

## In This Issue:

Hands On For DNA  
Dartmouth Promotes Cervical  
Cancer Screening and Prevention  
New Professorship Honors  
E. Elizabeth French  
DCMS Scores Again  
MedStock Rocks for CHaD

# DMS DIGEST

DARTMOUTH MEDICAL SCHOOL

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## Hands On For DNA

**DNA** took center stage when Lebanon High sophomores visited Dartmouth Medical School for discussion and demonstrations by medical school professors. More than 50 biology students and teacher Mary Maxfield participated in a pilot program spearheaded by Associate Dean for Medical Education David Nierenberg, MD, to help supplement the high school science curriculum.

Nierenberg said he became interested in building a relationship between Lebanon High School and DMS when his children took science courses there. "Public high schools with tight budgets encounter severe constraints developing laboratories to go with their science classes. It's the laboratory exercises that make science come alive for students. Gifted teachers like Ms. Maxfield are always looking for new ways to stimulate their students, while the medical school has superb teaching lab facilities that are not always in use, and superb faculty who love to teach," he said.

The visitors heard about DNA sequences, gel electrophoresis, restriction enzymes to cleave long DNA molecules into smaller pieces, and antibiotic resistance genes, topics that dovetailed with their high school biology curriculum on DNA. Connie Brinckerhof, PhD, professor of medicine and of biochemistry, began with a review of DNA structure and biochemistry, highlighting how gels and probes work to separate and identify DNA sequences. She showed an excerpt from the popular television series, X-Files, where the star agent suspected she had been infected by a virus from an alien culture. The FBI agent-scientist used a common research technique called a Southern Blot analysis to test if her cleaved DNA matched fragments prepared from the alien viral DNA.

Then Ronald Taylor, PhD, professor of microbiology and immunology, discussed bacteria and the challenge of antibiotic resistance, explaining how scientists can search for markers that indicate bacteria have integrated genes to become resistant to common antibiotics. Students moved to the teaching laboratory to observe and participate in experiments. Properly attired with safety goggles (to protect eyes against UV light) and latex gloves (to protect against lab

chemicals and pathogens), they helped pour an agar gel, loaded the gel with different digests of viral DNA, ran the gel, stained the DNA fragments of interest with an appropriate DNA probe, and looked for differences in the DNA fragments under UV light.

Assistant Superintendent Jacqui Guillette, who also accompanied the group, expressed appreciation for the opportunity DMS afforded to enrich the students' science foundation, noting that high school facilities are limited. Biology teacher Maxfield added, "This is an important component for us; students get to see state-of-the-art technology. It is extremely difficult to offer a similar experience to classes that meet for only 50 minutes each day."

Nierenberg hopes this pilot project will grow into a more substantial relationship between DMS and the science program at Lebanon High School next year, and perhaps begin to involve other neighboring school districts as well.

Lebanon High School biology students and Ronald K. Taylor, PhD, DMS professor of microbiology & immunology.

Photos by Lisa Bertrand

## Dartmouth Promotes Cervical Cancer Screening and Prevention

**F**or every four sexually active women in America, three have already been exposed to the sexually transmitted disease human papillomavirus (HPV). That means HPV affects 75 million American women, yet for many it is a silent infection without overt physical symptoms. Unfortunately, this virus assumes a multitude of shapes and sizes when it does become visible. There are over 150 different HPV types, with effects ranging from cervical cancer to hand and foot warts. HPV-associated cancers are found in the throat and mouth as well as the genital area. Despite these overwhelming statistics, HPV remains nearly anonymous among the general public.

Dartmouth Medical School physician Diane Harper, MD, MPH wants to change that. Harper, associate professor of community and family medicine and of obstetrics and gynecology, and a former MIT engineer, and her research team are working on projects to raise both awareness and prevention of HPV. Their studies may prevent millions of women from contracting HPV-related diseases like cervical cancer.

As the first step of the Dartmouth program, Harper is developing an HPV vaccine, using at least two of the cancer causing HPV types. Collaborating with industrial scientists, her goal is to provide protection against any infection with

those types of HPV, thus preventing cervical cancer. The vaccine has additional importance for young girls not yet sexually active and not yet exposed to HPV. Working with project coordinator Kazuyo Masuda, Harper hopes to enlist the participation of high school girls and college women for the vaccine study. According to Masuda, "Women who participate in this study may contribute to the health care of women, and will receive financial incentives." Those interested in learning more about the HPV vaccine can call Kazuyo Masuda at 603/650-2807.

Screening is a second important element of the Dartmouth program. Since many women unknowingly carry HPV, Harper stresses the importance of making the HPV test more accessible to women. She is designing a self-administered test for patients to use at home, and then mail to their doctors for analysis, partnering with Walter Noll, MD, professor of pathology, in the laboratory detection of HPV from the self-sampled devices.

"This method allows women who wouldn't otherwise be examined to receive the test. A lot of women are uncomfortable getting speculum exams and this eliminates much of



Diane M. Harper, MD

Photo courtesy of Dartmouth College Public Affairs Office

the discomfort since it is self-administered," Harper states. She is also investigating a tampon as a combined self-Pap smear and HPV test since, "Women are comfortable using a tampon and it provides similar HPV data to the swabs."

Self-sampling is now possible due to an advancement in the traditional Pap smear: liquid cytology. In liquid cytology, murky agents such as blood and mucous can be removed, leaving the cells more lucid for evaluation and rendering better results with increased information. Already liquid cytology has replaced 40% of traditional Pap smears, and Harper predicts that percentage will double within the next five years. The liquid Pap smear can test for the high-risk types of HPV, eliminating the need for additional tests, and increasing chances of pre-screening for harmful cancers. Jorge Gonzalez, MD, assistant professor of pathology, has instituted the liquid cytology method for Pap smear collection at DHMC.

Early detection of precursor lesions is the third element of Dartmouth's cervical cancer prevention. Once a patient receives an abnormal Pap result, the next step is colposcopy to examine the cervix under illuminated magnification using

acetic acid. However, colposcopy results are only correct 75% of the time due to the wide variation and inaccuracy of interpreting the changes, according to Harper, who is among less than 100 international experts in colposcopy. Working with Brian Pogue of the Thayer School of Engineering and Mary-Ann Mycek of the Physics Department, as well as a medical technology company, Harper instead supports the use of clearer biomarkers such as optical pattern scans or spectral signatures that discriminate between diseased and normal tissue. Spectral imaging is noninvasive for the patient, and it provides digital measurements at every pixel of an image in order to pinpoint any abnormalities. Spectral scans, the forefront of non-invasive diagnostic techniques, use many measures, including fluorescent and white light backscatter, to provide images that indicate abnormal tissue. Dartmouth is one of three sites in the world developing these scans for cervical cancer and its precursors.

In exploring the connections between HPV and cervical cancer, Harper is analyzing the cost effectiveness of improved screening and examining how advances will affect the quality of life for a woman with an abnormal Pap smear. With Anna Tosteson, ScD, associate professor of community and family medicine, she has gathered data on how false positive Pap smears *Continued on p. 2*