

Kosovo Project Launched

Kosovo medical school guests met with DMS leaders during their January visit. From left, former Dean James Strickler, Kosovo student Valbon Ajazaj, DMS Dean John Baldwin, and Dean Mazllum Belegu of Pristina University Medical School.



Photography by: Mark Washburn

Representatives from Kosovo's medical school visited Dartmouth Medical School through a cross-cultural outreach program to help the Kosovars rebuild their medical education and health care systems. Mazllum Belegu, MD, PhD, dean of the Pristina University Medical School, and medical students Melihate Mustafa and Valbon Ajazaj came to Hanover last month to launch the DMS Kosovo project. They spent a week meeting with Dartmouth medical faculty and students to discuss teaching, patient care and research.

Kosovo's health care problems are complex and challenging, Belegu explained. When the Serbian government expelled ethnic Albanian Kosovars from the university a decade ago, dual education systems were created. More than 400 doctors were fired from their faculty and hospital positions, said Belegu. "We had a parallel medical school in private houses outside the university and clinic buildings." The effort proved formidable; resources were scarce and hospital training was impossible.

Last summer the Albanian community cleaned up damaged buildings and reopened the University of Pristina. "Now our doctors are back in the hospital, but after 10 years we have lost many skills. The health situation is bad, and we have a lot to do just to improve conditions for our patients as well as for our students," said Belegu. The medical school has been working to provide facilities and equipment, reinstate instruction and training, and update knowledge and expertise. "As we were trying to reestablish our medical school, Dartmouth invited us to see how they are organized, and for that we are thankful. It has been busy but very stimulating. Everyone is friendly and helpful."

DMS Dean John Baldwin, MD, established the Dartmouth Medical School Kosovo project after he traveled to Pristina last summer at the invitation of the International Rescue Committee (IRC) to explore how Dartmouth could help revitalize Kosovo's only medical school and hospital. Project head is former DMS Dean James Strickler, MD, who co-chairs the board of directors of the IRC.

"The IRC has a strong presence in Kosovo, and it has facilitated the liaison with DMS," said Strickler, professor of community and family medicine, emeritus. "This is the beginning, we hope, of a long-term relationship."

Through the project, supported by a gift from Edwin C. Cohen's Blessing Way Foundation of New York, DMS medical faculty will provide expertise to help develop curriculum guidelines and other opportunities for assistance. Transportation for one of the Kosovar students was underwritten by Ohiyesa, a privately funded foundation founded by Dean Seibert, MD, associate professor of medicine, emeritus, who is also active in health relief work. The reward of this project, said Seibert, "is the real sense of hope and energy because people are getting their lives back together."

Belegu said he looks forward to exchanges at DMS to benefit faculty and students. Among the pressing needs he outlined were equipment for the university hospitals and preclinical facilities, fellowships for young staff to do research or refresh their clinical knowledge, and professionals to help improve basic instruction and clinical work. Already the Hanover Lions Club has helped fund an effort with the Cold Regions Research and Engineering Laboratory to send to Kosovo orthopedic and other medical supplies that Seibert gathered.

Strickler headed the medical school team that planned the week's agenda for the Kosovo visitors. In addition to focusing on primary care, psychiatry, computer and library services, the discussion encompassed admissions, undergraduate, graduate and continuing medical education. The guests toured the campus, the medical school and Dartmouth-Hitchcock Medical Center and met with medical center and college leaders as well.

"We thank Dartmouth Medical School and the IRC for the chance to enjoy your facilities and learn how medical students are organized," said Valbon Ajazaj, in his last year of medical school. "I hope your medical students will have an opportunity to visit us so they can see another world and a different culture."

Research Offers Clues to Antimicrobials

The race to stay ahead of bacteria that develop resistance to frequently used antibiotics may be paying off. Dartmouth Medical School (DMS) researchers have discovered how to block a pathway many bacteria use to infect organisms.

Ronald Taylor, PhD, professor of microbiology, and Christian LaPointe, a graduate student, have found a way to inhibit the enzyme that many types of bacteria need to infect and damage a variety of hosts, from plants to humans. Their work, reported in the January 14 issue of the *Journal of Biological Chemistry*, could provide a foundation for developing new agents to combat bacterial infections.

"In this age of antibiotics, people have come to expect a ready cure for the majority of common ailments caused by infectious microbes, from acne to ear aches. However, the microbes have been fighting back, and increasing numbers are becoming resistant to all available antibiotics at an alarming rate," says Taylor. "These recent findings may advance screening for additional compounds that can be developed into novel therapeutic or prophylactic antimicrobial agents, at a time when many of the mainstay antibiotics are no longer useful due to the development of resistant bacteria."

Taylor's laboratory has delineated mechanisms for a common bacterial enzyme or protease that bacteria need to secrete their toxins or other virulent factors that cause damage. Treating bacteria with compounds to prevent protease function could augment therapies against certain infectious diseases. For example, protease inhibitors have been used with success to inhibit replication of the Human Immunodeficiency Virus (HIV-1) in AIDS.

Their work, says Taylor, might be a useful adjunct to cystic fibrosis treatment by inhibiting the growth of *Pseudomonas* that colonizes patients' lungs and is notable for antibiotic resistance. It might also lead to useful approaches against infections such as meningitis by providing a way to clear bacteria without the potential complication of toxic shock associated with conventional treatments.

The researchers have identified the active site and biochemical pathway for type four prepilin peptidase (TFPP), a protease that cleaves the precursor form of pilin and related proteins prior to their secretion by bacteria. Pilins are protein building block subunits of hair-like fibers called pili that protrude from the bacterial surface and allow pathogenic bacteria to colonize on or in their hosts. Related proteins, termed pilin-like proteins, form channels across the bacterial membrane to facilitate the movement of toxins or other virulent factors the bacteria produce. If the TFPP function is absent, neither the pili nor the secretion apparatus forms, and pathogenic bacteria cannot spread or cause disease.

The Dartmouth investigators developed an assay to monitor TFPP activity in the laboratory and used the assay to identify a compound that inhibited the

activity. They tested TFPP activity in the *Vibrio cholerae* bacterium, which Taylor's laboratory studies. The organism causes cholera, a severe life-threatening diarrheal disease spread by ingestion of contaminated water or food and a large problem in many areas of the world. The recent findings could also lead to useful therapies in conjunction with the primary cholera treatment that relies heavily on rehydrating patients.

V. cholerae bacteria secrete two major virulent factors that are both needed to cause disease. One is cholera toxin (CT), which enters intestinal cells of infected individuals, causing copious fluid and electrolyte loss that leads to rapid dehydration serious enough to be fatal. The second factor is the toxin coregulated pilus (TCP) that allows the bacterium to colonize the human intestine. Without colonization, toxin production and delivery to the host cannot occur.

Each factor utilizes a different TFPP member during transport outside the bacterium, and both of these corresponding TFPPs, termed VcplD for toxin secretion and TcpJ for pilin secretion, were first discovered in Taylor's laboratory. These two proteases have served as model molecules to work out the mechanisms of action and inhibition for TFPPs that have been identified in at least 50 bacterial species.



Ron Taylor, PhD

Dartmouth Medical School Research Awards

New and competing awards to DMS, totalled \$2,899,369, for December. This brings the half-year total for FY2000 to \$38,667,420, up from \$35,646,971 for the same period last year.

Biochemistry

D. Compton	American Cancer Society	Restructuring the Mammalian Cell Nucleus during Mitosis
J. Dunlap	Pfizer Inc.	Identifying the Molecular Basis of Mammalian Circadian Rhythms
B. Trumpower	National Institute of General Medical Sciences	Mechanism of Respiration and Energy Transduction

Community & Family Medicine

P. Batalden	Hartford Foundation	Developing and Operating a Collaborative Program to Foster Academic Health Professional Leadership in Geriatrics
J. Wasson	Institute of Healthcare Improvement	Idealized Design of Clinical Office Practices

Pediatrics

W. Edwards	Vermont Oxford Network, Inc.	Effect of Aquaphor Emollient Ointment
E. Frank	State of New Hampshire	Bicycle Safety Programs
	State of NH-HSA	Buckle Up New Hampshire 2000
E. Larsen	Pediatric Oncology Group	Pediatric Oncology Group Per Case Reimbursement Contract
N. Tracy	University of NH	Promoting Early Identification and Support for Families of Young Children: The Early Connections Project