

Class of 2006 Celebrates New Beginning

Students, parents, friends and teachers gathered on September 20 to celebrate the first step in the medical careers of the 81 members of the Class of 2006 in a day-long program that focused on the core values of Dartmouth Medical School as they relate to medical and professional ethics. The morning sessions featured different aspects of medical education.



Lori Arviso Alvord, MD, associate dean for student and multicultural affairs, presents a white coat to Jean-Paul H. Dedam '06.

The students participated in a forum, "Introduction to Case Studies in Professional Behavior," led by Joseph F. O'Donnell, MD, senior advising dean, and later in a discussion about small group work with year two students and James M. Bell, MD, associate professor of medicine. Family and friends attended DMS faculty presentations designed to introduce them to the four-year medical school curriculum, with specific information about year one.

In the afternoon, everyone gathered back in Kellogg Auditorium for the formal presentation of the traditional white coats to the new students. Acting dean Ethan Dmitrovsky, MD, spoke about the relationship between science and medicine. "It may seem counter-intuitive that I selected as my topic today science and medicine, if the emphasis of our ceremony is on humanism and professionalism.

But this is not the case. We all would agree that scientific knowledge is an important aspect of being a physician. It is our genuine understanding of scientific principles that distinguishes our profession and it is the unique responsibility of physicians to translate basic scientific findings from the laboratory to the clinic. It is also this scientific knowledge that permits physicians to provide competent and compassionate care."

He went on to talk about the future of biomedicine and how we are moving much faster than was ever imagined when he was starting medical school. Finally, Dmitrovsky spoke about what students should do with the knowledge that they will acquire in medical school: "To address this question, I respectfully suggest that you consider drawing on the core values of Dartmouth Medical School. This is our commitment to excellence in scholarship, teaching, clinical care and, importantly, service. These missions are enhanced by each of us embracing the highest standards of personal and professional ethics. These include integrity, preserving confidentiality in your professional work and always placing your patients first while you serve their interests as well as those of the public health....



Class of 2006 members Roy Wade (left) and Alexander S. Ambly with guests after the white coat ceremony.

What sets our profession apart is that we become fully versed in the scientific bases of medicine and thereby acquire special skills that we can apply in our service to our patients and community. This service is our unique opportunity and privilege."

Then, O'Donnell spoke about the Class of 2006 mission statement regarding how they see their work as physicians in



Class of 2006 students from left, Kirstin I. Thode, Rajesh K. Joshi, Lisanne M. Palomar, Sandy Chan, Jinny E. Chang, and Alka Basil.

their communities, their nations and the world at large. Finally, David Nierenberg, MD, senior associate dean for medical education, discussed the importance of professionalism and the inherent responsibility that the white coat places on the shoulders of its recipients. He also noted how the class mission statement paralleled the mission statement worked out over many years by physicians across North America and Europe detailing the professional standards to which physicians need to hold themselves in their relationships with each other and with their patients.

The white coats were presented by Lori Arviso Alvord, MD, associate dean for student and multicultural affairs, and Sue Ann Hennessy, assistant dean for student affairs. Each student also received a copy of *The Lives of a Cell* by Lewis Thomas as a gift from Dmitrovsky. A reception followed for students and their families.

Deans Column

Each autumn the Life Sciences Symposium occurs at Dartmouth. This year's event, the ninth in the series, was titled "Proteomics and Genomics in Biology and Medicine." The scholarly presentations made it ever more evident that the separation between medical research and the technical part of medical practice is disappearing. Again this year, innovative, insightful and exciting concepts were presented, many of them applicable to understanding, diagnosing and treating disease. Symposia such as this force one to confront the pace and scope of change pervading medicine today.

In this same vein, the last nine years have also been a time of great change for Dartmouth Medical School. Since the first Life Sciences Symposium our basic science faculty has increased by over 20%, and the clinical faculty by more than that. The increase in graduate students has outpaced both. Extramural funding of research has more than doubled, and these years have seen several programmatic changes including the creation of the Genetics Department, the addition of various graduate degree programs, dramatic growth in CECS, expansion of the Norris Cotton Cancer Center and founding of the Neuroscience Center at Dartmouth. Unquestionably, DMS is securing a notable position in education, research and clinical expertise.

Parallel growth occurs between our programs here at DMS and the advances that captivate us each year at the Life Sciences Symposium. We live in an exhilarating time for medicine. After the symposium one of the distinguished speakers admitted to being jealous of our current students. I agree! They are beginning their careers at a time that has a fascinating and promising future. While I cannot predict what will be presented at the Life Sciences Symposium nine years hence, I am certain it will be dramatically different from today. Yet, DMS will be ready. We can be proud of our faculty's commitment to preparing our students for the evolving integration of clinical medicine and basic research that characterize this era.



William F. Hickey, M.D.
Senior Associate Dean for Academic Affairs
The Constantine and Joyce Hampers Professor

DMS Awarded Grant to Study Early Immunity

The National Institute of Allergy and Infectious Diseases has awarded Dartmouth Medical School \$7.2 million for an array of studies that traverse immunology, physiology and obstetrics/gynecology in a five-year program project headed by Charles Wira, PhD, professor of physiology.

DMS researchers are exploring the role sex hormones play in the body's rapid response protection system through collaboration that could lead to new approaches to combat infections and autoimmune diseases.

This comprehensive program focuses on a facet of the immune system called innate immunity, the first line of defense when bacteria or viruses invade the body. The innate response kicks in immediately to eradicate or reduce the potential infection.

In contrast, adaptive, or acquired, immunity occurs gradually with antibodies and T cells which encounter microbes and attack them, then set up the body to trigger an immune response on subsequent exposure. Only recently have researchers begun to appreciate the power of the innate system in humans.

Drawing on the talents of immunologists and endocrinologists, four DMS teams are scrutinizing the essential blood and epithelial cells of the innate immune system to define how the sex hormones – androgens, estrogens and progestins – shape the innate function in women and men. Collectively, they aim to understand how the innate and adaptive systems communicate, and if the early warning innate system can turn on an adaptive response. The work is expected to shed light on preventing and treating infections, including HIV and other sexually transmitted diseases, autoimmune disorders and gynecological cancers.

"The innate immune system is constitutive; it's always there," says Wira. "We're interested in seeing if it is in fact regulated



Charles Wira, PhD

by hormones and whether differences between men and women influence this protection. The cells we're studying are all key players in the innate system; they are immediately challenged and if they do their job completely, then the body doesn't initiate an immune response. But, if that level of protection is not sufficient, then they play an important role in stimulating the adaptive system to bring on this whole other level."

The work builds on a prior program project, which Wira also headed, on women's reproductive health and immunity that has revealed some intriguing clues to disease susceptibility and treatment potential. Recent work by John Fahey, PhD, and Wira, for example, has shown that the cells lining the uterus secrete a bacteria-killing molecule, whose activity is present during the menstrual cycle and is inactive in post menopausal women. "The message," says Wira, "is that that within the innate immune system, there are endogenous microbicides, which if they could be turned on, might lead to prevention of infection on conditions of exposure to a potential pathogen."

The four projects and their leaders are:

- The influence of female sex hormones on the epithelial cells that line the mucosal surface of the female reproductive tract: Wira and Fahey, research assistant professor of physiology.
- The effect of gender and steroid sex hormones on the function of blood cells called polymorphonuclear neutrophils, a critical element of the innate immune system: Paul Guyre, PhD, professor of physiology.
- The role of sex hormones on myeloid cells – the macrophages and dendritic cells, which are rapid effectors of innate immunity and are also involved in the adaptive response: Michael Fanger, PhD, professor of microbiology and immunology.
- The regulation of natural killer cells by androgens and estrogens in men and women, as well as how these cells are programmed to act in the female reproductive tract: Charles Sentman, PhD, assistant professor of microbiology and immunology.

Beginning this issue, different deans will have an opportunity to present their perspective in the Deans Column, which will rotate among deans each issue.

Imaging Studies Aim to Improve Breast Cancer Detection

A multidisciplinary team of Dartmouth doctors and engineers, in a joint effort to improve early breast cancer detection, is gearing up to test four novel, more comfortable breast imaging techniques in patients.

X-ray mammography, the most widely used method for breast cancer screening, has drawbacks. In a controversial report, its effectiveness in saving lives from breast cancer was questioned last year by a group of Danish researchers. A recent review by the US Preventive Services Task Force, however, has reaffirmed its use in women over 40 years of age, according to DMS physician Steven Poplack, MD, one of the investigators. Still, mammography remains limited by high rates of false-positives and false-negatives and is often uncomfortable.

Halfway through a five-year, \$7 million grant from the National Cancer Institute, Dartmouth Medical School and Thayer School of Engineering researchers, collaborating with the Norris Cotton Cancer Center, have amassed considerable informa-



Jon Gilbert Fox

Steven Poplack, MD

tion about breast tissue structure and behavior through their studies of different breast imaging alternatives. None of these techniques: magnetic resonance, infrared lasers, microwave imaging or electrical impedance spectroscopy, require breast compression or have known health hazards.

Starting next year, the investigators will test the methods they have developed in a formal clinical study involving 150 patients. Half the participants will be drawn from those who require a biopsy and the other half, the control group, will have received normal mammograms. The researchers plan

to examine each patient using all four techniques and then compare the results to the corresponding diagnoses of the biopsy group. Their goal is to collect data to assess the effectiveness of these newer imaging modes.

Preliminary results are encouraging, but it is too early to tell which of the techniques are effective. "The clinical study will give us that information," says Poplack, associate professor of radiology and of obstetrics and gynecology. "But even if only one of the modalities turns out to be able to detect breast cancer – especially in the settings where mammography has limitations – or proves to be diagnostic, then we will have made tremendous strides."

Dartmouth's program is considered unique because it is exploring the techniques, not in isolation, but in conjunction with each other. "This gives us a lot of data on each patient," says Keith Paulsen, PhD, an engineering professor and a principal investigator, "so that we can explore the intrinsic value of each method, their differences, and the value of using them in combination."

Dartmouth Site for Landmark Lung Cancer Screening Trial

Norris Cotton Cancer Center (NCCC) researchers have joined with colleagues across the country to launch the largest-ever lung cancer screening trial funded by the National Cancer Institute (NCI). The National Lung Screening Trial (NLST) aims to determine if screening people with either a sophisticated imaging technology called spiral computerized tomography (CT) or a standard chest X-ray before symptoms appear can reduce deaths from lung cancer.

William Black, MD, professor of radiology and of community and family medicine at Dartmouth Medical School, one of five co-chairs in the national study, helped develop the protocols for the study, which continues through 2009. Dartmouth-Hitchcock Medical Center is the only site in Northern New England for the NLST, which seeks to enroll an estimated 50,000 current and former smokers aged 55 to 74 through NCCC and 29 other comprehensive cancer centers nationwide.

"Lung cancer kills more people than cancers of the breast, prostate, colon and

pancreas combined and will claim nearly 155,000 lives this year," said Black. "Our hope is that this study will lead to saving lives."

Lung cancer rates in Northern New England have traditionally been above the national average. NCI statistics show that through 1994 (the last year for which national statistics are available) Maine, New Hampshire and Vermont were in the top half of states for lung cancer deaths per 100,000 population. In New Hampshire, current estimates are that 800 people will be diagnosed with lung cancer this year; of those, 700 are expected to die from the disease. In Vermont, the American Cancer Society (ACS) predicts 400 new cases of lung cancer this year and 400 deaths from the disease, and in Maine, 1,000 new lung cancer cases this year and 900 deaths from lung cancer.

To date, however, no scientific evidence has shown that screening or early detection of lung cancer can save lives. By the time it is detected, lung cancer has usually spread outside the lung in 15 to 30

percent of cases. Spiral CT, introduced in the 1990's, produces a three dimensional model of the lungs that can pick up tumors well under one centimeter (cm) in size, while chest X-rays detect tumors about one to two cm in size. But the acuity of spiral CT is also a drawback, for many of the lesions found turn out to be non-cancerous after additional follow-up.

NCI funded two research networks to conduct the NLST: the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial and the American College of Radiology Imaging Network, and is also collaborating with the ACS to organize grassroots recruitment efforts at NLST sites.

NLST will be a randomized, controlled study: participants will be randomly designated to receive either a chest X-ray or a spiral CT once a year for three years. Volunteers will receive their screenings free of charge.

To enroll or for more information, call 603-650-8747 or toll-free, 800-221-9994. Or log on to cancer.gov/NLST.

Dartmouth Distinguished Lecture Series Opens

The DMS Distinguished Lecture Series opened on Friday, October 11 with cancer biologist Craig Thompson, MD, DC '74, DMS '75, scientific director of the Abramson Family Cancer Research Institute, University of Pennsylvania. Thompson was so well received by the DMS community that his lecture was moved from Chilcott Auditorium to Kellogg Auditorium to accommodate everyone who wished to attend.

His lecture, "Apoptosis: How is it Regulated and Does it Really Contribute to Degenerative Diseases and Cancer?" was both scientifically astute and accessible to students and those from other fields. Thompson began with the way in which he was taught about cancer here at DMS in the 1970's, and then went on to outline what advances have taken place, especially with what is known about how the mechanism of apoptosis, or programmed cell death, functions, and how this is affecting the future of cancer research. In addition, he touched on some of the newest technologies that are helping in the fight against cancer, such as the PET scan, and how the

continuing scientific interest in the mechanisms of this disease has helped in their development.

Following clinical training in internal medicine at Harvard University and in medical oncology at the University of Washington, Thompson served on the faculties of the University of Michigan and the University of Chicago where he was also an Howard Hughes Medical Institute investigator, until assuming his post at Pennsylvania in 1999. Recently, he was appointed chair of the Howard Hughes Medical Institute Advisory Board.

The next lecturer in the series is Ronald M. Evans, PhD, an investigator at the Howard Hughes Medical Institute and professor at The Salk Institute for Biological Studies, on November 5 at 5 p.m. in Filene Auditorium in the Moore Psychology Building. The lecture "PPARs: The Complex Journey to Obesity," is preceded by a reception at 4:30 p.m. outside Filene. All are invited to both the reception and the lecture.

Evans' original discoveries over three decades have pioneered research in endocrinology, embryology and the treat-

ment of human disease. A member of the National Academy of Sciences, Evans received his BA in bacteriology and his PhD in microbiology from the University of California at Los Angeles.

The third lecturer will be Robert Kingston, PhD, from Massachusetts General Hospital, on Tuesday, December 3 at 5 p.m. in Filene Auditorium. His topic is: "Towards Establishing a Biochemical System to Understand Maintenance of Body Pattern." Kingston received his undergraduate degree from Harvard University and his PhD from the University of California, Berkeley. He did his postdoctoral fellowship at the Center for Cancer Research at the Massachusetts Institute of Technology. Since 1985, Kingston has served on the faculty at Harvard Medical School where he is professor of genetics and at Massachusetts General Hospital where he is a molecular biologist.

In 2003, on March 31, Stanley R. Korsmeyer, MD, will speak on the "Mitochondrial Gateway to Apoptosis." On Tuesday, May 27, Robert A. Weinberg, PhD, will give the final lecture for this academic year.

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