

In With the New: Class of 2007 Begins Training

DMS welcomed the medical class of 2007 with words of advice, encouragement, congratulations, and even a couple of songs. Starting his sixth week at DMS, Dean Stephen P. Spielberg opened by telling the class that they will “hold a special place in my heart as we learn our new professions together.” He then spoke of the distinct, collaborative environment at DMS and stressed that this community will nurture their minds as they enter the evolutionary world of medicine. “Things are changing rapidly in medicine,” Spielberg said, “which is why it is so vital for you to approach medical school as but the beginning of a life-long educational process.”

Following a hearty welcome from Dartmouth College President James



Christina Tseng, Shamon Mayer, Tim Gagne and Khushal Latifzai (from left) get to know each other at the “get acquainted lunch.”

Wright, Director of Admissions Andy Welch introduced the class of 2007. Welch began by revealing that 5,010 candidates applied to DMS and, of the five percent that were admitted, “the 78 students with the keenest sense of judgment have become the entering class of 2003.” Welch further praised the intellectual character of the new class, pointing out that, in addition to their undergraduate academic prowess, they have been published in nearly a dozen respected journals and six students already hold graduate degrees, including a PhD.



Sade Ajayi (left) and Seyi Akinbobola put their heads together during orientation.



Dean Stephen Spielberg connected with several fellow newcomers at the DMS Dean's Picnic at the Dartmouth Skiway.

Members of the class captained inter-collegiate teams, played professional hockey, volunteered for Mother Teresa's Missions of Charity in Calcutta and cleaned up the Mount

Everest Base Camp. Welch noted the diverse employment histories of the students, which include an ice-cream truck driver, an investment banker, a yacht builder and a manager of a café in Scotland.

Senior Associate Dean David Nierenberg then put some of the students' trepidations to rest as he shared a case study with the new class “to give you confidence as you set forth on your academic journey.” Associate Dean Lori Arviso Alvord added to his message, letting the students know that while this journey is not easy, DMS strives to ensure that no student goes through it alone and highlighted numerous resources for them to rely on.

Todd Burdette, '04, the DMS student government president, offered gems of advice as he addressed his new schoolmates for first time. Closing the

welcome session, Senior Advising Dean Joseph O'Donnell emphasized the words “joy” and “respect” in his speech, relying on Aretha Franklin to carry his message home.

Orientation for the new class involved several other functions throughout the week, including picnics, financial advising, computing classes and an overnight trip to Moosilauke Ravine Lodge.

The sessions culminate on September 19 with the white coat ceremony and an introduction to the privileges and responsibilities to the medical profession.



Two new students take time to truly orient themselves.

2003 Entering Medical Class

- 5,010 applicants
 - 588 interviewed
 - 259 admitted
- 78 entering students
 - 62 Dartmouth medical students
 - 15 Brown/Dartmouth students
 - 1 MD/PhD candidate
- 45% men, 55% women
- 26% international or students of color
- 8% racial or ethnic groups underrepresented in American medicine
- 23 states and 58 undergraduate institutions represented
- 5% acceptance rate

Deans Column

My first month here as dean of Dartmouth Medical School has convinced me how fortunate I am to be a part of this remarkable institution. I have had the pleasure of meeting with many of our faculty and some of our students and staff, and look forward to continuing to get to know the Dartmouth community. This has been a time for me to learn about the medical school, Dartmouth-Hitchcock Medical Center and Dartmouth College as a whole.



Flying Squirrel Graphics

Many of my impressions during the recruitment process have been confirmed. I am impressed by the dedication, enthusiasm and energy of individual scientists, physicians and students and how these features are expressed in teamwork, joint programs or cross-disciplinary initiatives aimed at taking a fresh, novel approach to problems ranging from basic molecular biology through health care delivery. I see strong alliances and a collaborative spirit between the medical school and Dartmouth-Hitchcock Medical Center and I am excited by opportunities to work across traditional departments and with the larger Dartmouth College community. I have greatly enjoyed meeting with alumni and other supporters of DMS; steadfast friends of the school have been so crucial to its success in the past and will be even more so in the future.

We will face many challenges at DMS and in medicine in general in the United States over the next years. Together, we have the chance to define the very best in education of our medical and graduate students in local and regional health care, while our research, clinical and educational activities have a national and international impact. Here at DMS, I am convinced we will pursue excellence in all spheres with a unique sense of vision and purpose, and I look forward to working with you all towards these goals.

Stephen P. Spielberg, MD, PhD

Stephen P. Spielberg, MD, PhD
Dean, Dartmouth Medical School
Vice President for Health Affairs, Dartmouth College

New Triggers for Cell Trash Can Found

Researchers have discovered a novel class of compounds that affects the cell's garbage disposal system which degrades proteins, opening a window for understanding a vital cell function as well as for treating heart disease and cancer.

The distinctive mechanisms of these compounds were reported in July in *Biochemistry* by Dr. Michael Simons, professor of medicine and of pharmacology and toxicology at DMS and head of cardiology at DHMC, with coauthors Dr. Mark Post, visiting associate professor of medicine, and colleagues from the University of Texas.

Just as cells produce proteins, they must also get rid of those they no longer need. Structures called proteasomes chew up proteins made within the cell — including viruses and other parasites — that are targeted for destruction.

Proteasomes are a complex of enzymes with a cylinder core and a lid on the top and bottom. "The proteins come in and are digested like a big garbage can," Simons said. Proteasomes are an attractive target for drug development because manipulating them to prevent or provoke degradation of a particular protein affects most cell activities.

In studying compounds that promote the formation of new blood vessels (angiogenesis), Simons and his colleagues found these compounds constituted a new class of inhibitor that changes the shape of the proteasome. "This is a completely different class of proteasome inhibitors with unusual mechanisms," Simons said. "It is a very unusual shape change; it does not fit any known patterns."

Generally proteasome inhibitors interact with protein-digesting enzymes on chains inside the proteasome cylinder. The new-found class, proline/arginine-rich peptides, instead

bind to the outside of the proteasome cylinder, triggering it to change shape in a way that limits the proteins they can ingest. The effects appear in all proteasomes, from yeast to humans.

Normal proteasomes look like regular circles; when the researchers add the peptide, the proteasome takes a dumbbell shape. Substances cannot easily get into the proteasome and its activity range is restricted. As a result, it will destroy only a small number of proteins.

Since the compounds do not act on the active site of an enzyme, but on its shape, their effects are reversible, meaning that treatment options are controllable. Moreover, the dual effects of stimulating and stopping growth offer intriguing therapeutic potential for both heart disease and cancer.

These peptides are especially powerful agents for inducing vessel growth and their angiogenic activity correlates with their ability to interact with certain proteasomes and change their shapes. They turn off degradation of master switch genes that activate several different angiogenic cascades.

Also, these peptides prevent degradation of a molecule that normally inhibits activity of nuclear factor kappa B that controls a number of cell processes including growth and inflammation. High levels of the molecule impede cell growth, which has implications for use against cancers.



Dr. Michael Simons

Mark Austin-Washburn



DMS Kosovo Project: Medical exchange students from the University of Pristina are studying at DMS for one month to enhance their skills. From left, Gani Abazi, Dean Stephen Spielberg, Ilir Hoxja and Dr. Joseph O'Donnell.

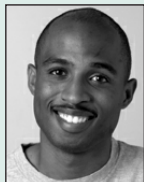
Flying Squirrel Graphics

Albert Schweitzer Fellows Find New Ways to Serve Community

The legacy of Albert Schweitzer, a renowned humanitarian and physician, is thriving at DMS. Eight ambitious second-year DMS medical students who are recipients of the Albert Schweitzer Fellowship are laying the foundations for their community service projects, taking on responsibilities ranging from consoling a patient on her deathbed to pirouetting across a ballet studio. The 2003 fellows, selected from a competitive pool of applicants by the New Hampshire/Vermont program, will contribute at least 200 hours of service towards filling the health needs of the community. While the fellows certainly have their work cut out for them, they are all eager to begin to enrich the lives of others and, ultimately, themselves through the rewarding process.



Shirin Sioshansi



Roy Wade



Elizabeth Eisenhardt



Emily Walker

among various groups in America. "We hope that DMS graduates will seek to learn about a patient's culture as they learn how to treat their illnesses," said Sioshansi, adding that the goal is to make it a permanent addition to the DMS curriculum.

I don't know what your destiny will be, but one thing I know: the only ones among you who will be really happy are those who have sought and found how to serve.

— Albert Schweitzer

Elizabeth Eisenhardt will build on her interest in the healing arts by teaching a ballet class to provide the medical community with a time to relax, to exercise and to be artistic. "I hope to instill an appreciation of the art, and to help teach music appreciation," she said. Eisenhardt plans on putting together a dance troupe to perform in local senior homes and hospitals. "That way," she said, "we will be able to inspire others and keep our souls healthy too!"

"In med school, we focus most of our energy in learning how to handle the outcome of a disease or health issue," said Emily Walker, "but we think it is extremely important to learn about methods to control and prevent diseases so they never become serious issues." She and Krista Heydt will lead a team of medical students to educate patients of the Good Neighbor Health Center on methods to maintain cardiovascular health and provide one-on-one support in making necessary lifestyle changes. "Many patients can make a significant impact in their long-term health by making a few changes in their eating habits, exercise regimen and stress level," Walker said. "I feel like it will make a big difference for people," added Heydt. "It will be like having your own personal trainer to strengthen your muscles — this just focuses on the heart muscle."

Joe Dwaihy is connecting literature with medicine in his efforts to provide companionship and conversation to hospice patients. He plans to write a book based on their life stories and his experiences with them in their final days. "There's a lot of prose by doctors, teachers and writers, but it is difficult to find something written by a student," said Dwaihy, who will focus his time on patients who are dying alone. "I believe I'm in a unique position to connect to hospice patients—they are vulnerable because they are faced with the end of life and I am vulnerable because I have so much to learn."

"We realized there is no 'safe' place for Hanover teens to go and talk about emerging drug and alcohol issues," said Katrina Mitchell, as she explained her motivation to start a peer support group for area teens. She and fellow medical student Christopher Jons will provide a forum for "at risk" teens to address substance abuse concerns in a positive, non-punitive environment. Mitchell and Jons will build off their experiences working with teens and, in addition to regular discussions and outreach, plan on incorporating community service activities, social activism and hiking trips to build a community of hope. "Teens are under so much pressure already," points out Mitchell, "that we feel that an easy, positive environment where they can rely on their peers and not be threatened with punishments will pull them through their struggles toward recovery."

Dr. Joseph O'Donnell, senior advising dean who directs the Schweitzer program, extolled the value of what can be accomplished when funds are combined with idealism of the young and an academic environment to nurture them. "Our students learn about patient care in lectures but the Schweitzer fellows are in a unique position to actually apply this knowledge to benefit themselves and the community," he said. "We hope this incredible program provides enrichment that extends beyond this one-year experience and enables our students to be Schweitzer fellows for life."

Past Schweitzer projects include smoking cessation programs, building and maintaining trails around DHMC, a resource guide for Teens, and the DMS Patient Partnership Program.



Krista Heydt



Joseph Dwaihy



Katrina Mitchell



Christopher Jons

Aspirin May Fight the Risk of Deadly Infections

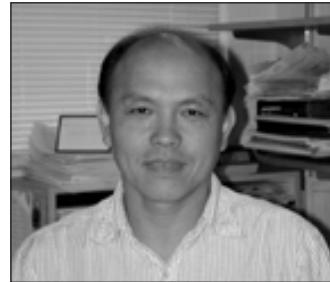
Adding to the benefits of aspirin, researchers have found that it is responsible for reducing toxic bacteria associated with serious infections. A study led by Dartmouth Medical School describes how salicylic acid — produced when the body breaks down aspirin — disrupts the bacteria's ability to adhere to host tissue, reducing the threat of deadly infections.

The investigation, reported in the July 15 issue of the *Journal of Clinical Investigation*, focused on the bacterium *Staphylococcus aureus* and its role in infections in animal tissue. *S. aureus* is a leading cause of serious systemic (often referred to as staph) infections and abscesses.

“Our research shows that salicylic acid, a byproduct of aspirin, impacted the stress system of the bacteria and reduced its ability

to cause infection,” said lead author Dr. Ambrose Cheung, professor of microbiology and immunology at DMS.

By disrupting this stress system, aspirin reduced the bacteria's capacity to adhere to host tissue. In addition, the salicylic acid disrupted the ability of *S. aureus* to produce toxins, which the bacteria require to propagate and spread to other tissue. As a result, the animals treated with aspirin have smaller abscesses and they have fewer number of bacteria in the infection. Aspirin did not cure it, notes Cheung, but it reduced the ability of the bacteria to cause infection.



Dr. Ambrose Cheung

The *S. aureus* bacteria are also responsible for sepsis, a blood poisoning disease that strikes 750,000 people in the US annually and is the leading cause of death in America's non-coronary intensive care units. Cases of sepsis are growing in number each year and

are becoming increasingly resistant to antibiotics, making aspirin a possibly invaluable option for treatment.

“The fact that aspirin has been used for pain treatment, to reduce mortality due to heart attacks, and can possibly reduce the risks of infection is incredible,” said Cheung. “We look forward to conducting future tests with aspirin in conjunction with antibiotic therapy.”

Beta-Carotene Supplement Could Increase Cancer Risk

Smokers and drinkers who take beta-carotene supplements to help prevent cancer may actually increase their risk, a study led by Dartmouth Medical School finds. The research, conducted at Norris Cotton Cancer Center and three other centers, provides a cautionary perspective regarding the alleged cancer-fighting attributes of beta-carotene and other antioxidants. It was published in the *Journal of the National Cancer Institute*.

Dr. John A. Baron, professor of medicine at DMS, and his colleagues found that for participants who smoked cigarettes and drank more than one alcoholic drink per

day, the vitamin A precursor beta-carotene doubled the risk of recurring adenomas.

Adenomas are benign tumors that can lead to colorectal cancer. In non-smokers or non-drinkers, beta-carotene supplementation was associated with a 44 percent decrease in the risk of colorectal adenoma recurrence, compared to those who received a placebo.

“The key point of the study was the supplements had different effects, depending on the smoking and drinking habits of the subjects,” Baron said. “These findings illustrate the complexity that we face in designing safe and effective chemopreventive strategies

for any cancer. A careful mix of animal studies, epidemiology and clinical trials is needed,” he said, to continue to determine successful methods of preventing cancer.

In addition to Baron, DMS authors were Dr. Bernard Cole, Dr. Maria Grau, Dr. Robert Greenberg and Leila Mott. They point out that the alcohol and smoking habits were reported by the subjects, so there is a potential for measurement error and association with other unknown lifestyle factors. Nonetheless, Baron and his co-authors conclude that, “Supplementation [with beta-carotene] was beneficial among subjects who did not drink or smoke but, if anything, increased risk among those who drank and/or smoked.”



Dr. John Baron

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