Initially, most medical students may not envision themselves working with leprosy patients in Egypt or traveling to Iran to determine the health needs of women. Yet, in an era of global health awareness and enhanced cultural sensitivity in patient care, more students are interested in supplementing their classroom education with first-hand medical experience outside the US.

Through a partnership between the Dartmouth International Health Group (DIHG) and the John Sloan Dickey Center for International Understanding at Dartmouth College, DMS students have the opportunity to acquire new insight on the dire health conditions that exist in countries around the world.

“The headlines may not be as prominent or attention-getting as war and violence,” said Dickey Center Director Kenneth Yalowitz, “but the long-term effects can be just as devastating, or even more.” With that in mind, the DIHG-Dickey Fellowships have sent more than 50 DMS students to over 20 different countries and are now looking to expand on this success in the near future.

“International exchange programs provide a wonderful opportunity for medical students to get exposed to community development,” said Dr. Dean Seibert, associate professor of medicine, in a recent presentation on his medical volunteerism in Honduras, Kosovo and Liberia.

Student fellows have completed an impressive array of projects in countries such as Swaziland, Russia, India, Slovenia and Cuba. Their work ranges from implementing new strategies to prevent cardiovascular disease in a Maori tribe in New Zealand to investigating the social challenges associated with malnutrition during pregnancy in Gambia.

The cultural immersions last a minimum of four weeks, the summer between students’ first and second years or during their fourth year. Over that period, DIHG fellows are personally involved with surmounting the health care hurdles prevalent in underdeveloped countries. Michael Cooley became frustrated at the lack of infrastructure in Ecuador where he helped communities record data on their patient populations. “I am much more aware of the obstacles that geography, poverty and politics play in preventing basic and inexpensive services from being provided to populations.” John Raser had a similar epiphany in Honduras where he worked at a rural clinic and promoted environmental public health initiatives. “It was remarkable to see how a small amount of resources can make a huge difference in a resource-poor area,” he said.

After working with Kosovar students who attended medical classes, Jennifer Keller noticed that there is an element of taking things for granted at DMS. “I realized the resources and education at DMS was not a right, but a privilege,” said Keller, now an anesthesiologist at DHMC. Other students made similar observations and are currently working to share the comparatively vast resources that a US education provides. JP Dedam’s efforts compiling data for his nutritional survey project in Nicaragua did not end upon his return. “The results from my survey found that people living in rural areas had no access to antibiotics and antiparasitic drugs, which is causing chronic malnutrition by untreated infection.” Dedam is helping on a new medical supplies collection program with several other medical students.

Although most students must travel thousands of miles, others can return home to accomplish their projects. Rodwell Mabaera decided to gather data on HIV patients in rural areas from his native Zimbabwe. “I am more determined to make my peers aware of what’s going on out there; that people wake up to the reality of AIDS each morning, that the HIV/AIDS figures have faces, places and communities attached to them.” Despite the deteriorating scenario in Zimbabwe, Mabaera plans on returning to continue this work after he obtains his degree.

The powerful learning experiences of the DIHG-Dickey Fellows have helped renew efforts to expand this and other international programs. A group of faculty from the College, DMS, Thayer and Tuck schools have recently formed a steering committee to examine and plan for new initiatives in global health at Dartmouth. One of the committee’s goals is to expose more students to the power of a cultural immersion. In reflecting on the impact of her trip to Zambia to care for AIDS patients, Shannon Lucas concluded that, “Once you open the door to an international experience like this, it can change your health care perspective for life.”
Deans Column

Good work. The term can be applied to much we do at DMS, whether in Hanover, Lebanon or even Kosovo. By examining the idea and impact of “good work,” we put ourselves in a position to take even more advantage of our efforts. I have invited Professor Howard Gardner, a world-renowned cognitive psychologist, educator and scholar from Harvard University to discuss his good work concept and how it applies to a life in medicine. The conference, “Good Work: Where Excellence and Ethics Meet,” will be Saturday, March 13 in Auditoriums E and F from 8 a.m. to 12:15 p.m.

Dr. Gardner has written about “good work” in many professions and has likened this concept to the “flow state” – when tasks and skills align to produce a fulfilling work state which counteracts burnout and cynicism and promotes well-being.

After Dr. Gardner’s talk, a Dartmouth panel will discuss ways to make more of our work “good work.” We’ll hear from: US Judge Mark Wolf, president of the Albert Schweitzer Fellowship program, which Dr. Gardner feels is an exceptional model to help socialize young professionals into a life of good work; James Strickler on our exchange program with Kosovo; Stephen Plume on the Northern New England Cardiovascular Disease Project that is improving the outcomes of cardiac surgery in our region; Gerald O’Connor on the progress of the Northern New England Cystic Fibrosis Consortium; Kathleen Allden, a human rights advocate, on working with refugees to improve their health care; Joyce DeLeo on the biology of pain and her work with young investigators; and DMS student Gary Maslow who has designed and implemented numerous programs for pediatrics and cancer patients. We will then elicit other stories of good work from our colleagues.

This should be an interesting session and I hope you will plan to be there so we can celebrate the good work we all do here.

Big Roles for Small RNA Molecules

What a difference a decade makes! Just over 10 years ago DMS geneticist Victor Ambros, PhD, discovered a new RNA molecule, surprising in its ultra small size and unconventional activity. Today these tiny RNAs appear abundant and varied.

Unlike their larger, better known messenger RNA relatives, they do not code for proteins. Yet the potential of these short nucleotide chains in regulating animal development and behavior is far reaching, he reported at the American Association for the Advancement of Science (AAAS) annual meeting February 15 in Seattle.

The finding of that first little RNA (ribonucleic acid) which Ambros, professor of genetics, Rosalind C. Lee, a research associate, along with a Harvard colleague, identified in a microscopic roundworm, was celebrated in the January 23 anniversary issue of Cell, which reviewed influential papers it published in its 30-year history.

Since that 1993 report, strides in technology have enabled scientists to document a panoply of genes for diverse mini RNAs. In a symposium at the 2004 annual AAAS meeting, Ambros highlighted work that continues to shed light on these modern RNAs and the critical roles they play in the expression of genetic information.

His recent studies of one class, called micro or miRNA, in the C. elegans worm, indicate that miRNAs function redundantly, meaning that miRNAs produced from different genes combine activity to regulate a common target. “In some cases one miRNA gene will become active at a certain time in development of the worm, then through a series of steps another miRNA becomes activated,” he explained.

With its relatively simple genetic apparatus, C. elegans is a model study organism. The findings, said Ambros, illustrate principles that are probably applicable to all miRNAs: “That different miRNAs are collaborating to regulate common targets and that miRNAs will function in developmental control pathways to control sequences of events in tissues (where there is) extensive differentiation.”

Another small RNA family is the small interfering RNA (siRNA) associated with gene silencing, where a gene essentially cancels itself by producing a double stranded RNA product. That silencing, or siRNA process, is distinct from the miRNA–based gene regulation where a gene is devoted to making a miRNA that then silences other genes to which it’s partially complementary. “In the case of a micro RNA the gene is acting in a developmental context as part of the normal regulatory circuitry,” Ambros explained.

In normal worms hundreds of genes in the germ line—the cells with the traits inherited by each generation—are silenced. Ambros speculated these are genes whose level needs to be controlled and it’s important for the biology of the germ line.

“Development of the germ line seems to involve widespread suppression of gene expression through this small RNA silencing mechanism. It is auto silencing, “Ambros said. “A diverse set of genes seems to be undergoing auto silencing to keep their own levels of expression low.”

His team has found siRNAs that match normal genes. “This means that they’re produced in the worms normally and are the agents for implementing the auto silencing. The small RNA is generated probably by the production of a double stranded RNA from the gene itself; so it’s a negative feedback mechanism.”

The big picture, Ambros said, stems from the stories of these little RNAs. With so many, for example, just in C. elegans, acting together or sequentially, many combinations can come into play in broad physiological and developmental contexts with considerable potential for gene regulation. Scientists can focus on these new gene families to answer key questions about heredity and development. The challenges escalate as the analyses become more complex, and the opportunities and answers become ever more exciting and wide ranging.
Models Target Antibiotic-Resistant Diseases

New biochemical studies may hold clues to more powerful malaria and pneumonia treatments that could save millions of lives worldwide. DMS research exploring why enzymes in organisms that cause pneumonia and malaria are becoming increasingly resistant to antibiotics could open a window to testing a new generation of drugs to combat these widespread diseases.

Malaria and pneumonia are responsible for more than 2 million deaths a year worldwide, said Dr. Bernard Trumpower, professor of biochemistry, who headed the study. His team used genetically modified yeast enzymes to pinpoint mutations responsible for antibiotic resistance of Pneumocystis jirovecii, which causes pneumonia that is the most serious and prevalent AIDS-associated opportunistic infection and a threat to other immuno-compromised patients.

Appearing in the January 23 Journal of Biological Chemistry, the study examines the mutations responsible for the diseases’ tolerance toward atovaquone (ATV), a drug that inhibits a respiratory enzyme called the cytochrome b$_{5}$ complex, essential for the pathogen’s survival. Lead author, Dr. Jacques Kessl, a research associate, said the study addresses evidence that malaria and pneumonia pathogens are increasing resistance to the ATV prescribed for the diseases by developing mutations that prevent the drug from acting on the b$_{5}$ complex.

“We were able to isolate the genetic mutations that enable the pathogens to resist the drug when it is introduced to our yeast samples,” said Trumpower. “As the genetically modified yeast strains now display atovaquone resistance identical to that found in pneumocystis, these yeast can be used to design new drugs to make the appearance of resistance more unlikely.”

The study builds on research in Trumpower’s lab using baker’s yeast as a surrogate disease model. Yeast can be manufactured in large quantities and easily modified to take on the qualities of more dangerous pathogens. The researchers genetically transferred the cytochrome b mutations from the ATV-resistant pneumocystis into the yeast which acquired similar resistance to ATV.

Additionally, the team used a computer program to construct molecular models of the enzymes. “We can now visualize the different mutations in three dimensions to predict how the enzyme will react to different changes,” said co-author Benjamin Lange, a research assistant. Other co-authors include colleagues from University of North Carolina and the Wolfson Institute for Biomedical Research in London.

Teachers Okay on Illnesses

Teachers have an overall positive attitude about having children with chronic illnesses in their classrooms, report Dartmouth researchers in the January Archives of Pediatrics & Adolescent Medicine.

With improved treatments and survival, children with complex chronic health conditions are likely to attend their local schools and spend most of their days in the school system. Previously, little was known about the educators’ concerns.

The researchers, led by Dr. Ardis Olson, associate professor of pediatrics and of community and family medicine, surveyed 384 school professionals (including 241 classroom teachers) in 23 elementary schools in six New Hampshire and Vermont communities served by DHMC. They measured the impact of having a child in the classroom with AIDS, asthma, congenital heart disease, diabetes mellitus, epilepsy and leukemia.

Educators responded to 13 statements about the academic impact on the child and on peers, personal risk or liability, and extra teacher time and demands. They felt AIDS and epilepsy had the most impact and asthma the least. Also, 53 percent were concerned about an emergency in the classroom and 27 percent about legal liability.

“Overall school professionals have positive attitudes about children with chronic health conditions in the classroom, but concerns about specific diseases and issues exist,” the authors conclude. “…. Health care professionals can help by providing educators with appropriate information about the risk and functional impact of childhood chronic health conditions.” Study co-authors are Drs. A. Blair Seidler, David Goodman, Richard Nordgren and Susan Gaelic.

Outpatient Settings Differ

Medical schools teach outpatient care through clerkships at varied ambulatory settings, such as academic medical center-based clinics (AMCs), affiliated residency teaching sites (ARTs) and community-based practices (CBPs). Their differences should be taken into account, report DMS researchers in the January Academic Medicine.

“Medical students may perform all of their ambulatory clerkships in one of these settings, and therefore may have missed crucial learning experiences, as we found that AMCs, ARTs and CBPs differ significantly in the patient symptoms and problems seen as well as the medical procedures and counseling skills that medical students encounter,” said lead researcher Dr. Patricia Carney, associate professor of community and family medicine.

Third-year DMS students collected data, using handheld computers, during family medicine clerkships. Documenting over 9,000 student/patient/preceptor encounters, they recorded information on symptoms, medical conditions, clinical activities (counseling and procedures) and the educational process.

The researchers found distinct differences by training setting. For example, symptoms occurred least frequently in ARTs; counseling skills were used most often in AMCs; general procedures were performed most often in CBPs. In AMCs, students were likely to observe preceptors conduct histories and physicals or do them together; in ARTs they more often did these independently. Students received more teaching about disease in AMCs, and more about patient management in ARTs. Students in ARTs and CBPs tended to work more independently.

The researchers caution that the findings are limited. Coauthors are Drs. David Nierenberg, Catherine Pipas, M. Scottie Eliassen and Stephen Genereaux.