important, especially when the patient is a child. But how do community pediatric practices adapt to offer the best care when faced with a child who has complex and often, multiple health needs? Reporting in May's issue of Pediatrics, Dartmouth Medical School researchers outline a process designed to help any practice become a state of the art "medical home" for such children.

Assessing the effectiveness of a model program they developed, Dr. W. Carl Cooley, adjunct associate professor in pediatrics, and Jeanne McAllister, research associate in pediatrics, review four practices in Vermont and New Hampshire that used their program to identify and implement changes to improve the care they deliver to children with special health care needs.

The concept of community-based "medical homes" — where care is managed through coordination of clinicians, educators, therapists, healthcare professionals, and caregivers — has been advocated by national health policy makers and the American Academy of Pediatrics as the best model for providing systematic yet individualized care to children with complex conditions and multiple needs.

Still, becoming an effective medical home can be difficult. "Introducing change into a busy pediatric practice is like trying

to repair a bicycle while riding it," the authors write. "Even the most motivated practice finds change difficult to implement. Many primary care providers believe that implementing the medical home concept is the right thing to do but question how they can do so and remain solvent."

To make the process easier, the authors developed a medical home improvement tool kit that allows practices to look at key functions of the medical home, assess their own operation, and identify the steps and strategies they will follow to become a medical home. The four participating practices all focused on improving different aspects of their medical home environment. They also introduced the role of a practice-based care coordinator and discovered the value of systematic consumer input to the design and operation of the medical home.

The success of the model program in these practices and across the country is encouraging, say the authors, who direct the Center for Medical Home Improvement within the Hood Center for Children at the Children's Hospital at DHMC. Establishing medical homes improves access to care, potentially makes more treatments available to children, strengthens the relationship between families and caregivers and ultimately provides the child with more comprehensive and effective care.

— Thaddeus Shattuck, DMS III

Medical Student for a Day



Andy Nordhoff

DMS rural health scholars hosted three New Hampshire state college students who attended several medical classes, observed clinics at DHMC and interacted with DMS students to obtain a strong sense of what to expect at medical school. The students are Adam Templeton (DMS I) (crouching), and from left, Christy Castro (DMS II), Annie Pearson (DMS I), Kate Donhauser (DMS I), James Wylie (University of New Hampshire), Steve Skinner (Plymouth State) and Allen Wellington (Keene State).

DARTMOUTH
MEDICAL
SCHOOL

DIGEST

DMS Communications

1 Rope Ferry Road (HB 7065)

Hanover, NH 03755-1404

Tel: (603) 650-1492 • Fax: (603) 650-1730

Email: dms.communications@dartmouth.edu

www.dartmouth.edu/dms/news

Hali Wickner, Editor

Andy Nordhoff, Associate Editor

Mark Cookson, Layout & Design