Dartmouth Medical School

DIGEST

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Neuroscience Center Forges New Links

The focus of the new Neuroscience Center at Dartmouth (NCD) is a quest of neuroscientists worldwide: understanding the complexity of the human brain, its processes and its structure. The center is constructed around a "triad" of neuroscience study: cognitive neuroscience, clinical neuroscience and molecular/cellular/systems neuroscience.

Research interests within the three areas of the triad are varied and cover a broad range of disciplines that include neurophysiology, neuroimmunology, behavioral neurology, psychopharmacology, neuro-oncology, neuroimaging and neuropsychology. The NCD provides a mechanism to bring together researchers, clinicians and educators from different departments and disciplines.

Officially established in July 2002, with a diverse advisory board, the NCD will forge a new link among Dartmouth College, Dartmouth Medical School and Dartmouth-Hitchcock Medical Center, integrating more than 90 faculty from 15 different departments.

"By collecting our various neuroscience experts under one umbrella," said Dr. Joyce DeLeo, associate professor of anesthesiology and of pharmacology and toxicology at Dartmouth Medical School and interim director of the NCD, "it will help focus our research and educational goals. Students interested in this field – at the undergraduate, graduate and post-doctoral levels – will benefit from this experience of [having] leading neuroscientists as teachers and mentors."

Showcasing part of a poster presentation at Neuroscience Day, from left, Flobert Y. Tanga, research assistant in anesthesiology, Vivianne Tawfik, MD/PhD student in pharmacology and toxicology and Dr. Raghavendra Vasudeva, research associate in anesthesiology.

At the 17th Annual Neuroscience Day at Dartmouth on January 31, Dr. Ethan Dmitrovsky, acting dean, said that the center "permits Dartmouth to expand its reach into neuroscience," an especially promising field since it explores the essential question of what it is that makes us human.

The daylong event provided an opportunity to learn more about the basic and clinical neuroscience research at Dartmouth and the people contributing. The two poster sessions totaled over 60 presentations that included a broad range of neuroscience related studies being conducted by faculty, postdoctoral researchers, graduate and undergraduate students, both from the College of Arts and Sciences and from DMS. A special guest lecture, "Neuroinformatics: A New Tool for Neuroscientists," was presented by Dr. Floyd E. Bloom, chair of neuropharmacology at the Scripps Research Institute. Ortho-NcNeil Pharmaceutical, Inc. provided support to the NCD for these activities, according to DeLeo, in their commitment to encourage, develop and help fund educational initiatives within the neurosciences.

Photos by Alexios N. Monopolis, DC '03

At Neuroscience Day, from left, Dr. Joyce A. DeLeo; Dr. Floyd E. Bloom, guest lecturer; Dr. Ethan Dmitrovsky and Dr. David W. Roberts.

Dartmouth's size allows the NCD to foster enhanced interaction and collaboration among all the neuroscientists, an approach that capitalizes on the strong interdisciplinary spirit here. NCD members are working with the advisory board to pursue funding opportunities and to coordinate their research projects for a cohesive program. The long-term goal is to produce a multifaceted entity that attracts the best minds and serves as a leader in the scientific community.

"The Neuroscience Center at Dartmouth will serve as the institution's focal point for people who have common but non-parallel interests in the vast arena of neuroscience," said Dr. William Hickey, senior associate dean for academic affairs, the Constantine and Joyce Hampers Professor of Pathology and NCD advisory board member. "Dartmouth will now have a defined central forum for the clinical, cognitive, psychological and basic science faculty. This will generate broader understanding and permit new areas of synergy to emerge. The center will also serve as a community for this particular group of scientists, and allow them to position themselves against the national background of the broad area of neuroscience. It will put Dartmouth on the map as having serious scientific activities in neuroscience. That will help us with everything from education to fund-raising to our relationships with the pharmaceutical industry."

New neuroscience courses are being developed at both the undergraduate and graduate level. "We really need to enhance the current courses – both laboratory as well as didactic," said DeLeo, "because what's offered right now focuses on cognitive sciences or psychological brain sciences and not on the neuroscience that I was trained in."

To that end, the NCD will spearhead several new undergraduate courses, perhaps eventually leading to a neuroscience major at Dartmouth. In addition, National Science Foundation curriculum development proposals are being pursued to facilitate graduate training and course development at the undergraduate and graduate level. Courses being considered include a new neuroscience lab course, clinical correlations using functional magnetic resonance imaging,

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Deans Column


Jon Gilbert Fox

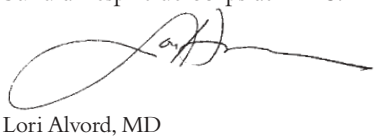
It is my pleasure to host this feature, and in this issue I'll highlight some new features of two departments.

Student Affairs: Last year, a program to support physical, mental and emotional wellness was started for medical students. Two DMS soccer teams were assisted with funding, and sports equipment is now available for students. Other initiatives included cooking clubs, massage therapy training, yoga classes and coffeehouses where students showcased their talents in the performing arts.

Multicultural Affairs: We are extremely pleased to welcome Shawn O'Leary to fill the position of director of multicultural affairs. An Ojibway tribal member, Shawn was most recently at the University of Maine. In addition, DMS and Dartmouth College worked together to bring Tommy Woon to the college as associate dean for diversity and pluralism. At Stanford, he developed a stress reduction program for medical students and will lead similar efforts here.

Students are working with Sharon Elementary School in Sharon, VT to teach children about a variety of cultures. They also hosted a film/forum on the Tuskeegee Syphilis Study and are beginning a variety of cultural competency initiatives. In a collaborative effort with the Dickey Center for International Understanding at Dartmouth College and the Bildner Endowment, DMS was pleased to host Dr. Roscoe Brown, a motivational speaker and a commander of the famed Tuskeegee airmen. With the suggestion and funding from Acting Dean Ethan Dmitrovsky, we have started a program to bring minority alumni to DMS to give grand rounds and serve as role models and mentors for students.

With the new programs and our incredible students, these departments continue to enhance support to students, and build an esprit de corps at DMS!



Lori Alvord, MD
Associate Dean of Student Affairs
and Multicultural Affairs
Assistant Professor of Surgery and of Psychiatry

DMS Advances Diabetes Work

DMS researchers exploring aspects of diabetes and its complications are helping to pave the way for improved understanding and treatment of this multifaceted disease.

Dr. Paul Beisswenger, professor of medicine, recently received two new grants from the National Institutes of Health for diabetes research and teaching to bridge the clinical and basic sciences and provide a fertile training ground for new investigators. His laboratory combines human populations studies with powerful analytic laboratory techniques to address questions of diabetic complications. The focus is on determining the role of enzymatic control of non-enzymatic glycation – spontaneous chemical reactions between sugars (such as glucose) and proteins – in the cellular and tissue damage associated with diabetes. Beisswenger studies factors that regulate toxic dicarbonyl compounds and their resultant advanced glycation endproducts (AGEs), which are produced in excess in diabetes and play an important role in the development of diabetic complications, and is at the forefront of the new research area of enzymatic deglycation.

One of the new grants will help Beisswenger expand his clinical research program and mentor younger investigators. The other will support a population-based study to determine risk factors for diabetic kidney disease by broadly examining family history, ethnic groups and lifestyle. Diabetes remains the leading cause of end stage renal disease in the US, yet it is still a mystery why some diabetics get kidney failure and some do not.

Now another recent DMS study published in the *American Journal of Renal Physiology* in January moves a step closer toward understanding the early pathological changes in diabetic kidney disease. The work could help identify new clinical markers for its detection, hopefully producing new therapeutic strategies to diminish these changes and reduce the progression to end-stage renal disease.

Dr. Frank Gesek, research assistant professor of pharmacology and toxicology, reported how urinary tumor necrosis factor (TNF) that is elevated during diabetes contributes to sodium retention and renal enlargement during the progression of diabetic kidney disease. He and his colleagues found that administration of a soluble TNF antagonist to diabetic rats reduces urinary TNF excretion and prevents sodium retention and renal enlargement. They concluded that urinary TNF contributes to early diabetic kidney disease and may serve as a valuable diagnostic marker. In addition, inhibition of TNF during diabetes may help to alleviate early pathological changes in diabetic nephropathy. Other DMS authors were Keith DiPetrillo and Bonita Coutermarsh, both of pharmacology and toxicology.

In other research, a DMS team led by Dr. Gustav Lienhard, professor of biochemistry, collaborated with colleagues from Harvard Medical School to develop a novel mouse model of lipoatrophic diabetes, highlighting leptin therapy as a successful tool to combat this rare form of type II diabetes. Lipoatrophic diabetes mellitus is marked by a lack of subcutaneous fat (lipoatrophy), high blood sugar (hyperglycemia) and high blood insulin (hyperinsulinemia). Although high levels of insulin accumulate in the bloodstream, patients are insulin resistant and glucose is not efficiently delivered to their body's cells, eventually resulting in severe eye, kidney, nerve and cardiovascular problems.

The disease is thought to have a strong genetic component and the new model, deficient in certain genes for insulin receptor substrate (IRS) proteins, could help scientists gain valuable insight into its genetic pathway. The researchers bred "double knockout mice," so called because they lack two specific genes. These mice had no fat tissue and became diabetic. Leptin, a protein secreted by fat cells, reversed the diabetes, they reported in the December 15, 2002 issue of *Genes & Development*.

Mice with a combined deficiency of IRS-1 and IRS-3, like humans with lipoatrophic diabetes, developed early onset severe lipoatrophy, hyperglycemia, hyperinsulinemia and insulin resistance. Since humans do not have a functional copy of the IRS-3 gene, IRS-1 may play a more significant role in human adipogenesis (fat development) and insulin homeostasis. The researchers completely reversed the hyperglycemia and hyperinsulinemia of IRS-1/3 double knockout mice within six days through administration of leptin, suggesting a role for leptin in treating lipoatrophic diabetes. Other DMS authors included Barbara Crute and Susanna Keller, both formerly of biochemistry.

Volunteers Bring Medical Care to Nicaragua

Medical school students and faculty joined Dartmouth undergraduates to help bring health care to rural Nicaragua in December through a two-week cross cultural service project of the college's Tucker Foundation.

Based in Siuna, the central town of Nicaragua's remote North Atlantic region, the Dartmouth medical team provided treatment and health education to residents throughout the area as part of a partnership led by Dr. Stuart Lord, dean of the Tucker Foundation, and now in its second year. They saw patients at the government sponsored Casa Mujeres, a high volume clinic serving mainly women and families. It is staffed with a Nicaraguan nurse and doctor and has the area's best-stocked pharmacy.

"We observed and delivered health care in a dramatically different environment," said Dr. William Young, associate professor of obstetrics and gynecology, a member of the Dartmouth medical contingent both years. "It was an opportunity for the medical students to spread their wings. They were truly treated as a doctor; people accepted their credentials and put trust in them. Faculty were available for advice, but gave the students freedom. They were almost running their own clinics." DMS student Sarah Conley, '03, agreed. "Medically for the first time, we were able to act as clinicians, yet have backup if needed."

The medical team also set up a mobile clinic in Yaoya, a remote area that lacked medical facilities. There, in a school, the kindergarten classroom became makeshift exam rooms with sheets and garbage bags hung with clothespins for curtains, child-size furniture for examination tables and head lamps worn by volunteers for light. Team members provided medical care and immunizations, conducted education programs and made house calls. Villagers traveled for up to two days, by some accounts, along rutted roads in buses or trucks, on horseback or foot to receive care or take a class.

Undergraduate volunteers assisted the medical students, learning as they went along to take histories and blood pressure and dispense medications. All together they served an estimated 700 patients. Working with the undergraduates, Conley noted, was a real connection to the college. Added

DMS student Jason Grassbaugh uses a demonstration doll.

Photos by Dr. William Young

Dr. William Young teaches birth techniques.

DMS students Paige Wickner (left) and Sarah Conley welcomed a newborn held by the proud grandmother and birth attendant.

DMS student Paige Wickner, '03, "The college volunteers made it all run smoothly. Moreover, showing them how to help with common procedures provided another kind of teaching experience."

The Dartmouth team built on a new cervical cancer prevention program and provided screening for many patients. "For many women this was their first pelvic exam. We ran assembly line Pap tests so that all the patients could be seen," said Young. Slides were prepared and shipped to Managua to be read. Women were notified via their local radio station when and where they could report for results in their area.

Rewards came in many ways. "Often we were the first point for any type of contact with health care; some people wanted to come and see the doctor and be reassured," Conley said. "We experienced the limitations of rural medicine and the challenge of how to do more. We sent a sick child with malaria to the hospital. Sometimes all we could give them was Tylenol and a bar of soap, and send them on their way."

"We were delivering medical care with few diagnostic tools and a limited formulary," said Wickner, who also learned the art of improvisation. "We used plastic baggies for gloves (until more arrived) and helped relocate a dislocated shoulder using cervical dilators as counter balance weights. It was an opportunity to see a wide range of patients with routine as well as rare problems not often encountered in the Upper Valley."

Most interesting, said Young, was working with traditional birth attendants or midwives, parteras in Spanish. All they bring to attend a birth is a blanket for sleeping on the floor while the mother is in labor.

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neuropathology, neuropharmacology, neurophysiology and genetics/behavior.

The NCD has been raising its visibility since its inception. It has established a neuroscience seminar series comprised of both internal and external lecturers and has assumed organizational oversight for future Neuroscience Day activities. As the neuroscience training program grows and establishes a record, the NCD is envisioned to become the core of a degree granting program in the neurosciences, producing and disseminating new knowledge in this exponentially growing field, educating and training the next generation of neuroscientists and fostering the spirit of science and multidisciplinary collaborations.

Members of the NCD advisory board besides DeLeo and Hickey include Dr. Alan Green, Raymond Sobel professor and chair of psychiatry; Dr. Gregory Holmes, professor of medicine and head of neurology; Dr. Robert Maue, professor of physiology and of biochemistry; Dr. David W. Roberts, professor of surgery (neurosurgery); and Dr. Surachai Supattapone, assistant professor of biochemistry and of medicine; as well as Dartmouth College faculty Dr. Scott Grafton, John Sloan Dickey Third Century Professor of Psychological and Brain Sciences and director of the Brain Imaging Center and Dr. Michael Gazzaniga, David T. McLaughlin Distinguished Professor of Psychological and Brain Sciences, dean of the Faculty of Arts and Sciences, and director of the Center for Cognitive Neuroscience.

– Tanisha Keshava, Dartmouth College '05

⋆ Further information about the NCD is available at their website: http://www.dartmouth.edu/dms/ncd

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Otherwise, they use what is available: dental floss to tie off the umbilical cord or the ubiquitous machete to cut it. The DMS team improvised its own birth kits stocked with soap, string for tying, razor blades and scissors for cutting and a bulb syringe to suction the baby. While there Young arranged for the midwives to receive cord clamps.

A flaming umbilical cord provided one unforgettable emergency home delivery experience for Young, Wickner and Conley. After delivering a retained placenta, the Dartmouth team asked the traditional birth attendant to show them how she tied and cut the cord, Young recalled. "What followed was unusual and remarkable, and provided some drama. The cord was tied with dental floss and cut. Camphor was applied to the end attached to the infant and [the cord was] set aflame. This veritable birthday candle was spectacular in the darkness of the little home."

Fourth-year medical students with facility in Spanish were targeted for their clinical ability. Future programs may include clinics for the elderly or children, expanded health teaching and patient education projects for other student levels that focus on public health and have greater enduring community benefits, said Young. "For example, we can treat parasites now, but making water potable and building sanitation systems will provide a long lasting benefit."

Meanwhile, after two years Dartmouth has made a contribution. "We brought people a sense of hope for the future," said Wickner, "giving them a sign that someone is thinking about them and cares."

Other DMS participants included: Dr. Dean Seibert, associate professor of medicine, Dr. E. Robert Greenberg, professor of community and family medicine, Alice Werbel, instructor of community and family medicine, Jason Grassbaugh, '03, and Hai Sun, an MD/PhD student in bioengineering. The Tucker Foundation sponsors the Siuna program in conjunction with Bridges to Community, a national organization that facilitates connections and immersions in diverse cultures. In addition to medical assistants, Dartmouth undergraduates participated as public health educators, construction crew and agricultural workers.

DARTMOUTH MEDICAL SCHOOL DIGEST

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